



GREAT SCIENCE  
2015 ANNUAL REPORT  
GREAT MEDICINE



# CHEMOCENTRYX

## An unwavering determination to execute on our plan was evident in 2015

ChemoCentryx (CCXI) was founded some years ago as an enterprise reflecting certain values and a vision. From the start, the CCXI team set a goal of offering patients powerful new medicines with distinct advantages. Specifically, by using novel orally-administered compounds that targeted the chemoattractant receptors of disease-causing inflammatory cells, we knew we should be able to beneficially alter diseased tissue at the level of the cellular microenvironment. By eliminating the attraction, accumulation, and persistent activation of the disease-causing cells in a given pathology, we aimed to stop ongoing tissue damage; providing the opportunity for organs to repair and rebuild and function more healthily.

The differentiating advantage of this approach for autoimmune diseases with chronic, destructive inflammation was clear: by targeting the natural specificity underlying chemoattractant receptor biology, we could offer safer and more efficacious therapy than the current, often noxious, standard of care treatments. These standard therapies include such things as high chronic doses of steroids, and other broadly immunosuppressant, nonspecific drugs that are still commonly used to this day. Later we learned how to operate on the same principle of chemoattractant receptor targeting in cancer, by stopping the cells that dampen down the body's anti-tumor response. In short, we aimed then -- as we aim now -- to take medicine to a more advanced level for the benefit of patients. With the advances we made in 2015, we believe that this goal is now more closely within reach.

## The excellent progress CCXI made in 2015 enables the next goal of being a late stage development company in 2016

CCXI advanced our pipeline considerably this past year, capturing opportunity as our lead programs matured. A key example was in our program involving a unique drug candidate known as CCX168, a powerful inhibitor of a part of the body's complement system, an ancient defense system that frequently causes organ damage in autoimmune diseases. We delivered positive Phase II data for CCX168 in the rare autoimmune disease known as ANCA-associated vasculitis or AAV (described below) from a trial concluded in 2015. We believe that data puts us on path to enter late stage, i.e. Phase III, clinical development for this disease in 2016.

We also embarked on a clinical initiative in cancer in 2015. Our drug CCX872 targets a chemoattractant receptor that is thought to guide tumor protecting (i.e., immune suppressing) cells to the environment of a growing tumor. We started clinical testing of CCX872 in patients with advanced pancreatic cancer in 2015, and data from that trial will be available in 2016.

## High value clinical programs in orphan and rare disease as well as immuno-oncology have become priorities for CCXI

In this letter I highlight two programs - CCX168 in orphan and rare disease and CCX872 in pancreatic cancer - as emblematic of programs where (a) CCXI controls directly, to some extent, the pace of clinical development over this coming year, and (b) where the programs will also yield additional clinical data this year. This latter point provides important ongoing validation of how we are executing on our long term plan, moving the pipeline ahead to what we believe will be eventual product approvals.

Orphan and rare diseases, as well as certain areas in cancer therapy, provide attractive routes for product development at CCXI. Orphan diseases can provide

a clinical and regulatory development path to approval that is tractable and affordable for a company of CCXI's size and stage of corporate maturity. As such, orphan and rare diseases provide in many ways an ideal path for some of the unique, wholly owned assets in our pipeline, as we pursue our ultimate goal of becoming a self-sustaining and profitable enterprise resulting from developing our innovative therapeutics. We at CCXI intend to continue our independent investment in orphan and rare disease, and to continue to keep developmental control of novel medicines like CCX168 in the hands of the Company. The same principles hold true for oncology. Clinical trials in cancer can sometimes be rapidly accomplished, and promising data can be expeditiously reviewed when warranted by regulatory bodies. Thus these two areas, orphan and rare disease and cancer, afford particularly attractive upside potential for CCXI and its investors.

## Changing the current treatment paradigm in orphan and rare disease is the goal with complement inhibitor CCX168

Even in the modern era, chronic high doses of steroids are administered to control certain autoimmune diseases. Steroids suppress immune function (and thus auto-immune activity), but steroids can be quite dangerous and difficult to manage over time. Side effects from steroids can, in fact, include death. Indeed, the single biggest cause of first year death after diagnosis in AAV is steroid-induced infections. The other noxious effects of chronic steroid use are risks of new onset diabetes, hypertension, psychiatric disorders, osteoporosis, glaucoma, cataracts, and other debilitations. As one clinician put it: "Clinically, we try to control the symptoms of a disease, such as vasculitis, by causing another illness: 'steroid disease'".

CCX168 is an orally-administered complement inhibitor targeting the C5a receptor (C5aR). We are developing CCX168 for several orphan and rare disease indications, including AAV and atypical Hemolytic Uremic Syndrome (aHUS), among others. CCX168 acts by blocking the destructive action of neutrophils that are activated as a consequence of the complement protein known as C5a binding to C5aR on their cell surface. Such activation occurs during autoimmune inflammation including in the vasculitis that occurs in AAV, where the activated neutrophils inflame and eventually destroy blood vessels. In 2015 CCXI concluded a Phase II clinical trial with CCX168 in AAV. The objective of the trial (known as the CLEAR trial) was to eliminate chronic high dose steroids from the standard of care regimen in AAV and replace the steroid with CCX168.

The CLEAR trial was successful.

Treatment with CCX168 met its primary endpoint of improving the symptoms of AAV without the need for chronic high doses of steroids (and their noxious effects). In addition, CCX168 treatment resulted in a more rapid and consistent beneficial response than the steroid-containing standard of care. There was even evidence of more rapid and sustained remission of AAV disease symptoms with CCX168 patients than those taking the full-steroid standard of care regimen.

Other benefits of CCX168 administration were found in the CLEAR trial. Treatment with CCX168 led to improvements in kidney function, as evidenced by improvements in a variety of kidney function measurements. Importantly too, patients themselves reported significant enhancements in "Quality of Life" measurements, which were markedly improved in CCX168 treatment groups, but not in the full-steroid taking standard of care treatment group.

The positive message from the CLEAR trial seems straightforward: with CCX168 therapy, chronic high doses of steroids are not required to get AAV under control. In fact, patients taking CCX168 may fare better (faster responses, more rapid and consistent remission, improvements in kidney function markers, and significantly improved patient reported outcomes in enhanced quality of life measurements) than those patients taking the traditional regimen of high dose chronic steroids.



We have obtained orphan drug status for CCX168 for ANCA disease in the US and Europe, as well as orphan drug status for CCX168 in another rare disease, atypical hemolytic uremic syndrome. Orphan drug status can provide certain key regulatory and marketing advantages. In addition to AAV, we are investigating other rare and ultra rare diseases with CCX168 and hope to be report on some of these findings in the not too distant future. As one industry veteran commented: "CCX168 has the potential to become a 'pipeline in a drug'". We at ChemoCentryx are committed to exploring fully that potential.

### Novel cancer treatment by inhibiting the cells that suppress the body's anti-tumor response is the goal of CCX872 in pancreatic cancer

As cancerous cells grow and form a larger tumor mass, they import other cells to surround the tumor as a type of insulating barrier against anti-tumor immune cells. These insulator cells are the so-called 'immune suppressor' cells, and they are drawn to the tumor via the action of chemoattractant receptors.

It is now thought that inhibiting the continued attraction and accumulation of the suppressor cells in the tumor microenvironment – via the inhibition of the chemoattractant receptors that guide the immune suppressor cells to the tumor – could lead to an intensified activation of the body's innate anti-tumor response, with better clinical outcomes for patients.

A chemoattractant receptor known as CCR2 is thought to bring a potent population of immune suppressor cells to pancreatic tumors, thus increasing the aggressive nature of those tumors. In 2015 we started a clinical trial in patients with non-resectable pancreatic cancer using CCX872, a potent, orally-administered inhibitor of CCR2. We are evaluating CCX872 in an ongoing, multi-center clinical trial in patients with non-resectable pancreatic cancer. Patients receive CCX872 in combination with FOLFIRINOX, one of the current standards of care in the treatment of pancreatic cancer. The primary efficacy measurement will be progression-free survival following completion of at least 24 weeks of treatment. But we look forward to earlier data as well with overall / objective response rates at 12 weeks. The trial enrolled extremely well throughout 2015, and in fact completed enrollment some months ahead of schedule, in the early part of 2016.

### We intend to manage the pipeline with a combination of partnered programs and independent investment

Obviously, our pipeline is deeper than the lead programs I have highlighted above. While we intend to retain control of the development of our lead programs, and invest in them accordingly, other programs will need to advance in the context of partnerships. For example, last year we published in the highly regarded journal *Lancet Diabetes and Endocrinology* positive Phase II clinical results from our drug candidate CCX140 in patients with chronic kidney disease in the context of type 2 diabetes. While diabetic nephropathy constitutes a massive clinical need, and commensurately a major commercial opportunity, the late stage development investments in diabetic nephropathy are larger than CCXI financial models entertain. Accordingly, we aspire to bring that program forward with a partner. Other opportunities in our development pipeline are similarly positioned. In short, our diverse and broad pipeline was designed to provide CCXI the option to invest independently in selected lead programs with revenues derived from partnering some of the other programs in our portfolio.

### We expect 2016 to include news and data to take us to the next stage of development for the Company

Emblematic of the overall progression and maturation of our program, we intend to become a late stage development company by the end of 2016. We will look forward to data from another Phase II clinical trial for CCX168 in AAV called CLASSIC. CLASSIC is essentially a safety study that will add to our understanding of how to use CCX168

in a therapeutic area currently dominated by steroid therapy. With the data from the above-mentioned CLEAR trial, and the safety data emerging from CLASSIC, CCXI will have end of Phase II meetings with both European and US regulatory agencies this year. It is our goal that this will result in the initiation of a Phase III registration trial for CCX168 in AAV by the end of the year. Additionally, we will continue other clinical work in additional orphan and rare disease indications with the unique CCX168 asset.

The cancer space will also be important for us in 2016. We look forward to advancing the pancreatic cancer trial of CCX872 in combination with FOLFIRINOX, and reporting initial overall response data in the second quarter of 2016, as well as initial progression free survival data by the end of 2016. Should those data be encouraging, the initiation of a definitive controlled trial of CCX872 in pancreatic cancer could follow. Such a definitive controlled trial may well constitute the major part of a registration package of CCX872 in pancreatic cancer. And, for cancer therapy, that may be just the beginning: apart from CCR2 in pancreatic cancer, other tumor types employ other chemoattractant receptors to bring immune suppressive cells into their unique tumor microenvironments. For example, we presented research at major cancer meetings in 2015 showing that our orally-administered inhibitor of the receptor known as CCR1, combined with an antibody against a checkpoint inhibitor, such as PD-L1, may be of utility in treating triple negative breast cancer which we have modeled in preclinical experiments. Combination therapy with CCXI inhibitors of chemoattractant receptors combined with checkpoint inhibitors may well constitute a big part of future immunoncology therapy. We look forward to exploring this more thoroughly in 2016.

### 2016 will be a year of real challenge but also key developments for CCXI

It is evident to all that strong headwinds for the biopharma industry are a prevailing feature of 2016 to date. Regrettably, our Company has not been immune to these forces, despite releasing what we consider to be robustly positive Phase II clinical data in January for CCX168.

Experience matters in tough times. Our Executive and our R&D teams are battle-hardened veterans of many tough campaigns in the biotech industry. We are accustomed to the sharp cycles, irrational as they may sometimes seem. We won't lose our way.

Valuable clinical assets matter too. Oftentimes in orphan and rare disease, clinical outcomes are not as familiar to the casual analyst as the data from more common diseases. If the robustly positive Phase II results from the CLEAR trial of CCX168 in AAV patients have been less than perfectly understood in some sectors, this only creates a more potent current value proposition for investors. Moreover, our clinical advances in such disease as AAV have been praised by those who matter most: the patients and clinicians who deal with that illness. We believe that we have fundamentally de-risked CCX168, our lead wholly-owned asset. Further, CCX168 is just one jewel ensconced in the trove of value that CCXI possesses.

In short, in challenging times in the industry, CCXI has the deep experience, the expertise, the broad talent; we have great novel medicines, and a plan which maps the way to prosperity.

I thank our in-house team of dedicated research professionals, our clinicians, our patients, and our current and future investors for being part of the ChemoCentryx community. Together, we will deliver on our promise of making better medicines for a better future.



# BROAD, WHOLLY OWNED CCXI PIPELINE

THERAPEUTIC AREA	DRUG: INDICATION (TARGET)	Preclinical	Phase I	Phase II	Phase III	Anticipated Milestones
Complement Inhibition in Orphan and Rare Disease	CCX168: ANCA ASSOCIATED VASCULITIS (C5AR)					AAV Phase II CLASSIC Trial top line results mid 2016 EOP2 meetings mid year Initiate Phase III 2H 2016 aHUS pilot Phase II early results in 2H 2016
	CCX168: ATYPICAL HEMOLYTIC UREMIC SYNDROME (C5AR)					
	CCX168: IGA NEPHROPATHY (C5AR)					
Immuno-Oncology	CCX872: PANCREATIC CANCER (CCR2)					Report data from pancreatic cancer study: Initial Overall Response Rate data 1H 2016 Initial Progression Free Survival data 2H 2016
	OTHER ONCOLOGY TARGETS: CXCR2, CCR1, CCR4, CCR6					
Chronic Kidney Disease	CCX140: DIABETIC NEPHROPATHY (CCR2)					Prepare for EOP2 meeting Partnering
Other Inflammatory and Autoimmune Diseases	VERCIRNON*: IBD: CROHN'S DISEASE (CCR9)					Explore partnering options to advance program in IBD Progress in TH17 disease
	CCX507: IBD: ULCERATIVE COLITIS (CCR9)					
	CCX991: PSORIASIS AND TH17 DISEASES (CCR6)					

\*also known as CCX282 or Traficet-EN

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, DC 20549**

**Form 10-K**

(Mark One)

**ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**  
For the fiscal year ended December 31, 2015

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  
(State or Other Jurisdiction of  
Incorporation or Organization)

94-3254365  
(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:**

<u>Title of Each Class</u>	<u>Name of Each Exchange on Which Registered</u>
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

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

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  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). 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

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

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 \$118.8 million, based on the closing price of the registrant's common stock on the NASDAQ Global Select Market of \$8.23 per share.

The number of outstanding shares of the registrant's common stock, par value \$0.001 per share, as of March 4, 2016 was 44,290,506.

**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 2016 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, 2015.

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**CHEMOCENTRYX, INC.**  
**FORM 10-K — ANNUAL REPORT**  
**For the Fiscal Year Ended December 31, 2015**

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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,” “estimate,” “intend,” “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;
- 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 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<sup>®</sup>, the ChemoCentryx logo, Traficet<sup>™</sup> and Traficet-EN<sup>™</sup> are our trademarks in the United States, the European Community, Australia and Japan. EnabaLink<sup>®</sup> and RAM<sup>®</sup> 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.

## Item 1. Business

### Overview

ChemoCentryx is a biopharmaceutical company focused on discovering, developing and commercializing orally-administered therapeutics to treat orphan and rare diseases, autoimmune diseases, inflammatory disorders and cancer. Our approach has been to target the chemoattractant system, a network of molecules including chemokine ligands and their associated receptors, as well as related chemoattractant receptors.

Chemokine ligands and their associated receptors, as well as related chemoattractant receptors are known to cause 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.

Expression of chemokines and their receptors play a dual role in the ability of cells to give rise to either benign or malignant progressively growing tumors. On the one hand, chemokines secreted by either the cancer-initiating cells or the normal cells surrounding them can help limit tumor development by increasing leukocyte migration toward the site, and inducing long-term anti-tumor immunity. On the other hand, they may facilitate survival, proliferation, and metastatic potential of tumor cells. The initially secreted chemokines at the tumor site play a key role defining the composition of the connective tissue and recruiting tumor infiltrating white blood cells bearing specific chemokine receptors.

Tumor cells are able to hijack the chemokine receptor/chemokine system for their own benefit. They “convert” infiltrating leukocytes into immuno-tolerant allies, since they are able to (1) attract suppressor T-cells and neutrophils, (2) hijack immature dendritic cells, avoiding their migration toward the lymph nodes and therefore antigen presentation, favoring a tolerogenic profile, and (3) participate in the recruitment and induction of myeloid-derived suppressor cells.

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 chemoattractant receptor, thereby blocking the negative inflammatory or suppressive response driven by that particular receptor, while leaving the rest of the immune system intact. Using our pioneering insights and proprietary technologies designed to better understand the chemoattractant system, we believe that we have established the broadest pipeline of novel drug candidates targeting chemoattractant 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.

Our pipeline comprises the following programs:

#### ***Orphan and Rare Diseases:***

- CCX168 is an orally-administered complement inhibitor targeting the C5a receptor (C5aR) and is being developed for orphan and rare diseases, including anti-neutrophil cytoplasmic antibody, or ANCA, associated vasculitis, or AAV, atypical hemolytic uremic syndrome, or aHUS, and immunoglobulin A-mediated nephropathy, or IgAN. CCX168 has successfully completed and reported positive clinical data from the first Phase II clinical trial in patients with AAV, known as the CLEAR trial. This study met its primary endpoint whereby treatment with CCX168 demonstrated numerical superiority and statistical non-inferiority in Birmingham Vasculitis Activity Score, or BVAS, response relative to standard of care. The second Phase II clinical trial in patients with AAV, the CLASSIC trial, is ongoing in North America and we expect to report top-line data from this trial in mid 2016. Following CLASSIC data in mid 2016, we plan to conduct end-of-Phase II meetings with regulatory

agencies and initiate the Phase III development program in patients with AAV by the end of 2016. Phase II pilot clinical trials with CCX168 in patients with aHUS and IgAN are ongoing.

***Immuno-Oncology:***

- CCX872 is being evaluated in patients with non-resectable pancreatic cancer, and is our second inhibitor of the chemokine receptor known as CCR2. CCX872 completed Phase I clinical development in healthy volunteers. A Phase Ib clinical trial in patients with advanced pancreatic cancer is ongoing. Having recently presented pharmacodynamic and pharmacokinetic, or PK, data from the first step of the study, we expect to report early objective response rate, or ORR, data in the first half of 2016 and initial progression free survival, or PFS, data in the second half of 2016.
- Chemoattractant Receptor Targets — CCR1, CCR4, CCR5, CXCR2, CXCR7 — We believe these chemokine and chemoattractant receptors play an important role in establishing a tumor microenvironment that suppresses a cytotoxic immune response. We have discovered small molecule inhibitors targeting these chemoattractant receptors, which may be developed in certain oncology indications targeting both solid and liquid tumors. We believe that such immunotherapeutic agents could be administered as stand-alone therapies or result in a synergistic effect when given in combination with traditional chemotherapies or other immunotherapies, such as programmed cell death protein 1, or PD-1/programmed death ligand 1, or PD-L1 antibodies.

***Chronic Kidney Disease:***

- CCX140 is an inhibitor of the chemokine receptor known as CCR2 (distinct from CCX872 above) and is being developed as an orally administered therapy for the treatment of diabetic nephropathy, or DN, a form of chronic kidney disease. We have successfully completed and reported positive data from a Phase II clinical trial in patients with DN. The trial met its primary endpoint by demonstrating that treatment with 5mg of CCX140 given orally once daily added to a standard of care angiotensin converting enzyme, or ACE, inhibitor or angiotensin II receptor blocker, or ARB treatment resulted in a statistically significant improvement in urinary albumin to creatinine ratio, or UACR, beyond that achieved with standard of care alone. We are preparing to conduct an end-of-Phase II meeting with the U.S. Food and Drug Administration, or FDA.

***Other Inflammatory and Autoimmune Diseases:***

- Th-17 cell-driven inflammation and CCR6 — Th-17 driven cells have been implicated in a variety of autoimmune and inflammatory diseases such as psoriasis, rheumatoid arthritis, and asthma. Th-17 cells express high levels of the chemokine receptor known as CCR6, which induces their migration to and activation within disease sites. We have a preclinical program in the inhibition of CCR6 which has produced several unique CCR6 inhibitor leads that are now being optimized through medicinal chemistry approaches, which we plan to advance to a clinical candidate.
- Vercirnon (also known as Traficet-EN, or CCX282) is an inhibitor of the chemokine receptor known as CCR9, and being developed as an orally administered therapy for the treatment of patients with moderate-to-severe Crohn's disease. Vercirnon is ready to continue development in Phase III with a partner, should an alliance partner be identified for this program.
- CCX507 is our second generation CCR9 inhibitor for the treatment of inflammatory bowel disease, or IBD. CCX507 has successfully completed Phase I clinical development, which demonstrated that CCX507 was safe and well-tolerated, and blocked CCR9 on circulating leukocytes. We also presented preclinical data with CCX507 in combination with an anti- $\alpha 4\beta 7$  or anti-TNF antibody showing combined treatment reduced the severity of colitis better than monotherapy with either drug alone.

All of our drug candidates are wholly owned and being developed independently by us. Our strategy also includes identification of next generation compounds related to our drug candidates, all of which have been internally discovered.

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

## Our Broad and Deep Wholly Owned Pipeline

THERAPEUTIC AREA	DRUG: INDICATION (TARGET)	PRECLINICAL	PHASE I	PHASE II	PHASE III	ANTICIPATED MILESTONES
Complement Inhibition in Orphan and Rare Diseases	CCX168: ANCA ASSOCIATED VASCULITIS (C5aR)					AAV Phase II CLASSIC Trial top line results mid 2016 EOP2 meetings mid 2016 Initiate Phase III End of 2016 aHUS pilot Phase II early results in 2016
	CCX168: ATYPICAL HEMOLYTIC UREMIC SYNDROME (C5aR)					
	CCX168: IgA NEPHROPATHY (C5aR)					
Immuno-Oncology	CCX872: PANCREATIC CANCER (CCR2)					Report data from pancreatic cancer study: - Initial ORR data 1H 2016 - Initial PFS data 2H 2016
	Other Oncology Targets: CXCR2, CCR1, CCR4, CCR6					
Chronic Kidney Disease	CCX140: DIABETIC NEPHROPATHY (CCR2)					Prepare for EOP2 meeting
Other Inflammatory and Autoimmune Diseases	VERCIRON*: IBD: CROHN'S DISEASE (CCR9)					Explore partnering options to advance program in IBD
	CCX507: IBD: ULCERATIVE COLITIS (CCR9)					
	CCX354: RHEUMATOID ARTHRITIS/MYELOMA BONE METASTASIS (CCR1)					CCR1 CCX354 completed Phase IIa
	CCX991: PSORIASIS AND TH17 DISEASES (CCR6)					Progress in TH17 disease

\* Also known as CCX282 or Traficet-EN.

## Orphan and Rare Diseases

In our orphan and rare disease program, our lead drug candidate is CCX168. CCX168 is a small molecule that targets the chemoattractant receptor known as C5aR, and is being developed for inflammatory and autoimmune diseases. CCX168 blocks the activity of complement C5a, a component of the complement system and the natural ligand for C5aR. The complement system is a group of proteins that work together to destroy foreign invaders (such as bacteria and viruses), trigger inflammation, and remove debris from cells and tissues. The complement system must be carefully regulated so it targets only unwanted materials and does not attack the body's healthy cells.

In the United States, under the Orphan Drug Act, the FDA has granted orphan drug designation for CCX168 for the treatment of AAV, including granulomatosis with polyangiitis or Wegener's granulomatosis, microscopic polyangiitis, and Churg-Strauss syndrome. The European Commission granted orphan drug designation for CCX168 for the treatment of granulomatosis with polyangiitis or Wegener's granulomatosis and microscopic polyangiitis.



Our most advanced clinical program in orphan and rare diseases is in patients with AAV. We also have pilot clinical trials that are ongoing in patients with aHUS and IgAN.

AAV, aHUS, and IgAN are all rare autoimmune diseases that are characterized by inflammation that often affects the kidneys.

### **ANCA-Associated Vasculitis (AAV)**

AAV is a rare, severe, and often fatal autoimmune disease that is caused by autoantibodies called anti-neutrophil cytoplasmic antibodies and is characterized by inflammation that can affect many different organ systems, and commonly involves the kidneys.

AAV affects approximately 40,000 people in the United States, with approximately 4,000 new cases each year, and more than 75,000 people in Europe, with at least 7,500 new cases each year.

### ***Limitations of Current Therapies***

AAV is currently treated with courses of immuno-suppressants (cyclophosphamide, or CYC, or rituximab, or RTX) combined with high dose glucocorticoid (steroid) administration. Following initial treatment, up to 30% of patients relapse within six to 18 months, and approximately 50% of all patients will relapse within three to five years.

The current standard of care for AAV is associated with significant safety issues. First year mortality is approximately 11% to 18%. The single greatest cause of premature mortality is not disease related adverse events, but rather infection that is thought largely to be a consequence of steroid administration. The multiple adverse effects of courses of steroid treatment (both initial courses and those that are repeated as a consequence of relapse) are major causes of both short-term and long-term disease and death. Such therapy-related adverse events contribute significantly to patient care costs, as well as to the diminution of quality of life for patients.

### ***Role of C5a and C5aR in AAV***

Complement C5a, acting through its receptor C5aR, is thought to play a pro-inflammatory role in AAV. Autoantibodies lead to the activation and increased adhesiveness of neutrophils to the walls of small blood vessels in different tissues and organs of the body. These accumulating adhering neutrophils initiate an inflammatory cascade in the small blood vessels by secreting pro-inflammatory cytokines and chemoattractants. Activation of the complement pathway occurs with production of C5a, one of the most potent pro-inflammatory mediators of the complement system. C5a, through binding to its receptor C5aR, induces expression of adhesion molecules and chemotactic migration of neutrophils, eosinophils, basophils, and monocytes.

### ***A Novel C5a Receptor Inhibitor CCX168***

CCX168 is a potent and highly specific inhibitor of the human C5a receptor. CCX168 is orally bioavailable and has demonstrated an excellent preclinical safety profile, consistent with its intended chronic use in patients. CCX168 does not affect formation of the C5b-9 terminal complement complex (or membrane attack complex), unlike the anti-C5-antibody, eculizumab. Therefore, CCX168 is believed not to increase the susceptibility to infections such as *Neisseria meningitides*.

The efficacy of CCX168 was demonstrated in a mouse model of the renal manifestations of AAV, which closely mimics 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

(one of the anti-neutrophil cytoplasmic antibodies that are implicated in AAV in humans). Levels of CCX168 in the blood of these mice were comparable to levels in the blood of patients participating in our Phase II CLEAR clinical trial with CCX168 in patients with AAV.

## ***Clinical Development***

### **CCX168 Phase I Clinical Trials**

We have completed two Phase I clinical trials with CCX168 in a total of 54 healthy subjects. The first 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 the second period, CCX168 doses of 1mg, 3mg, and 10mg once-daily for seven days, and 30mg and 50mg twice-daily for seven days, were studied. CCX168 was well-tolerated by clinical trial subjects in this clinical trial and no serious adverse events, or 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 sore throat. These adverse events typically were mild and dosing was not stopped as a result. In the second Phase I clinical trial in six healthy male subjects, the way CCX168 was metabolized in the body was studied after a single oral dose of 100mg CCX168. CCX168 was well-tolerated in this study.

### **CCX168 Phase II Clinical Trial**

We have completed the first Phase II clinical trial in 63 evaluable patients with AAV in Europe, known as the CLEAR trial. CLEAR was a randomized, double-blind, placebo-controlled clinical trial in patients with AAV. The aim of this trial was to provide effective therapy for AAV with an inhibitor of the C5a receptor while reducing toxicity associated with standard of care therapy by eliminating or reducing exposure to high dose systemic steroid use. The primary safety objective of this clinical trial was to evaluate the safety and tolerability of CCX168 in patients with AAV on background CYC or RTX treatment. The primary efficacy objective was to evaluate the efficacy of CCX168 based on the BVAS. BVAS measures AAV disease activity across all organ systems and is the most widely used and clinically validated outcome measure in AAV clinical trials. The higher the BVAS score, the higher the level of disease activity. The greater the reduction in BVAS score with treatment, the greater the disease improvement. The secondary objectives of this clinical trial included assessment of the feasibility of reducing or eliminating the use of steroids in the treatment of patients with AAV without the need for rescue steroid 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, or eGFR, hematuria, and proteinuria with CCX168 compared to standard of care treatment.

The CLEAR trial met its primary endpoint based on the BVAS response at week 12 in patients receiving CCX168, compared to those patients receiving the high dose steroid-containing standard of care. Specifically, all treatment groups receiving CCX168 demonstrated a statistically significant ( $P=0.002$ ) non-inferior clinical efficacy outcome when compared to standard of care. The study contained two CCX168 treated groups: one group which received CCX168 with a low dose of steroids (one third the steroid in the standard of care group), in which the BVAS response was 86% at week 12 versus 70% for standard of care;  $P=0.002$  for non-inferiority. A separate group received CCX168 without steroids; in this group the response was 81% ( $P=0.01$  for non-inferiority). Following adjudication of BVAS data from the follow-up period, the previously reported BVAS response of 75% for the standard of care group was found to be 70% and the resulting P-values were revised accordingly. The BVAS response data for the CCX168 groups remain unchanged. The revised P-values are presented above. Standard of care treatment included a placebo to CCX168, and all treatment groups received a standard background immunosuppressant (CYC or RTX) as well. The primary endpoint of BVAS response was prospectively defined as the proportion of patients with a decrease from baseline of at least 50% in BVAS plus no worsening in any body system.

Other beneficial changes were noted, including in pre-specified secondary endpoints:

- 1) CCX168 exhibited a more rapid onset of improvement than standard of care treatment, as evidenced by beneficial changes in proteinuria (measured as UACR); also rapid beneficial reductions from baseline in BVAS, as well as reductions in the levels of MCP-1 (a marker of kidney inflammation) found in the urine;
- 2) improvements in eGFR and hematuria were seen in all three treatment groups, indicating these disease activities did not require high dose chronic steroid administration to be controlled; and
- 3) improvements in “Quality of Life” (as defined by the visual analogue scale of the EuroQOL-5D-5L) and measurements based on the Short Form-36 were seen in CCX168 treatment groups, but not in the standard of care group.

Taken together, these results suggest that CCX168, a target-specific complement inhibitor, may be able to replace chronic steroids in the treatment of AAV with at least equal efficacy. CCX168 also appeared safe and well-tolerated in the trial. There were no observations that would prevent further clinical development of CCX168. We also recently completed the long-term toxicology program with CCX168. The results provide support for chronic dosing of CCX168 in future clinical trials.

A second Phase II clinical trial, the CLASSIC trial, is ongoing in North America. CLASSIC is a randomized, double-blind, placebo controlled Phase II clinical trial in patients with either newly diagnosed or relapsing AAV who require either CYC or RTX treatment. Eligible patients are randomized in a 1: 1:1 ratio to receive either placebo plus CYC or RTX plus full dose starting steroids; 10mg CCX168 twice daily plus CYC or RTX plus full dose starting steroids; or 30mg CCX168 twice daily plus CYC or RTX plus full dose starting steroids. The treatment period is 12 weeks, with a 12-week follow-up period. The aim of the CLASSIC trial is different from the CLEAR trial. The CLASSIC trial is mainly a regulatory and safety trial. As such, the main goal of CLASSIC is to evaluate the safety of CCX168 when given with high dose steroid-containing standard of care treatment, which also includes CYC or RTX. Therefore, the primary safety objective of this clinical trial is to evaluate the safety and tolerability of CCX168 in patients with AAV on background CYC or RTX treatment. The primary efficacy objective is to evaluate the efficacy of CCX168 based on BVAS. A total of 42 patients have been enrolled in this trial.

### **Atypical Hemolytic Uremic Syndrome (aHUS)**

aHUS is a genetic, chronic, rare disease that is caused by the formation of blood clots within small blood vessels, or thrombosis, throughout the body. aHUS affects both adults and children and can progressively damage vital organs, including the kidneys, but also other organs such as the brain, heart, lungs, gastrointestinal tract, and pancreas. These clots can cause serious medical problems if they restrict or block blood flow.

As a result of clot formation in small blood vessels, people with aHUS experience kidney damage and acute kidney failure that lead to end-stage renal disease, or ESRD, in about half of all cases. These life-threatening complications prevent the kidneys from filtering plasma and eliminating waste products from the body effectively.

### ***Limitations of Current Therapies***

Current aHUS treatment has limited efficacy or is very expensive, and as a result, is not a practical option for many patients with aHUS.

Plasma exchange or infusion has decreased mortality from 50% to 25% in patients with aHUS. In patients with complement factor H, or CFH, mutations, plasma exchange or infusion resulted in partial or complete remission in approximately 60% of patients. Plasma exchange with immunosuppressive therapy such as steroids and azathioprine or mycophenolate mofetil and RTX resulted in long-term dialysis-free survival in 60% to 70%

of patients. Patients may become non-responsive to plasma exchange or infusion. It is also debatable whether renal transplantation is appropriate for patients with aHUS with ESRD as the disease recurs in approximately 50% of patients after transplantation, and graft failure occurs in 80% to 90% with recurrent disease.

Eculizumab (Soliris) has been approved by the FDA for treatment of patients with aHUS to inhibit complement-mediated thrombotic microangiopathy. Eculizumab treatment improves the disease based on platelet count, lactate dehydrogenase, hemoglobin, and serum creatinine levels, and need for plasma exchange, infusion, or dialysis. Eculizumab is an anti-C5 antibody, designed to block the conversion of C5 to C5a and C5b. Eculizumab needs to be administered by frequent intravenous infusion, is associated with an increased risk of *Neisseria* infections, and can cost approximately \$500,000 per year in the United States.

### ***Role of C5a and C5aR in aHUS***

aHUS often results from a combination of environmental and genetic factors. The genes associated with aHUS provide instructions for making proteins involved in regulating the complement system. In aHUS, the regulatory proteins that prevent uncontrolled activation of the complement system are defective due to gene mutations. The resulting uncontrolled activation of the complement system, including uncontrolled production of the anaphylatoxin C5a, results in damage to the vasculature and organs such as the kidneys.

The fact that C5a and its receptor C5aR play a role in the pathogenesis of aHUS is supported by studies in mice. Mice deficient in CFH develop proliferative glomerulonephritis, which is improved in mice where both the CFH and C5aR genes are deleted. Mice lacking C5aR were significantly protected from functional renal disease as assessed by blood urea nitrogen levels. This is relevant as loss-of-function CFH mutations are relatively common in humans with aHUS. In addition, C5a can prime neutrophils and enhance neutrophil activation. C5a, acting on C5aR, is a potent neutrophil chemoattractant and agonist, which triggers neutrophil aggregation. Further, C5a activates endothelial cells, promoting retraction and increased permeability.

CCX168, as a potent and specific inhibitor of C5aR, may therefore be effective in the treatment of patients with aHUS. Compared to intravenously administered eculizumab, CCX168 is a convenient, orally administered treatment. CCX168 blocks the effect of C5a without compromising the formation of the C5b-9 terminal complement complex (or membrane attack complex), which is important in fighting *Neisseria* infections. Since CCX168 is a small molecule, manufacturing cost is anticipated to be lower than the protein-based drugs such as eculizumab. As a small molecule, CCX168 has a shorter plasma half-life (terminal half-life is approximately 70 hours) than eculizumab (272 hours, according to eculizumab prescribing information). Therefore, in the event of an undesirable adverse event requiring discontinuation of treatment, plasma clearance would be faster with CCX168.

### ***Clinical Development***

In collaboration with external scientists, we have demonstrated that CCX168, when added to the serum of patients with aHUS, reduces the size of thrombus (blood clot) formation on vascular endothelial cells that has been stimulated by the aHUS serum. The positive effect of CCX168 was concentration dependent, and the magnitude of the effect was similar to that observed with eculizumab or soluble complement receptor 1.

Based on these encouraging in vitro findings, we have commenced a Phase II pilot clinical trial with CCX168 in up to ten patients with aHUS who are on dialysis. The primary efficacy objective of the trial is to evaluate whether treatment with CCX168 may reduce thrombosis formation in chronic dialysis patients with aHUS. We, through our external collaborator, plan to report early results from this proof-of-concept trial in 2016.

### ***Immunoglobulin A Nephropathy (IgAN)***

IgAN is a form of glomerulonephritis, or inflammation of the filtration units of the kidneys called glomeruli. The damage caused by IgAN results from abnormal deposits of immunoglobulin A, or IgA, complexes in the glomeruli. This immune complex deposition is associated with complement activation.

One of the kidney's most important jobs is to filter toxic waste products, such as creatinine, from the blood, and the glomeruli play a key role in this process. As more glomeruli are damaged by the IgA immune complexes, protein is spilled into the urine, and the kidney progressively loses its ability to clear waste products from the body. In some patients with IgAN, this loss of kidney function progresses to chronic kidney failure, which requires dialysis treatment or a kidney transplant.

### ***Limitations of Current Therapies***

Renin-angiotensin-aldosterone system, or RAAS, blockers such as ACE inhibitors and ARBs are recommended when proteinuria is higher than 0.5g per day. Doses are titrated up to achieve blood pressure below 130/80 mmHg in patients with proteinuria less than 1g per day and below 125/75 mmHg if proteinuria is higher than 1g per day. Steroids are used in patients with persistent proteinuria higher than 1g per day despite optimal RAAS blockade. Immunosuppressive treatment with CYC or azathioprine is not recommended unless there is crescentic IgAN with deteriorating kidney function. Fish oil is also used. RAAS blockers have limited efficacy. Steroids are associated with an increased risk of infection and other adverse effects including osteoporosis, cataracts, peptic ulcer disease, new onset hypertension and diabetes, and mental disturbances. Immunosuppressive treatment such as with CYC is associated with an increased risk of infertility, cystitis, and cancer. Therefore, there exists an unmet medical need for safe and effective therapies for patients with IgAN.

### ***Role of C5a and C5aR in IgAN***

IgAN is an autoimmune disease in which auto-antibodies are inappropriately made against IgA. The immunoglobulin immune complexes are deposited in the glomeruli of the kidney, and may lead to activation of the complement system and production of C5a. The end result is kidney inflammation which leads to inappropriate spilling of protein in the urine, and impairment of the ability of the kidney to filter the blood of waste products such as creatinine. Consequently, this can ultimately lead to kidney failure and dialysis.

As a potent and specific inhibitor of C5aR, CCX168 may be effective in treating patients with IgAN. Because of its unique mechanism of action, CCX168 has the potential to be synergistic to RAAS blockade, and could also potentially reduce the dosing requirements for steroids as well as immunosuppressive drugs.

### ***Clinical Development***

We have an ongoing Phase II pilot study with CCX168 in up to 20 patients with IgAN who have residual proteinuria (protein in the urine) despite being on a stable maximum tolerated dose of a RAAS inhibitor for at least eight weeks. The objective of the trial is to evaluate whether treatment with CCX168 may be synergistic to RAAS blockade, and potentially improve proteinuria in patients with IgAN.

### ***CCX168 Commercialization Strategy***

We plan to develop CCX168 independently or in the context of a co-development partnership and retain meaningful commercial rights to CCX168 in certain orphan indications such as AAV, aHUS, and IgAN. CCX168 is one of the two compounds in our renal disease portfolio and an integral part of our forward integration plan.

### ***Immuno-Oncology***

In oncologic disease, tumors can profoundly subvert inflammatory and effector immune responses. In the tumor cellular microenvironment, CCR2 bearing cells are thought to largely have an immunosuppressive behavior. These are the so-called myeloid derived suppressor cells, or MDSCs. These cells effectively help tumors hide from the body's cytotoxic immune response to tumor cells. Inhibiting CCR2, and thus the MDSCs controlled by CCR2, could therefore lead to the liberation of the cytotoxic immune response against the tumor



cells, tumor shrinkage, and improved patient survival. We have an ongoing clinical development program for the treatment of patients with advanced pancreatic cancer with our drug candidate CCX872, our second inhibitor of the chemokine receptor known as CCR2.

### ***Understanding Pancreatic Cancer***

Pancreatic cancer is a rare but deadly cancer. It is the 15th most common cancer worldwide but the fourth highest cause of cancer-related death. In the United States in 2014, approximately 46,000 people are expected to develop pancreatic cancer, and 40,000 of those patients are expected to succumb to the disease. Primarily due to the aging of the population, the incidence of pancreatic cancer is predicted to increase to 62,000 new cases per year by 2030. Pancreatic adenocarcinoma, which represents 85% of all pancreatic cancers, is characterized by rapid progression and a dismal prognosis. Because of the deep location of the pancreas in the abdomen and the lack of markers of early disease, most cancers remain asymptomatic until they obstruct the biliary tract, which usually occurs with tumors of the pancreatic head, or until they become metastatic. Hence, less than 15% of patients initially present with a resectable cancer (stage 1 or 2), while the majority of patients have either a locally advanced, nonresectable, stage 3 cancer or a metastatic, stage 4 cancer at the time of diagnosis. Even with the best current treatment, the median overall survival of these patients is less than one year, an outlook that has remained largely unchanged over the last few decades.

The dismal prognosis of this cancer results from the combination of the late diagnosis, the early metastatic dissemination, and resistance to most chemotherapies. The main factors explaining this resistance to treatment include a very high rate of activation of the Kirsten rat sarcoma viral oncogene, or KRAS, mutations, a propensity for both local extension and distal spreading, the presence of a dense stromal tissue surrounding the tumor that results in a hypoxic, hypovascularized environment with high interstitial pressure, which may impede drug delivery, and ultimately the loss of immune control. Therapeutic interventions that improve the prognosis of patients with pancreatic cancer are urgently needed.

### ***Limitations of Current Therapies***

Current standard of care regimens are not only limited by modest efficacy but also by significant toxicity. For patients with nonresectable cancer (stage 3 or 4), FOLFIRINOX (oxaliplatin, irinotecan, leucovorin, and 5-fluorouracil) or a combination of gemcitabine and nanoparticle albumin-bound-, or nab-, paclitaxel are considered standard treatments, but the median overall survival of patients remains less than one year. Further, these treatments often are poorly tolerated. FOLFIRINOX is associated with a high rate of Grade 3-4 adverse events, can rarely be administered for more than six months, and is mostly prescribed to patients with excellent performance status. Frail, elderly patients usually receive palliative treatment. Extensive research is ongoing to identify novel agents with improved efficacy and a reduced toxicity profile, including chemotherapies with improved formulations of currently available agents, therapies targeted against specific oncogenic pathways, or cancer vaccines.

### ***Role of CCR2 in Pancreatic Cancer***

Human pancreatic tumors are characterized by a highly immunosuppressive microenvironment. In the tumor cellular microenvironment, CCR2 bearing cells are thought to be largely of an immunosuppressive behavior; these are the so-called MDSCs. These cells effectively help tumors hide from the body's cytotoxic immune response to tumor cells. Inhibiting CCR2, and thus the MDSCs controlled by CCR2, could therefore lead to the liberation of the cytotoxic immune response against the tumor cells, and improved patient survival.

### ***Clinical Development***

CCX872 is a potent and selective inhibitor of the human CCR2. The objective of using a CCR2 inhibitor such as CCX872 is to reduce the suppressive myeloid cell presence in the tumor and, in doing so, slow the

progression of disease in these patients. We believe that CCX872 may represent a promising novel immunotherapeutic approach. Drugs that block CCR2 have shown evidence of activity in patients with pancreatic cancer as well as in a mouse orthotopic pancreatic cancer model.

### **Phase I Clinical Trials**

We completed a first-in-human Phase I clinical trial in healthy subjects. This clinical trial was a combined single-and-multiple-ascending dose clinical trial in 40 subjects. The clinical trial was conducted in the Netherlands. CCX872 doses of 3mg, 10mg, 30mg, 100mg, and 300mg were given as a single dose in the first study period and once-daily doses for seven days in the second study period. Data showed that CCX872 was well-tolerated and appeared to be safe in healthy volunteers at all dose levels studied. There were no SAEs or dropouts due to adverse events in the trial. The most common adverse events reported by subjects receiving CCX872 in the multi-dose period were dizziness, diarrhea, and headache. These events typically were mild in intensity and did not result in dosing discontinuation. The results showed that CCX872 was safe and well-tolerated, and suitable for chronic dosing in patients. CCX872 was able to block CCR2 in the circulation, and it had a predictable dose-linear PK profile.

Our Phase Ib study for CCX872 explores a novel approach (CCR2 inhibition) for the treatment of patients with stage 3 and 4 pancreatic cancer. Beyond the field of pancreatic cancer, the results of this study will also advance our understanding of the role of chemokines in solid tumors and of the potential for chemokine receptor inhibitors as therapeutic options in cancer patients when combined with standard of care regimens. The primary aim of this study is to evaluate whether orally administered CCX872 is safe and can improve the progression of disease in up to 54 patients with nonresectable pancreatic cancer being treated with FOLFIRINOX, one of the current standard of care treatments for this disease. Enrollment in the trial occurs in two stages, Part A (single dose) and Part B (multiple dose). Part A has been completed. Results showed that a single oral dose of 150-mg CCX872 was well-tolerated and safe in this study. The PK profile in patients with pancreatic cancer was in line with the PK profile observed in healthy volunteers in the previous clinical trial. CCX872 was effective in blocking CCR2 in circulating cells as measured by CCR2 occupancy and internalization assays, as well as migration assays. Successful completion of Part A led to initiation of Part B. Enrollment in Part B is ongoing. We expect to report initial ORR data from Part B of the trial in the first half of 2016 and initial PFS data in the second half of 2016.

### **Preclinical Development in Immuno-Oncology**

One of the most exciting advances in oncology in decades is the recent observation that modifiers of the activity of the patient's own immune system can profoundly enhance their response to chemotherapy.

A critical cellular component of this response are the MDSCs, which inhibit the activity of the effector T cells, and thus dampen the immune response of the body to the tumor. These MDSCs express chemokine and chemoattractant receptors that they use to migrate to the tumor microenvironment. We believe that blocking these chemokine receptors with small molecule antagonists could be effective either as stand-alone therapies for certain cancers or by synergistic effect when given in combination with traditional chemotherapies or other immunotherapies.

We have discovered small molecule inhibitors that target these chemoattractant receptors, and one or more of them may be developed in certain oncology indications targeting both solid and liquid tumors.

In our preclinical research, we are conducting studies with various chemokine receptor inhibitors in combination with check point inhibitors, such as those inhibiting the programmed death-ligand 1, or PD-L1, pathway, that we believe may result in a greater anti-tumor effect, than with check-point inhibition alone.

A growing body of data suggests that a number of chemokine receptors, including, but not limited to, CCR1, CCR2, CCR5, and CXCR2, may play diverse roles in cancer growth, cancer metastasis, cancer angiogenesis, or

the composition of the tumor microenvironment. Given the potential role of chemokine receptors in cancer cell survival, the combination of chemokine receptor antagonists with traditional chemotherapeutic agents or with immunotherapy, such as programmed cell death protein-1, or PD-1, or PD-L1 inhibitors is an attractive strategy because it may result in greater efficacy and/or allow dose reductions of the chemotherapeutic drugs and therefore limit systemic side effects.

## **Chronic Kidney Disease**

In our chronic kidney disease program, our lead drug candidate, CCX140, is an inhibitor of the chemokine receptor known as CCR2 and is being developed as an orally administered therapy for the treatment of DN. We have successfully completed a Phase II, placebo-controlled, clinical trial in patients with this disease.

DN is a form of chronic kidney disease, characterized by the gradual loss of kidney function. It is most common among people with Type 2 diabetes and hypertension and affects an estimated 26 million adults in the United States. Diabetes has become the primary cause of kidney disease in the United States and the associated incidence of DN is also on the rise. Twenty million people in the United States are estimated to have diabetes and 40% of all diabetics will develop DN. Clinically, DN is characterized by a progressive increase in urine albumin, or albuminuria, and a decline in glomerular filtration rate, hypertension, and a high risk of cardiovascular morbidity and mortality.

### ***Limitations of Current Therapies***

Management of DN includes treatment of the underlying Type 2 diabetes and/or hypertension. Blood pressure medications such as ACE inhibitors and ARBs are commonly prescribed to control hypertension and slow the progression of DN. Nevertheless, most patients continue to have a decline in kidney function. About 20% of patients eventually progress to ESRD and require hemodialysis, peritoneal dialysis, or renal transplant. DN is a serious medical condition and needs treatments with new mechanisms of action that target pathways other than the RAAS in order to slow or reverse the progression of the disease.

### ***Role of CCR2 in Diabetic Nephropathy***

The chemokine receptor known as CCR2 has been identified as a main driver of inflammatory 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 DN. Levels of MCP-1 (also known as CCL2), the main ligand for CCR2, are elevated in the kidneys of patients with DN. MCP-1 is produced by kidney cells in response to such factors as high blood glucose levels and physical stresses. As a result, MCP-1 level in the urine is a strong indicator of renal damage and correlate well with albuminuria and interstitial macrophage numbers.

CCX140 is our CCR2 inhibitor which successfully completed a Phase II clinical trial in type 2 diabetics and more recently a Phase II clinical trial in patients with DN. While historically DN was not considered an inflammatory disease, there is now clear evidence of the role of macrophages in this disease. Kidney biopsies from patients with DN show elevated numbers of macrophages in the glomeruli, which are the basic filtering units 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.

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 DN 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 benefits 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***

<b>Biological Parameter</b>	<b>Effect of CCR2 Inhibition</b>
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 inhibitor of CCR2 which is required for monocytes to infiltrate the inflamed kidney, where they differentiate into macrophages. While CCX140 is not the first CCR2 inhibitor 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 inhibitors in that it has been shown preclinically to be free of the cardiovascular safety signals associated with other CCR2 inhibitors. CCX140 has been shown in a number of preclinical toxicology studies to be suitable for evaluation in humans for chronic use in DN.

***Clinical Development***

Our clinical development strategy was to first assess the safety and tolerability of CCX140 in healthy subjects, then in patients with type 2 diabetes and normal renal function, and finally to evaluate the drug in patients with DN. As a precursor to our clinical trials in patients with DN, we completed a 159-patient randomized Phase II clinical trial to assess the safety and tolerability of CCX140 in patients with type 2 diabetes, one of the most common causes of nephropathy. We also completed a 332-patient randomized Phase II clinical trial to assess the efficacy, safety, and tolerability of CCX140 in patients with DN.

**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 with no SAEs observed in these Phase I clinical trials. The 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 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 10mg dose group.

## **CCX140 Phase II Clinical Trial in Diabetic Nephropathy**

We have completed a Phase II clinical trial in patients with DN. A total of 332 patients were enrolled in a randomized, double-blind, placebo-controlled clinical trial. The goals of this clinical trial was to evaluate the efficacy, safety, and tolerability of CCX140 in patients with DN. The primary efficacy objective was evaluation of the effect of CCX140 on albuminuria. Secondary efficacy objectives were evaluation of the effect of CCX140 on HbA1c and eGFR. The three treatment groups consisted of standard of care, ACE inhibitor or ARB plus placebo (control group), 5mg and 10mg of CCX140 once-daily plus standard of care. The treatment duration was 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 were included in this clinical trial. The key efficacy endpoint was a change from baseline in first morning UACR, a major indicator of renal health. The target sample size of the trial was increased from 135 to 270 patients and the dosing duration was extended from 12 weeks to 52 weeks, following completion of long-term toxicology studies that allowed extension of dosing beyond 12 weeks. Because of better than anticipated enrollment towards the end of the enrollment period, a total of 332 subjects were ultimately enrolled in the trial.

The Phase II trial met its primary endpoint by demonstrating that treatment with 5mg of CCX140 given orally once daily added to a standard of care regimen of ACE and ARB treatment resulted in a statistically significant ( $p=0.01$ ) improvement in UACR, beyond that achieved with standard of care alone. The maximum treatment effect (24% reduction) was reached at 12 weeks, and sustained reduction in albuminuria induced by CCX140 relative to standard of care alone observed over the full year (UACR at each one of the 10 time points over the 52-week treatment period in the patients who received 5mg CCX140 continuously for 52 weeks, were below those of the standard of care alone group). A dose of 10mg CCX140 per day did not provide more improvement in albuminuria as compared to the 5mg dose. CCX140 did not affect systematic blood pressure, suggesting that the beneficial effect of CCX140 is mediated locally in the kidney micro-environment, possibly through a beneficial reduction in renal inflammation. CCX140 was well-tolerated with a low overall dropout rate over the 52-week treatment period (10%). No safety issues were observed that would prevent further clinical development of CCX140 in DN.

We are preparing to conduct an end-of-Phase II meeting with the FDA, at which time the clinical results from the CCX140 program will be reviewed in detail and a Phase III clinical program will be discussed. We plan to further develop CCX140 in the context of a partnership.

## **Other Inflammatory and Autoimmune Diseases**

### **Inflammatory Bowel Disease, or IBD/Crohn's Disease and Ulcerative Colitis**

IBD refers to two diseases — Crohn's disease and ulcerative colitis — both characterized by inflammation of the gastrointestinal tract. Crohn's disease can cause inflammation in any part of the digestive tract but often affects the tail end of the small intestine. Ulcerative colitis is inflammation of the large intestine. Both Crohn's disease and ulcerative colitis are chronic and recurring inflammatory conditions. Researchers believe that these conditions occur when the body's inflammatory cells become over-reactive and mount a destructive inflammatory response. Current treatments for IBD include steroids, 5-aminosalicylic acids, immunosuppressive therapies, such as azathioprine or biologic agents such as TNF- $\alpha$  inhibitors and integrin inhibitors, such as the anti- $\alpha 4\beta 7$  antibody, vedolizumab, and when all else fails, surgery.

### ***Vercirnon***

Our drug candidate Vercirnon 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.



We completed nine clinical trials with vécirnon 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 vécirnon was effective in inducing a clinical response over a 12-week treatment period. The results also indicated that vécirnon was effective in maintaining clinical remission over an additional 36-week treatment period. Vécirnon was safe and well-tolerated in all clinical trials completed to date. Data from the first of four Phase III clinical trials, the SHIELD-1 study, conducted by our former collaboration partner, Glaxo Group Limited, or GSK, an affiliate of GlaxoSmithKline, investigating vécirnon in 608 patients with moderate-to-severe Crohn's disease, did not achieve the primary endpoint of improvement in clinical response and the key secondary endpoint of clinical remission. Results from SHIELD-4, a second induction study showed higher Crohn's disease activity index, or CDAI, response and remission rates with 500mg vécirnon twice daily compared to 500mg once daily. This is in contrast to the lack of dose response observed in the SHIELD-1 trial, and the response observed in the population of patients who completed 12 week dosing in SHIELD-4 was similar to the positive results from the Phase Iib PROTECT-1 clinical trial conducted by us. We are evaluating a potential future development and funding strategy for vécirnon. The assets, including vécirnon, all clinical study data, and IND are wholly owned by us.

### ***Second Generation CCR9 Inhibitor CCX507***

Also in the area of IBD, our drug candidate CCX507 builds on our expertise in the area of CCR9 inhibitors and IBD. CCX507 is a second generation CCR9 inhibitor. CCX507 is selective for CCR9 relative to all other chemokine receptors, orally bioavailable, and has an excellent preclinical safety profile. CCX507 has a greater potency towards CCR9 than vécirnon. We completed Phase I clinical development, which demonstrated that CCX507 was safe and well-tolerated, and blocked CCR9 on circulating leukocytes. Additionally, preclinical data of CCX507 in combination with an anti- $\alpha$ 4 $\beta$ 7 antibody or anti-TNF showed that combined treatment reduced the severity of colitis better than monotherapy with either drug alone. We plan to move CCX507 forward to Phase II clinical trials, potentially in conjunction with a strategic partner.

### **TH17 Driven Diseases and CCR6**

One of the most intriguing areas of current research in immunology involves a newly discovered type of helper T cells known as Th17 cells. There is a large amount of preclinical and clinical data that implicate Th17 cells, as well as Interleukin 17, or IL-17, in the development of a large number of autoimmune diseases, including psoriasis, rheumatoid arthritis, asthma, and multiple sclerosis.

Activated Th17 cells isolated from chronically inflamed human tissues produce high levels of TNF- $\alpha$  and other cytokines. A hallmark of Th17 cells is that they express high levels of the chemokine receptor known as CCR6, which is not found on Th1 and Th2 cells. High levels of the CCR6 chemokine ligand, CCL20, have been found in psoriatic skin, in rheumatoid arthritis joint biopsies, and in asthmatic lungs.

We believe that these are potential therapeutic opportunities for a CCR6 inhibitor. We have produced several unique CCR6 inhibitor leads, which are now being optimized through medicinal chemistry approaches.

We have shown in preclinical models that an orally bioavailable, small molecule inhibitor of the chemokine receptor known as CCR6 confers protection against IL17-mediated inflammation. We have generated potent orally bioavailable CCR6 inhibitors that inhibit CCL20-mediated chemotaxis of both human and mouse CCR6-positive cells. The utility of CCR6 inhibition was tested in preclinical models of psoriasis, and demonstrated that animals treated with our CCR6 inhibitor were protected against imiquimod induced skin thickening. Histological

analysis of the skin confirmed the protective effect of our CCR6 inhibitor compared to an aqueous vehicle control and significantly reduced ear-thickening induced by intradermal injections of Interleukin 23, or IL-23, a cytokine that is important for the terminal differentiation and pathogenicity of Th17 cells.

The mechanism of action for CCR6 inhibitors is different from other therapeutics targeting IL-17, because inhibition of CCR6 disrupts the recruitment of infiltrating leukocytes into the epidermis upon skin damage, thereby protecting against epidermal hyperplasia, or an abnormal increase in the number of cells on the skin. Thus, pharmacological inhibition of CCR6 with an orally bioavailable small molecule inhibitor mitigates IL-17-driven inflammation in psoriasis models, and its distinct mechanism of action suggests it may offer additional efficacy when added to current standard of care.

Recent work by others in the field has also revealed potential roles for CCR6 inhibitors in the treatment of colorectal cancer, or CRC. Specifically, in a mouse CRC model, mice that are genetically deficient in CCR6, as well as wild-type mice treated with a CCR6 inhibitor develop fewer intestinal polyps.

### ***CCR4 Inhibitor for Atopic Autoimmune Disorders***

CCR4 is expressed primarily on 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. CCR4 has also been identified on populations of T-Regulatory cells, or Treg cells, including those that are known to be important in the tumor microenvironment; thought to be a protective element in the tumor. An emerging concept in cancer therapy is that the elimination of tumor protecting Treg cells from the tumor microenvironment could be an important part of the future therapies in immuno-oncology.

CCX6239 is a novel, orally administered CCR4 inhibitor with potential utility in the treatment of conditions discussed above. We have shown in preclinical models that CCX6239 blocks the mobilization of white blood cells controlled by CCR4.

### ***CXCR6 Inhibitor for Liver Diseases***

Infection, chemical and metabolic insults to the liver can lead to a vigorous T-cell response in that organ. Resultant inflammation and liver damage can often result from persistent attempts by the immune system to deal with the underlying insults. 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 inhibitors 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 chemoattractant 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 chemoattractant 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, and several 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 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.

### **Former Strategic Alliance with GSK**

We had a development and commercialization agreement with GSK which ended in November 2013. For former collaboration compounds that were originally licensed to GSK and were subsequently returned to us, we are free to develop and commercialize such compounds either independently or with another partner. In the event we elect to continue to develop and commercialize drug candidates covered under this former agreement, including vercirnon, CCX168 and CCX832, we would be subject to future royalties to GSK. With respect to vercirnon, we would be subject to a reverse royalty to GSK of 3% on annual worldwide net sales only if a regulatory agency were to deem one of GSK's SHIELD trials to be a pivotal Phase III clinical trial. With respect to CCX354, we would not be subject to any reverse royalty to GSK on sales. With respect to CCX168 and CCX832, we would be subject to reverse royalties to GSK of 3% on annual worldwide net sales, not to exceed \$50.0 million in royalties for each.

### **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, manufacturing, salts and polymorphs, dosage, combinations 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 716 issued or allowed patents and approximately 214 pending patent applications, with claims relating to all of our current clinical-stage drug candidates. There are approximately 20 issued or allowed patents and 26 patent applications pending for

CCX168, our lead drug candidate in the C5aR program. With respect to our drug candidates in the CCR2 program, we have approximately 70 issued or allowed patents and 6 patents pending worldwide relating to their chemical composition or use thereof. With respect to our drug candidates in the CCR9 and CCR1 programs, we have approximately 363 issued or allowed patents and 116 patents pending worldwide relating to their chemical composition or use thereof. We have approximately 80 patents issued or pending for our other preclinical-stage compounds in the C5aR, CCR2, CXCR7, CCR4, CXCR2 and CCR6 programs. We have approximately 37 issued patents relating to other small molecule compounds and approximately 155 issued patents relating to our novel biological discoveries and our proprietary screening and drug development technologies.

For our lead drug candidates, CCX168, CCX872 and CCX140, our issued primary patents will expire on dates ranging from 2026 to 2031, not including patent term extensions or supplementary protection certificates that may be available in some countries. 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 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 AAV, DN and other renal diseases, IBD, 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.

CCX168, our C5aR inhibitor, if approved for marketing by the FDA or other regulatory agencies for the treatment of AAV, might compete with current treatments, such as steroids, CYC, RTX, azathioprine, methotrexate, and mycophenolate mofetil. If CCX168 were approved for the treatment of aHUS, it would potentially compete with eculizumab (Soliris).

CCX872, our second CCR2 inhibitor, if approved by the FDA or other regulatory agencies for the treatment of pancreatic cancer, might compete with treatments that are currently available, such as chemotherapeutic drugs including gemcitabine and nab-paclitaxel, or new treatments in development.

CCX140, our first CCR2 inhibitor, if approved for marketing by the FDA or other regulatory agencies for the treatment of DN, might 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 DN.

Our CCR9 small molecule inhibitors such as CCX507 and vercirnon for the treatment of IBD, might compete against existing IBD treatments such as Remicade, Humira, and other TNF- $\alpha$  inhibitors, anti- $\alpha$ 4B7 antibodies such as vedolizumab (Entyvio), immunomodulatory drugs and steroids and potentially against other novel IBD drug candidates that are currently in development. Remicade is a humanized monoclonal antibody targeted to TNF- $\alpha$ , indicated for the treatment of Crohn's disease, ulcerative colitis, rheumatoid arthritis, psoriasis, psoriatic arthritis and ankylosing spondylitis. Humira, a similar drug, is also a human monoclonal antibody that acts as a TNF- $\alpha$  inhibitor. Marketed by AbbVie in the United States and Europe, Humira is approved for the treatment of Crohn's disease, ulcerative colitis, rheumatoid arthritis, psoriatic arthritis, juvenile idiopathic arthritis, plaque psoriasis, and ankylosing spondylitis. Biosimilar drugs to Humira, for example, may also become available to treat patients with IBD.

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, Alexion, Amgen, AstraZeneca, Biogen Idec, Bayer, Bristol-Myers Squibb, Elan, Roche/Genentech, 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 and chemoattractant research and related drug development include Pfizer, GSK, Bristol-Myers Squibb, Merck, AstraZeneca, Boehringer-Ingelheim, Takeda, Sanofi, Incyte, Alexion, 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. We rely on contract manufacturing organizations to produce our 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.

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 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 which has recently completed a Phase II clinical trial in patients with DN in Europe. One of the Phase II clinical trials with CCX168 in patients with AAV has also been conducted in Europe. The second clinical trial is being conducted in North America. We have opened an IND in the United States. prior to commencing the Phase II clinical trial in the United States. All of our clinical trials are designed to comply with FDA regulatory requirements so that the data from all 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 CCX168, and for other drug candidates we develop independently prior to filing for regulatory approval 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.
- 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. An exception might be drugs developed for an orphan indication, where smaller clinical trials might be acceptable to the FDA and the EMA.

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 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. Fast track designation, accelerated approval, breakthrough therapy designation and priority review do not change the standards for approval, but may expedite the development or approval process. When appropriate, we intend to seek fast track designation, accelerated approval, breakthrough therapy designation and priority review, as applicable for our drug candidates. We cannot predict whether any of our drug candidates will obtain such designations or approvals, or the ultimate impact, if any, of such designations or approvals 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.

### ***Orphan Drug Designation***

In the United States, under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition. Such diseases and conditions are those that affect fewer than 200,000 individuals in the United States, or if they affect more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a drug available in the United States for these types of diseases or conditions will be recovered from sales of the drug. Orphan drug designation must be requested before submitting an NDA. If the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by that agency. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, but it can lead to financial incentives, such as opportunities for grant funding toward clinical trial costs, tax advantages and user-fee waivers.

If a drug that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the drug is entitled to orphan drug marketing exclusivity for a period of seven years. Orphan drug marketing exclusivity generally prevents the FDA from approving another application, including a full NDA, to market the same drug or biological product for the same indication for seven years, except in limited circumstances, including if the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. For purposes of small molecule drugs, the FDA defines “same drug” as a drug that contains the same active chemical entity and is intended for the same use as the drug in question. A designated orphan drug may not receive orphan drug marketing exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Orphan drug marketing exclusivity rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

The criteria for designating an orphan medicinal product in the EU are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. The application for orphan designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the marketing authorization application if the orphan designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.



The ten-year market exclusivity in the EU may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if:

- the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- the applicant consents to a second orphan medicinal product application; or
- the applicant cannot supply enough orphan medicinal product.

### ***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 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 extended coverage to approximately 32 million previously uninsured Americans. The Affordable Care Act contained a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse, which impacted existing government healthcare programs and resulted 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:

- imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs" to specified federal government programs;

- increased the minimum level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1%;
- required collection of rebates for drugs paid by Medicaid managed care organizations;
- required manufacturers to participate in a coverage gap discount program, under which they must agree to offer 50% 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; and
- mandated a further shift in the burden of Medicaid payments to the states.

The Affordable Care Act also established 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. In August, 2011, the President signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee did not achieve a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments, will remain in effect through 2025 unless additional Congressional action is taken. In January 2013, the President signed into law the American Taxpayer Relief Act of 2012, or the ATRA, which, among other things, further 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 if 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 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;
- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- the federal Physician Payment Sunshine Act, which requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and applicable manufacturers and group purchasing organizations to report annually to CMS ownership and investment interests held by physicians (as defined above) and their immediate family members and payments or other "transfer of value" to such physician owners;
- 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; state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

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 EU 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 marketing authorization that is valid for all EU Member States. The mutual recognition procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing 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, 2015, we had 58 full-time employees, 26 of whom hold Ph.D.s, M.D.s or both. Of our total workforce, 45 employees are engaged in research and development, and 13 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 \$33.2 million, \$33.8 million and \$33.5 million in research and development in the years 2015, 2014, and 2013, 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](http://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.

### **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](http://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](http://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.

## 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, 2015 and 2014 was \$47.3 million, and \$46.9 million, respectively. As of December 31, 2015, we had an accumulated deficit of \$267.1 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. 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. In November 2013, our agreement with our former collaboration partner, Glaxo Group Limited, or GSK, an affiliate of GlaxoSmithKline ended. 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 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 drug candidates, CCX140, CCX168, CCX872, vercirmon, CCX507 and CCX354 and 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 PK 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 demonstrate safety and efficacy in clinical trials or result in commercially successful products. For example, in August 2013, our former collaboration partner, GSK, reported the first of four Phase III studies, the SHIELD-1 study, investigating vercirmon in patients with moderate-to-severe Crohn's disease, did not achieve the primary endpoint of improvement in clinical response and the key secondary endpoint of clinical remission, and GSK subsequently reverted to us all rights to vercirmon and its two identified back-up compounds. In addition, in November 2013, GSK reverted to us all rights to CCX354 and its two identified back-up compounds, and GSK declined its last option to license CCX168 under our agreement with GSK.



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, or ethics committee, or EC, approval to conduct a clinical trial at a prospective site;
- the need to successfully complete, on a timely basis, preclinical safety pharmacology or toxicology 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;
- 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.

Further, chemokine receptors and chemoattractant 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 CCX140 and CCX168. As of the date of this Annual Report on Form 10-K, six of our drug candidates have been tested in human beings. Although we have not observed significant harmful side effects in prior studies of our drug candidates, later trials could reveal such side effects. The PK 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 PK results were not as favorable in humans as in earlier preclinical animal studies. We have not completed studies on the long-term effects associated with the use of our drug candidates, CCX168, for example. Completion of studies of these long-term effects may be required for regulatory approval and would delay our introduction of our 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 our drug candidates depends on our ability to develop and market such drug candidates or find partners to co-develop and commercialize such drug candidates, and if we fail in these initiatives, our ability to generate future revenue could be significantly reduced.***

We may retain commercial rights to certain of our drug candidates or find partners for their co-development and commercialization. Any of the following events or factors could have a material adverse effect on our ability to generate revenue from the commercialization of our drug candidates:

- We may be unable to successfully complete the clinical development of our drug candidates;
- 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 our drug candidates;
- We may not be able to identify a suitable co-development partner;
- We or any of our future partners may fail to fulfill responsibilities in a timely manner or fail to commit sufficient resources to the development, regulatory approval, and commercialization efforts related to our drug candidates;
- 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;
- Our drug candidates must be manufactured in compliance with requirements of FDA and similar foreign regulatory agencies and in commercial quantities sufficient to meet market demand;
- Our drug candidates may not achieve market acceptance by physicians, patients and third party payors;
- Our drug candidates may not compete successfully against alternative products and therapies; and
- We or any pharmaceutical company may independently develop products that compete with our drug candidates.

***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. 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 good clinical practices, or GCPs, 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 protocols or GCPs, 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. Our ability to develop and commercialize our drug candidates will depend upon our ability to identify financing or collaboration arrangements and there can be no assurance that we will be successful in identifying or implementing any such arrangement.

As of December 31, 2015, we had approximately \$76.3 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 success of any strategic alliance with potential future collaboration partners;
- 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 not be able to obtain orphan drug exclusivity for CCXI68 for the treatment of AAV.***

In the United States, under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition. Such diseases and conditions are those that affect fewer than 200,000 individuals in the United States, or if they affect more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a drug available in the United States for these types of diseases or conditions will be recovered from sales of the drug. Orphan drug designation must be requested before submitting an NDA. If the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by that agency. Orphan drug designation



does not convey any advantage in or shorten the duration of the regulatory review and approval process, but it can lead to financial incentives, such as opportunities for grant funding toward clinical trial costs, tax advantages and user-fee waivers.

If a drug that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the drug is entitled to orphan drug marketing exclusivity for a period of seven years. Orphan drug marketing exclusivity generally prevents the FDA from approving another application, including a full NDA, to market the same drug or biological product for the same indication for seven years, except in limited circumstances, including if the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. For purposes of small molecule drugs, the FDA defines “same drug” as a drug that contains the same active chemical entity and is intended for the same use as the drug in question. A designated orphan drug may not receive orphan drug marketing exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Orphan drug marketing exclusivity rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

The criteria for designating an orphan medicinal product in the European Union, or EU, are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. The application for orphan designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the marketing authorization application if the orphan designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The ten-year market exclusivity in the EU may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if:

- the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- the applicant consents to a second orphan medicinal product application; or
- the applicant cannot supply enough orphan medicinal product.

The FDA granted orphan drug designation for CCX168 for the treatment of aHUS and AAV, including granulomatosis with polyangiitis or Wegener’s granulomatosis, microscopic polyangiitis, and Churg-Strauss syndrome. The European Commission granted orphan drug designation for CCX168 for the treatment of granulomatosis with polyangiitis or Wegener’s granulomatosis and microscopic polyangiitis. However, we cannot assure you that we will be able to obtain or maintain orphan drug exclusivity for CCX168, if it is approved for the treatment of aHUS and/or AAV in any jurisdiction, in a timely manner or at all, or that a competitor will not obtain orphan drug exclusivity that could block the regulatory approval of CCX168 for several years. If we are unable to obtain or maintain orphan drug exclusivity in the United States or the EU, our

ability to generate sufficient revenues may be negatively affected. If a competitor is able to obtain orphan exclusivity that would block CCX168's regulatory approval, our ability to generate revenues would be significantly reduced, which would harm our business prospects, financial condition and results of operations.

***We may form additional strategic alliances in the future with respect to our 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 programs that we believe will complement or augment our existing business. For example, we plan to find a partner for the development and commercialization of CCX140, and we may seek to find a partner or alternative financing arrangements with respect to the completion of clinical development and commercialization of vercirnon. We face significant competition in seeking appropriate strategic partners or other alternative arrangements 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 current or future drug candidates and programs because our research and development pipeline may be insufficient, our drug 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 drug 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 drug candidates could also delay the development and commercialization of our drug 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 as described in a January 2014 publication by the nomenclature committee of the International Union of Pharmacology. 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 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. 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.***

We currently have limited experience in, and we do not own facilities for, manufacturing our 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.

We currently rely on a single source supplier for API and drug product for each of our drug candidates. 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 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 third parties to assist us in the marketing and distribution of our products. 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. 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 any 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. 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 third parties, any future product revenue will be materially adversely affected.

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

As of December 31, 2015, we had 58 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 CCX168 and Phase Ib clinical trial for CCX872, 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 chronic kidney disease, including DN, IBD, 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 but not limited to, AbbVie, Alexion, Amgen, AstraZeneca, Biogen Idec, Bayer, Elan, GlaxoSmithKline, Johnson & Johnson, Merck, Merck Serono, Roche/Genentech, 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 and chemoattractant research and related drug development include, but not limited to, Pfizer, GlaxoSmithKline, Bristol-Myers Squibb, Merck, Takeda, Sanofi, Incyte, Alexion 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 AAV, DN and other renal disease, IBD, rheumatoid

arthritis, other autoimmune diseases, metabolic diseases, inflammatory disorders, and cancer. 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.

***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.

***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 our business. 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.

***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, or the JOBS Act, and we 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 have elected 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 following the year in which we completed our initial public offering, 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 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 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 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 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, independent contractors, principal investigators, CROs, consultants, vendors and collaboration partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.***

We are exposed to the risk of that our employees, independent contractors, principal investigators, CROs, consultants, vendors and collaboration partners may engage in fraudulent or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities

to us that violate: FDA regulations, including those that require the reporting of true, complete and accurate information to the FDA; manufacturing standards we have established; federal and state healthcare fraud and abuse laws and regulations; and laws that require the reporting of true, complete and accurate financial information or data. In particular, 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. These activities could also include 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 misconduct by employees and other third parties, 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 civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other U.S. federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

***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 of 1986, as amended, 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 vercirnon.***

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 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 our 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. 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 alleged 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. In October 2013, the Opposition Division of the European Patent Office verbally announced a decision against the opposition filed by Millennium, with a written decision following in January 2014. In this decision, the patent was maintained in amended form. Millennium did not appeal this decision. Thus, the decision to maintain the patent became final in April 2014. The patent has meanwhile been revalidated in all designated states. It can now only be invalidated nationally by filing a nullity action before a national court.

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.

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.



***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 716 issued or allowed patents and approximately 214 pending patent applications, with claims relating to all of our current clinical-stage drug candidates. There are approximately 20 issued or allowed patents and 26 patent applications pending for CCX168, our lead drug candidate in the C5aR program. With respect to our drug candidates in the CCR2 programs, we have approximately 70 issued or allowed patents and 6 patents pending worldwide relating to their chemical composition or use thereof. With respect to our drug candidates in the CCR9 and CCR1 programs, we have approximately 363 issued or allowed patents and 116 patents pending worldwide relating to their chemical composition or use thereof. We have approximately 80 patents issued or pending for our other preclinical-stage compounds in the C5aR, CCR2, CXCR7, CCR4, CXCR2 and CCR6 programs. We have approximately 37 issued patents relating to other small molecule compounds and approximately 155 issued patents relating to our novel biological discoveries and 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, in September, 2011, the President 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.

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 technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees and consultants that are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could otherwise become known or be independently discovered by our competitors. In addition, intellectual property laws in foreign countries may not protect our intellectual property to the same extent as the laws of the United States.

***We may become subject to third parties' claims alleging infringement of patents and proprietary rights or seeking to invalidate our patents or proprietary rights, which would be costly, time consuming and, if successfully asserted against us, delay or prevent the development and commercialization of our products.***

There has been substantial litigation and other proceedings regarding patent and other intellectual property rights in the pharmaceutical and biotechnology industries. We may be subject to third-party claims in the future against us or our collaborators that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages, including treble damages and attorney's fees if we are found to be willfully infringing a third party's patents. Further, if a patent infringement suit were brought against us or our collaborators, we or they could be forced to stop or delay research, development, manufacturing or sales of the product or drug candidate that is the subject of the suit. As a result of patent infringement claims, or in order to avoid potential claims, we or our collaborators may choose to seek, or be required to seek, a license from the third party and would most likely be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we or our collaborators were able to obtain a license, the rights may be nonexclusive, which would give our competitors access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or forced to redesign it, or to cease some aspect of our business operations if, as a result of actual or threatened patent infringement claims, we or our collaborators are unable to enter into licenses on acceptable terms. This could harm our business significantly.

In addition to infringement claims against 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 USPTO to determine the priority of invention. We may also become involved in similar opposition proceedings in the European Patent Office regarding our intellectual property rights with respect to our products and technology.

***Restrictions on our patent rights relating to our drug candidates may limit our ability to prevent third parties from competing against us.***

Our success will depend, in part, on our ability to obtain and maintain patent protection for our drug candidates, preserve our trade secrets, prevent third parties from infringing upon our proprietary rights and operate without infringing upon the proprietary rights of others. Composition-of-matter patents on APIs are generally considered to be the strongest form of intellectual property protection for pharmaceutical products as they apply without regard to any method of use. Entirely new individual chemical compounds, often referred to as new chemical entities, are typically entitled to composition-of-matter coverage. However, we cannot be certain that the current law will remain the same, or that our drug candidates will be considered novel and non-obvious by the USPTO and courts.

In addition to composition-of-matter patents and patent applications, we also have filed method-of-use patent applications. This type of patent protects the use of the product only for the specified method. However, this type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if these competitors do not actively promote their product for our targeted indication, physicians may prescribe these products “off-label.” Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute.

Patent applications in the United States and most other countries are confidential for a period of time until they are published, and publication of discoveries in scientific or patent literature typically lags actual discoveries by several months or more. As a result, we cannot be certain that we and the inventors of the issued patents and applications that we may in-license were the first to conceive of the inventions covered by such patents and pending patent applications or that we and those inventors were the first to file patent applications covering such inventions. Also, we have numerous issued patents and some patent applications pending before the USPTO and the patent protection may lapse before we manage to obtain commercial value from them, which might result in increased competition and materially affect our position in the market.

***We may be subject to claims that we or our employees or consultants have wrongfully used or disclosed alleged trade secrets of our employees’ or consultants’ former employers or their clients. These claims may be costly to defend and if we do not successfully do so, we may be required to pay monetary damages and may lose valuable intellectual property rights or personnel.***

Many of our employees were previously employed at universities or biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could hamper our ability to commercialize, or prevent us from commercializing our drug candidates, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

***Some of our intellectual property which is discovered through government funded programs is subject to federal regulation such as “march-in” rights, certain reporting requirements, and a preference for U.S. industry. Compliance with such regulations may limit our exclusive rights, subject us to expenditure of resources with respect to reporting requirements, and limit our ability to contract with foreign manufacturers.***

Some of our existing drug candidates, including CCX140, and some of our research and development work were funded, at least in part, by the U.S. government and are therefore subject to certain federal regulations. For example, some of our research and development work on vaccine adjuvants and immunomodulation for biothreat applications was funded by government research grants. In addition, as noted on several of our patents including U.S. Patent Nos. 7,884,110; 7,622,583; 7,776,877; 8,198,309 and 8,093,247, inventions covering various CCR9 and CCR2 inhibitors were supported at least in part by National Institutes of Health funding (U19-AI056690-01). Under the “march-in” provisions of the Bayh-Dole Act, the government may have the right under limited circumstances to require us to grant exclusive, partially exclusive or non-exclusive rights to third parties for intellectual property discovered through the government funded program. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the new invention or because action is necessary to alleviate health or safety needs of the public. Intellectual property discovered under the government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. Such intellectual property is also subject to a preference for U.S. industry, which may limit our ability to contract with foreign product manufacturers for products covered by such intellectual property. We plan to apply for additional U.S. government funding, and it

is possible that we may discover compounds or drug candidates as a result of such funding. Intellectual property under such discoveries would be subject to the applicable provisions of the Bayh-Dole Act.

### **Risks Related to Government Regulation**

*The regulatory approval process is expensive, time consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our drug candidates.*

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, which regulations differ from country to country. We are not permitted to market our drug candidates in the United States until we receive approval of a new drug application, or NDA, from the FDA. We have not submitted an application for or received marketing approval for any of our drug candidates. Obtaining approval of an NDA can be a lengthy, expensive and uncertain process. In addition, failure to comply with FDA and other applicable U.S. and foreign regulatory requirements may subject us to administrative or judicially imposed sanctions, including:

- warning letters;
- civil and criminal penalties;
- injunctions;
- withdrawal of approved products;
- product seizure or detention;
- product recalls;
- total or partial suspension of production; and
- refusal to approve pending NDAs or supplements to approved NDAs.

Prior to receiving approval to commercialize any of our drug candidates in the United States or abroad, we must demonstrate with substantial evidence from well controlled clinical trials, and to the satisfaction of the FDA and other regulatory authorities abroad, that such drug candidates are safe and effective for their intended uses. Results from preclinical studies and clinical trials can be interpreted in different ways. Even if we believe the preclinical or clinical data for our drug candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. Administering any of our drug candidates to humans may produce undesirable side effects, which could interrupt, delay or halt clinical trials of our drug candidates and result in the FDA or other regulatory authorities denying approval of our drug candidates for any or all targeted indications.

Regulatory approval of an NDA or NDA supplement is not guaranteed, and the approval process is expensive and may take several years. The FDA also has substantial discretion in the approval process. Despite the time and expense exerted, failure can occur at any stage, and we could encounter problems that cause us to abandon or repeat clinical trials, or perform additional preclinical studies and clinical trials. The number of preclinical studies and clinical trials that will be required for FDA approval varies depending on the drug candidate, the disease or condition that the drug candidate is designed to address, and the regulations applicable to any particular drug candidate. The FDA can delay, limit or deny approval of a drug candidate for many reasons, including, but not limited to, the following:

- a drug candidate may not be deemed safe or effective;
- FDA officials may not find the data from preclinical studies and clinical trials sufficient;
- the FDA might not approve our or our third party manufacturer's processes or facilities; or
- the FDA may change its approval policies or adopt new regulations.

If any of our drug candidates fails to demonstrate safety and efficacy in clinical trials or does not gain regulatory approval, our business and results of operations will be materially and adversely harmed.

***Even if we receive regulatory approval for a drug candidate, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and subject us to penalties if we fail to comply with applicable regulatory requirements.***

Once regulatory approval has been granted, the approved product and its manufacturer are subject to continual review by the FDA and/or non-U.S. regulatory authorities. Any regulatory approval that we receive for our drug candidates may be subject to limitations on the indicated uses for which the product may be marketed or contain requirements for potentially costly post-marketing follow-up studies to monitor the safety and efficacy of the product. The FDA also has authority to require a risk evaluation and mitigation strategy, or REMS, as part of an NDA or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria or requiring treated patients to enroll in a registry. In addition, if the FDA and/or non-U.S. regulatory authorities approve any of our drug candidates, we will be subject to extensive and ongoing regulatory requirements by the FDA and other regulatory authorities with regard to the labeling, packaging, adverse event reporting, storage, advertising, promotion and recordkeeping for our products. The FDA strictly regulates the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. If we receive marketing approval for any of our drug candidates, physicians may nevertheless prescribe our products to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability and government fines.

In addition, manufacturers of our drug products are required to comply with cGMP regulations, which include requirements related to quality control and quality assurance as well as the corresponding maintenance of records and documentation. Further, regulatory authorities must approve manufacturing facilities before they can be used to manufacture our drug products, and such facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations. If we or a regulatory authority discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory authority may impose restrictions on that product, the manufacturer or us, including imposition of a REMS or requesting recall or withdrawal of the product from the market or suspension of manufacturing. If we, our drug candidates or the manufacturing facilities for our drug candidates fail to comply with regulatory requirements of the FDA and/or other non-U.S. regulatory authorities, we could be subject to administrative or judicially imposed sanctions, including:

- warning letters;
- civil or criminal penalties;
- injunctions;
- suspension of or withdrawal of regulatory approval;
- suspension of any ongoing clinical trials;
- voluntary or mandatory product recalls and publicity requirements;
- refusal to approve pending applications for marketing approval of new drugs or supplements to approved applications filed by us;
- restrictions on operations, including costly new manufacturing requirements; or
- seizure or detention of our products or import bans.



The regulatory requirements and policies may change and additional government regulations may be enacted for which we may also be required to comply. For example, the Food and Drug Administration Safety and Innovation Act of 2012 required the FDA to issue guidance on permissible forms of internet and social media promotion of regulated medical products, and the FDA issued a number of draft guidance documents relating to social media and may soon specify new restrictions on this form of product promotion. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or in other countries. If we are not able to maintain regulatory compliance, we will not be permitted to market our future products and our business will suffer.

***The availability of adequate third-party coverage and reimbursement for newly approved drugs is uncertain, and failure to obtain adequate coverage and reimbursement from third-party payors could impede our ability to market any future products we may develop and could limit our ability to generate revenue.***

There is significant uncertainty related to the third-party payor coverage and reimbursement of newly approved drugs. The commercial success of our future products in both domestic and international markets depends on whether such third-party coverage and reimbursement is available for our future products. Governmental payors, including Medicare and Medicaid, health maintenance organizations and other third-party payors are increasingly attempting to manage their healthcare expenditures by limiting both coverage and the level of reimbursement of new drugs and, as a result, they may not cover or provide adequate reimbursement for our future products. These payors may not view our future products as cost-effective, and coverage and reimbursement may not be available to our customers or may not be sufficient to allow our future products to be marketed on a competitive basis. Third-party payors are exerting increasing influence on decisions regarding the use of, and coverage and reimbursement levels for, particular treatments. Such third-party payors, including Medicare, are challenging the prices charged for medical products and services, and many third-party payors limit or delay coverage and reimbursement for newly approved healthcare products. In particular, third-party payors may limit the covered indications. Cost-control initiatives could cause us to decrease the price we might establish for products, which could result in lower than anticipated product revenues. If the prices for our drug candidates decrease or if governmental and other third-party payors do not provide adequate coverage or reimbursement, our prospects for revenue and profitability will suffer.

***Failure to obtain regulatory approvals in foreign jurisdictions will prevent us from marketing our products internationally.***

We intend to seek a distribution and marketing partner for CCX140 and may market future products in international markets. In order to market our future products in the EEA (which is comprised of the 28 Member States of the EU plus Norway, Iceland and Liechtenstein) and many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EEA, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

- The Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use of the European Medicines Agency, or EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.
- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member State through the Mutual

Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

We have had limited interactions with foreign regulatory authorities, and the approval procedures vary among countries and can involve additional clinical testing, and the time required to obtain approval may differ from that required to obtain FDA approval. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one or more foreign regulatory authorities does not ensure approval by regulatory authorities in other foreign countries or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. We may not be able to file for regulatory approvals and even if we file we may not receive necessary approvals to commercialize our products in any market.

***Healthcare reform measures could hinder or prevent our drug candidates' commercial success.***

In the United States, there have been and we expect there will continue to be a number of legislative and regulatory changes to the healthcare system in ways that could affect our future revenues and profitability and the future revenues and profitability of our potential customers. Federal and state lawmakers regularly propose and, at times, enact legislation that would result in significant changes to the healthcare system, some of which are intended to contain or reduce the costs of medical products and services. For example, in March 2010, the President signed one of the most significant healthcare reform measures in decades, the Affordable Care Act. It contained a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse measures, all of which impacted existing government healthcare programs and resulted in the development of new programs. The Affordable Care Act, among other things:

- imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell “branded prescription drugs” to specified federal government programs;
- increased the minimum level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1%;
- required collection of rebates for drugs paid by Medicaid managed care organizations;
- required manufacturers to participate in a coverage gap discount program, under which they must agree to offer 50% 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; and
- mandated a further shift in the burden of Medicaid payments to the states.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. In August, 2011, the President signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee did not achieve a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, triggering the legislation’s automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments, will remain in effect through 2025 unless additional Congressional action is taken. In January 2013, the President signed into law the American Taxpayer Relief Act

of 2012, or the ATRA, which, among other things, further 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. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our potential customers and accordingly, our financial operations.

There likely will continue to be legislative and regulatory proposals at the federal and state levels directed at containing or lowering the cost of health care. We cannot predict the initiatives that may be adopted in the future or their full impact. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of health care may adversely affect:

- our ability to set a price we believe is fair for our products;
- our ability to generate revenues and achieve or maintain profitability; and
- the availability of capital.

Further, 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 IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial. In light of widely publicized events concerning the safety risk of certain drug products, regulatory authorities, members of Congress, the Governmental Accounting Office, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the recall and withdrawal of drug products, revisions to drug labeling that further limit use of the drug products and establishment of risk management programs that may, for instance, restrict distribution of drug products or require safety surveillance and/or patient education. The increased attention to drug safety issues may result in a more cautious approach by the FDA to clinical trials and the drug approval process. Data from clinical trials may receive greater scrutiny with respect to safety, which may make the FDA or other regulatory authorities more likely to terminate or suspend clinical trials before completion, or require longer or additional clinical trials that may result in substantial additional expense and a delay or failure in obtaining approval or approval for a more limited indication than originally sought.

Heightened Congressional scrutiny on the adequacy of the FDA's drug approval process and the agency's efforts to assure the safety of marketed drugs resulted in the enactment of legislation addressing drug safety issues, the FDA Amendments Act of 2007, or FDAAA. This legislation provided the FDA with expanded authority over drug products after approval, including the authority to impose the requirement for a REMS to assure the safe use of the drug, either as a condition for product approval or after a product is approved on the basis of new safety information. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of our drug candidates, if approved. The FDA's exercise of this authority under FDAAA has resulted in delays or increased costs during the period of product development, clinical trials and regulatory review and approval, and increased costs to assure compliance with new post-approval regulatory requirements. Given the serious public health risks of high profile adverse safety events with certain drug products, the FDA may require, as a condition of approval, costly risk management programs which may include safety surveillance, restricted distribution and use, patient education, enhanced labeling, special packaging or labeling, expedited reporting of certain adverse events, preapproval of promotional materials and restrictions on direct-to-consumer advertising.

***If we fail to comply with healthcare regulations, we could face substantial penalties and our business, operations and financial condition could be adversely affected.***

Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud

and abuse and patients' rights are and will be applicable to our business. We could be subject to healthcare fraud and abuse and patient privacy regulation by both the federal government and the states in which we conduct our business. The regulations that may affect our ability to operate include, without limitation:

- the federal Anti-Kickback Statute, which prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the federal False Claims Act, which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, false claims, or knowingly using false statements, to obtain payment from the federal government, and which may apply to entities like us which provide coding and billing advice to customers;
- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- 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; and
- 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.

Further, there has been a recent trend in the increase of federal and state laws and regulations regarding payments and other transfers of value paid to physicians and other healthcare providers and entities. The Affordable Care Act imposes new requirements to report certain financial arrangements with physicians and others, including reporting any "transfers of value" made or distributed to prescribers and other healthcare providers and reporting any investment interests held by physicians and their immediate family members during each calendar year. Manufacturers are required to submit reports to the government by the 90<sup>th</sup> day of each calendar year. In addition, certain states mandate that we comply with a state code of conduct, adopt a company code of conduct under state criteria, disclose marketing payments made to physicians and other healthcare providers, and/or report compliance information to the state authorities. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply in multiple jurisdictions with different compliance and reporting requirements increases the possibility that a pharmaceutical company may run afoul of one or more of the requirements.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, the exclusion from participation in U.S. federal or state health care programs and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our ability to operate our business and our financial results. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

## **Risks Related to the Securities Markets and an Investment in Our Stock**

*There may not be a viable market for our common stock or the price of our common stock may be volatile, and stockholders may not be able to sell their shares at prices that are attractive to them.*

There was no public market for our common stock prior to our initial public offering in February 2012, the trading volume of our common stock on the NASDAQ Global Select Market has been limited and there can be no assurance that an active and liquid trading market for our common stock will develop or be sustained. We cannot predict the extent to which investor interest in our company will lead to the development or maintenance of an active trading market on the NASDAQ Global Select Market or otherwise or how liquid that market might become. If an active public market does not develop or is not sustained, it may be difficult for stockholders to sell their shares of common stock at prices that are attractive to them, or at all. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or drugs, drug candidates or technologies by using our shares of common stock as consideration.

Stockholders may also be unable to sell their shares of common stock at prices that are attractive to them due to fluctuations in the market price of our common stock. The market prices for securities of biotechnology and pharmaceutical companies have historically been highly volatile. Since the commencement of trading in connection with our initial public offering in February 2012, the publicly traded shares of our common stock have themselves experienced significant price and volume fluctuations. During the year ended December 31, 2015, the price per share for our common stock on the Nasdaq Global Select Market ranged from a low sale price of \$5.40 to a high sale price of \$9.46. This market volatility is likely to continue. These and other factors could reduce the market price of our common stock, regardless of our operating performance. In addition, the trading price of our common stock could change significantly, both over short periods of time and the longer term, due to many factors, including, but not limited to, those described elsewhere in this “Risk Factors” section and the following:

- results from, and any delays in, clinical trial programs relating to our drug candidates, including the ongoing and planned clinical trials for CCX168, CCX140, CCX872, CCX507, and other drug candidates;
- announcements of regulatory approvals or disapprovals of our drug candidates, including CCX168 and CCX140, or delays in any regulatory agency review or approval processes;
- failure or discontinuation of any of our research programs;
- announcements relating to future collaborations;
- general economic conditions in the United States and abroad;
- acquisitions and sales of new products, technologies or business;
- delays in the commercialization of any of our drug candidates;
- market conditions in the pharmaceutical, biopharmaceutical and biotechnology sectors;
- the issuance of new or changed securities analysts’ reports or recommendations regarding us, our competitors or our industry in general;
- actual and anticipated fluctuations in our quarterly operating results;
- disputes concerning our intellectual property or other proprietary rights;
- introduction of technological innovations or new products by us or our competitors;
- manufacturing issues related to our drug candidates for clinical trials or future products for commercialization;
- market acceptance of our future products;



- deviations in our operating results from the estimates of analysts, or other analyst comments;
- third party payor coverage and reimbursement policies;
- new legislation in the United States relating to the sale or pricing of pharmaceuticals;
- FDA or other U.S. or foreign regulatory actions affecting us or our industry;
- product liability claims or other litigation or public concern about the safety of our drug candidates or future drugs;
- our ability to obtain necessary intellectual property licenses including, if necessary, those relating to vercirnon and other CCR9 drug candidates;
- the outcome of any future legal actions to which we are party;
- sales of our common stock by our officers, directors or significant stockholders;
- additions or departures of key personnel; and
- external factors, including natural disasters and other crises.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that have been often unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our management would be diverted from the operation of our business.

***The ownership of our common stock is highly concentrated, and these stockholders could delay or prevent a change of control.***

As of March 4, 2016, our officers and directors, together with holders of 5% or more of our outstanding common stock and their respective affiliates, beneficially owned approximately 70% of our outstanding common stock. Accordingly, these stockholders, acting as a group, have significant influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets or any other significant corporate transaction. The interests of these stockholders may not be the same as or may even conflict with the interests of our other stockholders. For example, these stockholders could delay or prevent a change of control of our company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

***Future sales of our common stock or securities convertible or exchangeable for our common stock may depress our stock price.***

Persons who were our stockholders prior to the sale of shares in our initial public offering continue to hold a substantial number of shares of our common stock that they are able to sell in the public market, subject in some cases to certain legal restrictions. If our stockholders or holders of our options or warrants sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. The perception in the market that these sales may occur could also cause the trading price of our common stock to decline. As of December 31, 2015, we had 44,185,506 shares of common stock outstanding. Of these shares, approximately 26,332,965 are freely tradeable, without restriction, in the public market. In addition, approximately 16,126,074 of the outstanding shares of common stock, and an additional

150,000 shares of common stock issuable upon exercise of outstanding warrants that we issued to Bio-Techne Corporation (formerly Techne Corporation), or Bio-Techne, in connection with our initial public offering, are eligible for sale in the public market, subject to volume limitations under Rule 144 under the Securities Act of 1933, as amended, or the Securities Act, with respect to shares held by directors, executive officers and other affiliates. In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans are eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act and, in any event, we have filed a registration statement permitting shares of common stock issued on exercise of options to be freely sold in the public market. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Certain holders of shares of our common stock, warrants to purchase our capital stock and the shares of common stock issuable upon exercise of those warrants are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. In addition, certain of our directors and executive officers have established, programmed selling plans under Rule 10b5-1 of the Exchange Act, for the purpose of effecting sales of our common stock. Any sales of securities by these stockholders, or the perception that those sales may occur, including the entry into such programmed selling plans, could have a material adverse effect on the trading price of our common stock.

***If we sell shares of our common stock in future financings, common stockholders may experience immediate dilution and, as a result, our stock price may decline.***

We may from time to time issue additional shares of common stock at a discount from the current trading price of our common stock. As a result, our common stockholders would experience immediate dilution upon the purchase of any shares of our common stock sold at such discount. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, preferred stock or common stock. For example, in connection with our initial public offering, in February 2012, we issued Bio-Techne a warrant with a ten-year term to purchase up to 150,000 shares of our common stock at an exercise per share equal to 200% of the initial public offering price of a share of our common stock and such warrant, if exercised, would likely be exercised at a time when the exercise price of such warrant represented a discount to the trading price of our common stock. If we issue common stock or securities convertible into common stock, our common stockholders would experience additional dilution and, as a result, our stock price may decline.

***Our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.***

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expenses related to our drug candidates or future development programs;
- if any of our drug candidates receives regulatory approval, the level of underlying demand for these drug candidates and wholesalers' buying patterns;
- addition or termination of clinical trials or funding support;
- our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under such arrangements, or the termination of such arrangements;
- any intellectual property infringement lawsuit in which we may become involved;
- regulatory developments affecting our drug candidates or those of our competitors; and

- our ability to secure new government contracts and allocation of our resources to or away from performing work under government contracts.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

***We have broad discretion in the use of our cash and may not use it effectively.***

Our management has broad discretion over the use of our cash. Because of the number and variability of factors that will determine our use of cash, stockholders may not agree with how we allocate or spend our cash. We may pursue collaborations or clinical trials that do not result in an increase in the market value of our common stock and that may increase our losses, or we may place our cash in investments that do not produce significant investment returns or that may lose value. Our failure to allocate and spend our cash effectively would have a material adverse effect on our financial condition and business and could cause our stock price to decline.

***Provisions of our charter documents or Delaware law could delay or prevent an acquisition of our company, even if the acquisition would be beneficial to our stockholders, and could make it more difficult for our stockholders to change management.***

Provisions of our amended and restated certificate of incorporation and amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. In addition, these provisions may frustrate or prevent any attempt by our stockholders to replace or remove our current management by making it more difficult to replace or remove our board of directors. These provisions include:

- a classified board of directors so that not all directors are elected at one time;
- a prohibition on stockholder action through written consent;
- a requirement that special meetings of stockholders be called only by the chairman of the board of directors, the chief executive officer, the president or by the board of directors;
- an advance notice requirement for stockholder proposals and nominations;
- the authority of our board of directors to issue preferred stock with such terms as our board of directors may determine; and
- a requirement of approval of not less than 66 2/3% of all outstanding shares of our capital stock entitled to vote to amend any bylaws by stockholder action, or to amend specific provisions of our certificate of incorporation.

In addition, Delaware law prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person who, together with its affiliates, owns or within the last three years has owned 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. Accordingly, Delaware law may discourage, delay or prevent a change in control of our company.

***Our employment agreements with our named executive officers may require us to pay severance benefits to any of those persons who are terminated in connection with a change of control of us, which could harm our financial condition or results.***

Our named executive officers are parties to employment agreements providing for aggregate cash payments of up to approximately \$5.2 million for severance and other benefits and acceleration of vesting of stock options

with an intrinsic value of \$0.9 million as of December 31, 2015 in the event of a termination of employment in connection with a change of control of us. The accelerated vesting of options could result in dilution to our stockholders and harm the market price of our common stock. The payment of these severance benefits could harm our financial condition and results. In addition, these potential severance payments may discourage or prevent third parties from seeking a business combination with us.

***We do not anticipate paying any cash dividends on our capital stock in the foreseeable future, therefore capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.***

We have never declared or paid cash dividends on our capital stock. We do not anticipate paying any cash dividends on our capital stock in the foreseeable future. We currently intend to retain all available funds and any future earnings to fund the development and growth of our business. In addition, any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

***If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, our stock price and trading volume could decline.***

The trading market for our common stock depends, in part, on the research and reports that securities or industry analysts publish about us or our business. As of January 2016, we had research coverage by only two securities analysts. In the event one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price would likely decline. In addition, if our operating results fail to meet the forecast of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

#### **Item 1B. Unresolved Staff Comments**

Not applicable.

#### **Item 2. Properties**

Our corporate headquarters are located in Mountain View, California, where we lease 35,755 square feet of office and laboratory space. In April 2004, we entered into a ten-year lease agreement for that facility. In August 2012, we entered into an amendment to the lease agreement for the same facility to extend the term of the lease through April 2019.

We believe that our existing facilities are adequate for our current needs, as the facility has sufficient laboratory space to house additional scientists to be hired as we expand. When our leases expire, we may exercise our renewal options or look for additional or alternate space for our operations and we believe that suitable additional or alternative space will be available in the future on commercially reasonable terms.

#### **Item 3. Legal Proceedings**

We are not currently a party to any legal proceedings.

#### **Item 4. Mine Safety Disclosures**

Not Applicable.

## PART II

### Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

#### Market Information

Our common stock has been traded on the NASDAQ Global Select Market since February 8, 2012 under the symbol "CCXI." Prior to such time, there was no public market for our common stock. The following table sets forth the high and low sales prices per share of our common stock on the NASDAQ Global Select Market for the quarterly periods indicated.

	Sales Price of Common Shares	
	High	Low
<i>Fiscal 2015</i>		
First Quarter	\$9.20	\$6.51
Second Quarter	9.46	6.50
Third Quarter	9.19	5.40
Fourth Quarter	8.30	5.46
<i>Fiscal 2014</i>		
First Quarter	\$8.25	\$5.58
Second Quarter	7.19	4.70
Third Quarter	6.07	4.41
Fourth Quarter	8.50	4.06

#### Holder of Common Stock

As of March 4, 2016, there were approximately 52 holders of record of our common stock. Certain shares are held in "street" name and accordingly, the number of beneficial owners of such shares is not known or included in the foregoing number.

#### Dividend Policy

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors.



## Equity Compensation Plan Information

The following table summarizes securities available under our equity compensation plans as of December 31, 2015 <sup>(1)</sup>.

<u>Plan Category</u>	<u>Shares Issuable Upon Exercise of Outstanding Options, Warrants and Rights<sup>(3)</sup></u>	<u>Weighted Average Exercise Price of Outstanding Options, Warrants and Rights<sup>(4)</sup></u>	<u>Number of Securities Available for Future Issuance<sup>(5)</sup></u>
Equity compensation plans approved by security holders: <sup>(2)</sup>	7,914,930	\$8.52	2,292,090
Equity compensation plans not approved by security holders:	—	—	—
Total	<u>7,914,930</u>	<u>\$8.52</u>	<u>2,292,090</u>

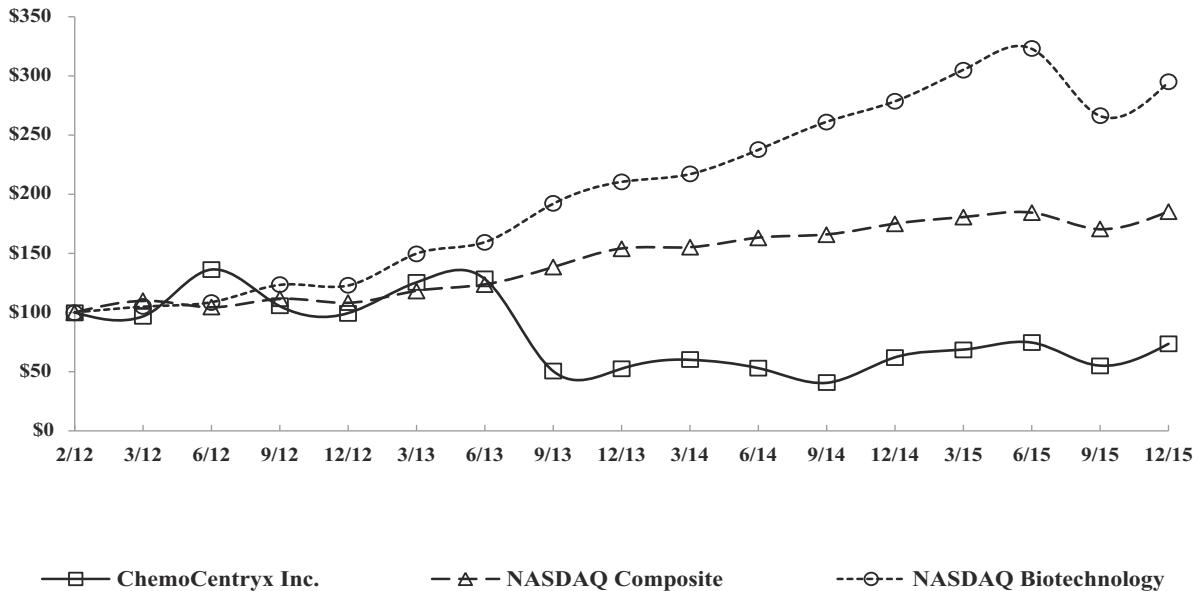
- (1) In January 2012, we effected a one-for-two reverse split of our common stock. All historical common stock and per share information has been changed to reflect the stock split and is referred to in this chart “as adjusted.”
- (2) Consists of our Amended and Restated 1997 Stock Option/Stock Issuance Plan, our Amended and Restated 2002 Equity Incentive Plan and our 2012 Equity Incentive Award Plan, our Non-Employee Director Compensation Policy and our Employee Stock Purchase Plan, or ESPP.
- (3) Includes 7,847,449 shares subject to outstanding stock option awards and 67,481 shares subject to outstanding restricted stock unit awards as of December 31, 2015.
- (4) Calculated exclusive of outstanding restricted stock unit awards.
- (5) Of these shares, 2,157,641 shares were available for stock option awards and restricted stock unit awards, and 134,449 were available for the ESPP, in each case as of December 31, 2015.

## Performance Graph

The information contained in this Performance Graph section shall not be deemed “soliciting material” or to be “filed” with the SEC, for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any filing of ChemoCentryx, Inc. under the Securities Act of 1933, as amended, or the Exchange Act.

The following graph shows a comparison from February 8, 2012 (the date our common stock commenced trading on the NASDAQ Global Select Market) through December 31, 2015 of cumulative total return for our common stock, the NASDAQ Composite Index and the NASDAQ Biotechnology Index. Such returns are based on historical results and are not intended to suggest future performance. Data for the NASDAQ Composite Index and the NASDAQ Biotechnology Index assume reinvestment of dividends.

**COMPARISON OF 47 MONTH CUMULATIVE TOTAL RETURN\***  
Among ChemoCentryx Inc., the NASDAQ Composite Index, and the NASDAQ Biotechnology Index



\*\$100 invested on 2/8/12 in stock or 1/31/12 in index, including reinvestment of dividends.  
Fiscal year ending December 31.

	2/8/ 2012	3/31/ 2012	6/30/ 2012	9/30/ 2012	12/31/ 2012	3/31/ 2013	6/30/ 2013	9/30/ 2013	12/31/ 2013	3/31/ 2014	6/30/ 2014	9/30/ 2014	12/31/ 2014	3/31/ 2015	6/30/ 2015	9/30/ 2015	12/31/ 2015
ChemoCentryx Inc.	100.00	96.91	136.36	105.73	99.45	125.64	128.55	50.55	52.64	60.27	53.18	40.91	62.09	68.64	74.82	55.00	73.64
NASDAQ Composite	100.00	110.15	104.74	111.74	108.43	118.27	123.77	138.49	154.12	155.36	163.30	166.03	175.07	180.78	184.54	170.72	185.42
NASDAQ Biotechnology	100.00	105.12	108.69	123.53	123.13	149.65	159.53	192.22	210.56	217.21	237.76	261.26	278.70	304.94	323.27	266.36	295.15

## Item 6. Selected Financial Data

The following selected financial data have been derived from our audited financial statements. The information set forth below is not necessarily indicative of future results and should be read in conjunction with “Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Item 8. Financial Statements and Supplementary Data” included elsewhere in this Annual Report on Form 10-K.

	Years Ended December 31,				
	2015	2014	2013	2012	2011
(in thousands except share and per share data)					
<b>Consolidated Statement of Operations Data:</b>					
Revenues:					
Collaborative research and development revenue from related party	\$ —	\$ —	\$ 6,060	\$ 5,419	\$ 31,673
Operating expenses:					
Research and development	33,183	33,815	33,541	34,569	28,359
General and administrative	14,506	13,584	11,634	10,480	7,615
Total operating expenses	47,689	47,399	45,175	45,049	35,974
Loss from operations	(47,689)	(47,399)	(39,115)	(39,630)	(4,301)
Interest income	384	494	501	533	402
Interest expense	—	(24)	(59)	(794)	(734)
Other income	—	—	—	—	16
Net loss	\$ (47,305)	\$ (46,929)	\$ (38,673)	\$ (39,891)	\$ (4,617)
Basic and diluted net loss per share <sup>(1)</sup>	\$ (1.08)	\$ (1.08)	\$ (0.95)	\$ (1.13)	\$ (1.10)
Shares used to compute basic and diluted net loss per share	43,889,677	43,275,276	40,916,138	35,406,922	4,210,704

(1) See Note 2 within the notes to our audited consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for a description of the method used to compute basic and diluted net loss per share.

	As of December 31,				
	2015	2014	2013	2012	2011
(in thousands)					
<b>Consolidated Balance Sheet Data:</b>					
Cash, cash equivalents and investments	\$ 76,289	\$ 114,620	\$ 149,874	\$ 118,956	\$ 96,086
Working capital	66,541	66,139	127,430	93,180	81,962
Total assets	78,155	116,981	152,422	122,323	101,551
Non-current equipment financing obligations	—	—	16	379	947
Accumulated deficit	(267,096)	(219,791)	(172,862)	(134,189)	(94,298)
Total stockholders’ equity	72,507	108,606	145,308	110,346	75,997

## **Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.**

*You should read the following discussion and analysis of financial condition and results of operations together with "Item 6. Selected Financial Data" and our financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion and other parts of this Annual Report on Form 10-K contain forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations and intentions. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in "Item 1A. Risk Factors" of this Annual Report on Form 10-K.*

### **Overview**

ChemoCentryx is a biopharmaceutical company focused on discovering, developing and commercializing orally-administered therapeutics to treat orphan and rare diseases, autoimmune diseases, inflammatory disorders and cancer. Our pipeline comprises the following programs:

#### ***Orphan and Rare Diseases:***

- CCX168 is an orally-administered complement inhibitor targeting the C5a receptor (C5aR) and is being developed for orphan and rare diseases, including anti-neutrophil cytoplasmic antibody, or ANCA, associated vasculitis, or AAV, atypical hemolytic uremic syndrome, or aHUS, and immunoglobulin A-mediated nephropathy, or IgAN. CCX168 has successfully completed and reported positive clinical data from the first Phase II clinical trial in patients with AAV, known as the CLEAR trial. This study met its primary endpoint whereby treatment with CCX168 demonstrated numerical superiority and statistical non-inferiority in Birmingham Vasculitis Activity Score, or BVAS, response relative to standard of care. The second Phase II clinical trial in patients with AAV, the CLASSIC trial, is ongoing in North America and we expect to report top-line data from this trial in mid 2016. Following CLASSIC data in mid 2016, we plan to conduct end-of-Phase II meetings with regulatory agencies and initiate the Phase III development program in patients with AAV by the end of 2016. Phase II pilot clinical trials with CCX168 in patients with aHUS and IgAN are ongoing.

#### ***Immuno-Oncology:***

- CCX872 is being evaluated in patients with non-resectable pancreatic cancer, and is our second inhibitor of the chemokine receptor known as CCR2. CCX872 completed Phase I clinical development in healthy volunteers. A Phase Ib clinical trial in patients with advanced pancreatic cancer is ongoing. Having recently presented pharmacodynamic and pharmacokinetic, or PK, data from the first step of the study, we expect to report early objective response rate data in the first half of 2016 and initial progression free survival, or PFS, data in the second half of 2016.
- Chemoattractant Receptor Targets — CCR1, CCR4, CCR5, CXCR2, CXCR7 — We believe these chemokine and chemoattractant receptors play an important role in establishing a tumor microenvironment that suppresses a cytotoxic immune response. We have discovered small molecule inhibitors targeting these chemoattractant receptors, which may be developed in certain oncology indications targeting both solid and liquid tumors. We believe that such immunotherapeutic agents could be administered as stand-alone therapies or result in a synergistic effect when given in combination with traditional chemotherapies or other immunotherapies, such as programmed cell death protein 1, or PD-1/programmed death ligand 1, or PD-L1 antibodies.

#### ***Chronic Kidney Disease:***

- CCX140 is an inhibitor of the chemokine receptor known as CCR2 (distinct from CCX872 above) and is being developed as an orally administered therapy for the treatment of diabetic nephropathy, or DN,

a form of chronic kidney disease. We have successfully completed and reported positive data from a Phase II clinical trial in patients with DN. The trial met its primary endpoint by demonstrating that treatment with 5mg of CCX140 given orally once daily added to a standard of care angiotensin converting enzyme, or ACE, inhibitor or angiotensin II receptor blocker, or ARB treatment resulted in a statistically significant improvement in urinary albumin to creatinine ratio, or UACR, beyond that achieved with standard of care alone. We are preparing to conduct an end-of-Phase II meeting with the U.S. Food and Drug Administration, or FDA.

***Other Inflammatory and Autoimmune Diseases:***

- Th-17 cell-driven inflammation and CCR6 — Th-17 driven cells have been implicated in a variety of autoimmune and inflammatory diseases such as psoriasis, rheumatoid arthritis, and asthma. Th-17 cells express high levels of the chemokine receptor known as CCR6, which induces their migration to and activation within disease sites. We have a preclinical program in the inhibition of CCR6 which has produced several unique CCR6 inhibitor leads that are now being optimized through medicinal chemistry approaches, which we plan to advance to a clinical candidate.
- Vercirnon (also known as Traficet-EN, or CCX282) is an inhibitor of the chemokine receptor known as CCR9, and being developed as an orally administered therapy for the treatment of patients with moderate-to-severe Crohn's disease. Vercirnon is ready to continue development in Phase III with a partner, should an alliance partner be identified for this program.
- CCX507 is our second generation CCR9 inhibitor for the treatment of inflammatory bowel disease, or IBD. CCX507 has successfully completed Phase I clinical development, which demonstrated that CCX507 was safe and well-tolerated, and blocked CCR9 on circulating leukocytes. We also presented preclinical data with CCX507 in combination with an anti- $\alpha 4\beta 7$  or anti-TNF antibody showing combined treatment reduced the severity of colitis better than monotherapy with either drug alone.

All of our drug candidates are wholly owned and being developed independently by us. Our strategy also includes identification of next generation compounds related to our drug candidates, all of which have been internally discovered.

Since commencing our operations in 1997, our efforts have focused on research, development and the advancement of our drug candidates into and through clinical trials. As a result, we have incurred significant losses. We have funded our operations primarily through the sale of convertible preferred and common stock, contract revenue under our collaborations, government contracts and grants and borrowings under equipment financing arrangements. In February 2012, we completed our initial public offering, or IPO, pursuant to which we received net proceeds of \$45.0 million, after underwriting discounts, commissions and offering expenses. We also received gross proceeds of \$12.0 million from concurrent private placements of common stock at the IPO price of \$10.00 per share. In addition, the outstanding principal amount of \$10.0 million and accrued interest under a convertible note we had issued to Bio-Techne Corporation (formerly Techne Corporation), or Bio-Techne, one of our principal stockholders, automatically converted into shares of our common stock in connection with our IPO at a conversion price equal to the IPO price.

In April 2013, we completed a follow-on public offering of 5,750,000 shares of our common stock at \$12.00 per share. We received net proceeds of \$64.4 million, after deducting underwriting discounts, commissions and offering expenses. As of December 31, 2015, we had an accumulated deficit of \$267.1 million. We expect to continue to incur net losses as we develop our drug candidates, expand clinical trials for our drug candidates currently in clinical development, expand our research and development activities, expand our systems and facilities, seek regulatory approvals and engage in commercialization preparation activities in anticipation of FDA approval of our drug candidates. In addition, if a product is approved for commercialization, we will need to expand our organization. Significant capital is required to launch a product and many expenses are incurred before revenues are received. We are unable to predict the extent of any future losses or when we will become profitable, if at all.



## **JOBS Act**

In April 2012, the JOBS Act was enacted. Section 107 of the JOBS Act provides that an emerging growth company can utilize the extended transition period provided in Section 7(a)(2)(B) of 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 have elected 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 other companies.

Subject to certain conditions set forth in the JOBS Act, as an emerging growth company, we intend to rely on certain of these exemptions, including without limitation, providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404 and implementing any requirement that may be adopted regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements (auditor discussion and analysis). These exemptions will apply for a period of five years following the completion of our IPO 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.

## **Critical Accounting Policies and Significant Judgments and Estimates**

The preparation of our consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of our financial statements as well as the reported revenues and expenses during the reported periods. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in the Notes to our consolidated financial statements appearing at the end of this Annual Report on Form 10-K, we believe that the following critical accounting policies relating to revenue recognition, clinical trial expenses and stock-based compensation are most important to understanding and evaluating our reported financial results.

### ***Revenue Recognition***

We have generated revenue principally from collaborative research and development agreements with pharmaceutical companies. We recognize revenue in accordance with the criteria outlined in the Securities and Exchange Commission's Topic 13 and Accounting Standards Codification, or ASC, 605-25 and by the Financial Accounting Standards Board, or FASB. Following these accounting pronouncements, revenue is recognized when the following criteria have been met:

- persuasive evidence of an arrangement exists;
- delivery has occurred and risk of loss has passed;
- the seller's price to the buyer is fixed or determinable; and
- collectability is reasonably assured.

Any amounts received in advance of performance are recorded as deferred revenue until earned. Under collaboration agreements, we may receive payments for non-refundable up-front fees, reimbursement for research and development services, milestone payments, license fees and royalties. In assessing the appropriate revenue recognition related to a collaboration agreement, we first determine whether an arrangement includes multiple elements, such as the delivery of intellectual property rights and research and development services. For

multiple element arrangements entered into prior to our adoption of Accounting Standards Update, or ASU No.2009-13, Revenue Recognition — Multiple Deliverable Revenue Arrangements, on January 1, 2011, intellectual property rights granted were not considered to be separable from the activity of providing research and development services because the intellectual property right does not have stand-alone value separate from the research and development services provided or evidence of fair value does not exist for the undelivered research and development services. Accordingly, we account for our collaboration agreements as a combined unit of accounting. The revenue from up-front payments is recognized on a straight-line basis over the estimated term of the research and development obligations covered under the research and development collaboration agreement. We periodically review the basis for our estimates, and we may change the estimates if circumstances change. These changes can significantly increase or decrease the amount of revenue recognized. As we applied our policy to our collaboration arrangements, we made judgments which affected the pattern of revenue recognition. For instance, in our former arrangement with Glaxo Group Limited, or GSK, an affiliate of GlaxoSmithKline, we were obligated to provide research and development services. We recognized revenue from up-front payments over the estimated period of our performance of the research and development services, which ended in October 2013, the completion date of the Phase II clinical trial for the last of the drug candidates to be developed under the GSK alliance. In February 2012, we shortened the term of our performance obligation and associated period over which the up-front payments were recognized under our arrangement with GSK following the decision by us and GSK not to advance CCX832 or its two designated back-up compounds. This change in estimate was accounted for prospectively and we revised the estimated period of performance prospectively in 2012 to end by October 2013, which increased the annualized revenue recognition by approximately \$0.9 million per year.

We follow the milestone method of recognizing revenue from milestones and milestone payments are recorded as revenue in full upon achievement of the milestone if there is substantive uncertainty at the date the arrangement is entered into that the event will be achieved and the achievement of the milestone is based on our performance.

#### ***Clinical Trial Accruals and Related Expenses***

We accrue and expense costs for clinical trial activities performed by third parties, including clinical research organizations, or CROs, and clinical investigators, based upon estimates made as of the reporting date of the work completed over the life of the individual study in accordance with agreements established with CROs and clinical trial sites. Some CROs invoice us on a monthly basis, while others invoice upon milestones achieved and the expense is recorded as services are rendered. We determine the estimates of clinical activities incurred at the end of each reporting period through discussion with internal personnel and outside service providers as to the progress or stage of completion of trials or services, as of the end of each reporting period, pursuant to contracts with numerous clinical trial centers and CROs and the agreed upon fee to be paid for such services. The significant factors considered in estimating accruals include the number of patients enrolled and the percentage of work completed to date. Costs of setting up clinical trial sites for participation in the trials that are paid for in advance are expensed over the estimated set-up period. While the set-up periods vary from one arrangement to another, such set-up periods generally take from two to six months. Such set-up activities include clinical site identification, local ethics committee submissions, regulatory submissions, clinical investigator kick-off meetings and pre-study site visits. Clinical trial site costs related to patient enrollments are accrued as patients are entered into the trial.

To date, we have not experienced significant changes in our estimates of clinical trial accruals after a reporting period. However, due to the nature of estimates, we cannot assure you that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical trials.

## ***Stock-Based Compensation***

Stock-based compensation cost is measured at the grant date, based on the fair value of the award, and is recognized as an expense over the employee's requisite service period on a straight line basis. The fair value of the stock options is estimated using the Black-Scholes valuation model. We recorded non-cash stock-based compensation expense of \$9.0 million, \$8.2 million, and \$6.2 million for the years ended December 31, 2015, 2014, and 2013, respectively. At December 31, 2015 and 2014, we had \$12.6 million and \$13.1 million, respectively, of total unrecognized stock-based compensation expense, net of estimated forfeitures, related to employee stock options that will be recognized over a weighted-average period of 2.36 years and 2.56 years, respectively. We expect to continue to grant stock options in the future, and to the extent that we do, our actual stock-based compensation expense recognized in future periods will likely increase.

Prior to our IPO, our board of directors, with the assistance of management and independent consultants, performed fair value analyses for the valuation of our common stock. For grants made on dates for which there was no contemporaneous valuation to utilize in setting the exercise price of our common stock, and given the absence of an active market for our common stock prior to our IPO in February 2012, our board of directors determined the fair value of our common stock on the date of grant based on several factors, including:

- important developments in our operations, most significantly related to the clinical development of our lead drug candidates at that time, vercirnon and CCX140;
- equity market conditions affecting comparable public companies;
- the likelihood of achieving a liquidity event for the shares of common stock, such as an IPO or an acquisition of us, given prevailing market conditions; and
- that the grants involved illiquid securities in a private company.

## **Results of Operations**

### ***Revenues***

We have not generated any revenue from product sales. For the year ended December 31, 2013 our revenues were derived from contract revenue, up-front payments and development milestone payments from our former collaborator partner, GSK. Total revenues, as compared to the prior years, were as follows (in thousands):

	<u>Year Ended December 31,</u>		
	<u>2015</u>	<u>2014</u>	<u>2013</u>
GSK			
Contract revenue	\$—	\$ —	\$2,299
Recognition of up-front payments	—	—	3,761
Total revenues	<u>\$—</u>	<u>\$ —</u>	<u>\$6,060</u>
Dollar decrease	\$—	\$(6,060)	
Percentage decrease	—	(100%)	

Our product development and commercialization agreement with GSK ended in November 2013, and therefore no revenue was recorded in 2014 and 2015. The decrease in total revenues from 2013 to 2014 was due to funding of clinical support in 2013 from our former partner, GSK, for CCX168, our C5aR inhibitor, for the treatment of AAV.

### ***Research and development expenses***

Research and development expenses represent costs incurred to conduct basic research, the discovery and development of novel small molecule therapeutics, development of our suite of proprietary drug discovery

technologies, preclinical studies and clinical trials of our drug candidates. We expense all research and development expenses as they are incurred. These expenses consist primarily of salaries and related benefits, including stock-based compensation, third-party contract costs relating to research, formulation, manufacturing, preclinical study and clinical trial activities, laboratory consumables, and allocated facility costs. Total research and development expenses, as compared to the prior years, were as follows (in thousands):

	<u>Year Ended December 31,</u>		
	<u>2015</u>	<u>2014</u>	<u>2013</u>
Research and development expenses	\$33,183	\$33,815	\$33,541
Dollar (decrease) increase	\$ (632)	\$ 274	
Percentage (decrease) increase	-2%	1%	

The decrease in research and development expense from 2014 to 2015 was primarily attributable to lower expenses associated with CCX507, our second generation CCR9 inhibitor, due to the completion of Phase I clinical development in 2014 and CCX140, our CCR2 inhibitor, due to the completion of our Phase II clinical trial in patients with DN in 2014. These decreases were partially offset by higher expenses associated with CCX168, our C5aR inhibitor, due to the ongoing Phase II CLEAR and CLASSIC trials for the treatment of AAV in 2015, our Phase II pilot clinical trials in patients with aHUS and IgAN, and higher costs associated with CCX872, our second generation CCR2 inhibitor, as our clinical trial in patients with advanced pancreatic cancer continues to enroll and treat patients.

The increase in research and development expenses from 2013 to 2014 was primarily attributable to higher expenses associated with CCX168 due to patient enrollment in the CLEAR trial and initiation of the CLASSIC trial in North America in 2014. This increase was partially offset by lower expenses associated with CCX140 due to the completion of the Phase II clinical trial in patients with DN and CCX872 due to the timing of Phase I related activities.

The following table summarizes our research and development expenses by project (in thousands):

	<u>Year Ended December 31,</u>		
	<u>2015</u>	<u>2014</u>	<u>2013</u>
Development candidate (Target)			
CCX168 (C5aR)	\$14,920	\$13,051	\$ 3,909
CCX872 (CCR2 2G)	2,934	1,619	2,804
CCX140 (CCR2)	1,867	3,512	12,008
CCX507 (CCR9)	117	2,662	2,724
Other (CCR1, C5aR 2G, CCR2 3G, CCR9 3G, CCR4, CCR6, CXCR7, Other)	<u>13,345</u>	<u>12,971</u>	<u>12,096</u>
Total research and development	<u>\$33,183</u>	<u>\$33,815</u>	<u>\$33,541</u>

We track specific project expenses that are directly attributable to our preclinical and clinical development candidates that have been nominated and selected for further development. Such project specific expenses include third-party contract costs relating to formulation, manufacturing, preclinical studies and clinical trial activities. Unlike our early stage research and drug discovery programs, we allocate research and development salaries, benefits or indirect costs to our development candidates and we have included such costs in the project specific expenses. All remaining research and development expenses are reflected in "Other" which represents early stage drug discovery programs. Such expenses include unallocated employee salaries and related benefits, stock-based compensation, consulting and contracted services to supplement our in-house laboratory activities, laboratory consumables and allocated facility costs associated with these earlier stage programs.

At any given time, we typically have several active early stage research and drug discovery projects. Our internal resources, employees and infrastructure are not directly tied to any individual research or drug discovery

project and are typically deployed across multiple projects. As such, we do not maintain information regarding these costs incurred for our early stage research and drug discovery programs on a project specific basis. We expect our research and development expenses to increase as we advance our development programs further and increase the number and size of our clinical trials. The process of conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time consuming. We or our partners may never succeed in achieving marketing approval for any of our drug candidates. The probability of success for each drug candidate may be affected by numerous factors, including preclinical data, clinical data, competition, manufacturing capability and commercial viability. Our strategy includes entering into additional partnerships with third parties for the development and commercialization of some of our independent drug candidates.

Most of our product development programs are at an early-to-mid-stage; therefore the successful development of our drug candidates is highly uncertain and may not result in approved products. Completion dates and completion costs can vary significantly for each drug candidate and are difficult to predict for each product. Given the uncertainty associated with clinical trial enrollments and the risks inherent in the development process, we are unable to determine the duration and completion costs of the current or future clinical trials of our drug candidates or if, or to what extent, we will generate revenues from the commercialization and sale of any of our drug candidates. We anticipate we will make determinations as to which programs to pursue and how much funding to direct to each program on an ongoing basis in response to the scientific and clinical success of each drug candidate, as well as ongoing assessment as to each drug candidate's commercial potential. We will need to raise additional capital or may seek additional strategic alliances in the future in order to complete the development and commercialization of our drug candidates, including CCX168, CCX140, and vercirnon.

#### *General and administrative expenses*

Total general and administrative expenses were as follows (in thousands):

	<u>Year Ended December 31,</u>		
	<u>2015</u>	<u>2014</u>	<u>2013</u>
General and administrative expenses	\$14,506	\$13,584	\$11,634
Dollar increase	\$ 922	\$ 1,950	
Percentage increase	7%	17%	

General and administrative expenses consist primarily of salaries and related benefits, including stock-based compensation and travel expenses, in executive, finance, business and corporate development and other administrative functions. Other general and administrative expenses include allocated facility-related costs not otherwise included in research and development expenses, legal costs of pursuing patent protection of our intellectual property, and professional fees for auditing, tax, and legal services.

The increase from 2014 to 2015 was primarily due to increases in stock based compensation expense for stock option grants and restricted stock unit awards, intellectual property related expenses, and professional fees. Further, travel expenses and professional fees relating to our business development efforts also contributed to the increase.

The increase from 2013 to 2014 was primarily due to an increase in employment-related expenses, including stock-based compensation expense for stock option grants and restricted stock unit awards, intellectual property-related expenses, and professional service expenses relating to corporate governance and our business development efforts.

We expect that general and administrative expenses will increase in the future as we expand our operating activities and incur additional costs associated with being a public company. These public company related increases will likely include, but not be limited to, investor and public relations expenses, legal and accounting related fees, and expenses associated with preparing to meet the requirements pursuant to the Sarbanes-Oxley Act of 2002.



### ***Other income (expense)***

Other income (expense) primarily consists of interest income earned on our marketable securities and interest expense incurred on our equipment financing obligations. Total other income, net, as compared to prior years was as follows (in thousands):

	<u>Year Ended December 31,</u>		
	<u>2015</u>	<u>2014</u>	<u>2013</u>
Interest income	\$384	\$494	\$501
Interest expense	—	(24)	(59)
Total other income (expense), net	<u>\$384</u>	<u>\$470</u>	<u>\$442</u>
Dollar increase (decrease)	(86)	28	
Percentage increase (decrease)	-18%	6%	

The decrease in total other income, net from 2014 to 2015 was primarily due to a decrease in interest income earned on lower cash balances, which was partially offset by a decrease in interest expense as a result of full repayment of our equipment financing debt in the fourth quarter of 2014.

The increase in total other income, net from 2013 to 2014 was primarily due to a decrease in interest expense as a result of repayment of our equipment financing debt in 2014, and a shift in the composition of the portfolio to treasuries and other government sponsored agency securities in 2014.

### **Liquidity and Capital Resources**

As of December 31, 2015, we had approximately \$76.3 million in cash, cash equivalents and investments. The following table shows a summary of our cash flows for each of the three years ended December 31, 2015, 2014, and 2013 (in thousands):

	<u>Year Ended December 31,</u>		
	<u>2015</u>	<u>2014</u>	<u>2013</u>
Cash provided by (used in)			
Operating activities	\$(39,327)	\$(34,315)	\$(33,318)
Investing activities	33,884	38,339	(31,668)
Financing activities	2,191	1,793	66,784

*Operating activities.* Net cash used by operating activities increased to \$39.3 million for the year ended December 31, 2015, from \$34.3 million for the same period in 2014 due primarily to changes in working capital items and a higher net loss. Net cash used by operating activities increased to \$34.3 million for the year ended December 31, 2014, from \$33.3 million for the same period in 2013 due primarily to a higher net loss in 2014.

*Investing activities.* Net cash provided by or used in investing activities for periods presented primarily relate to the purchase, sale and maturity of investments used to fund the day-to-day needs of our business. Following our February 2012 IPO and the follow-on public offering in April 2013, we invested the majority of our net proceeds received in short-term and long-term investments. We financed property and equipment purchases through equipment financing facilities. Proceeds from collaboration agreements and common stock issuances are used for general working capital purposes, such as research and development activities and other general corporate purposes.

*Financing activities.* Net cash provided by financing activities was \$2.2 million for the year ended December 31, 2015 compared to \$1.8 million for the same period in 2014. Net cash provided by financing activities for the years ended December 31, 2015 and 2014 were primarily derived from proceeds from the exercise of stock options and purchases from contributions to our 2012 Employee Stock Purchase Plan.

Net cash provided by financing activities was \$1.8 million for the year ended December 31, 2014 compared to \$66.8 million for the same period in 2013. This decrease was primarily due to the receipt of net proceeds of \$64.4 million from the issuance of common stock in the follow-on public offering completed in April 2013 after underwriting discounts, commissions and offering expenses. We believe that our existing cash, cash equivalents and investments as of December 31, 2015 will be sufficient to meet our anticipated cash requirements for at least the next 12 months. However, our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially.

Our future capital requirements are difficult to forecast and will depend on many factors, including:

- the terms and timing of any other collaborative, licensing and other arrangements that we may establish;
- the initiation, progress, timing and completion of preclinical studies and clinical trials for our drug candidates and potential drug candidates;
- the number and characteristics of drug candidates that we pursue;
- the progress, costs and results of our clinical trials;
- the outcome, timing and cost of regulatory approvals;
- delays that may be caused by changing regulatory approvals;
- the cost and timing of hiring new employees to support continued growth;
- the costs involved in filing and prosecuting patent applications and enforcing and defending patent claims;
- the cost and timing of procuring clinical and commercial supplies of our drug candidates;
- the cost and timing of establishing sales, marketing and distribution capabilities; and
- the extent to which we acquire or invest in businesses, products or technologies.

### Contractual Obligations and Commitments

The following is a summary of our long-term contractual cash obligations as of December 31, 2015 (in thousands).

	Payments Due by Period				
	Total	Less than One Year	1-3 Years	3-5 Years	More than 5 Years
Operating lease <sup>(1)</sup>	\$3,061	\$894	\$1,852	\$315	\$—
Total contractual obligations	\$3,061	\$894	\$1,852	\$315	\$—

(1) We lease our facility in Mountain View, California. The lease expires in 2019.

We enter into contracts in the normal course of business with CROs for clinical trials and clinical supply manufacturing and with vendors for preclinical research studies, research supplies and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

### Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements (as defined by applicable SEC regulations) that are reasonably likely to have a current or future material effect on our financial condition, results of operations, liquidity, capital expenditures or capital resources, except warrants and stock options.

## **Recent Accounting Pronouncements**

In May 2015, the Financial Accounting Standards Boards, or FASB, issued a comprehensive new standard on revenue from contracts with customers. The standard's core principle is that a reporting entity will recognize revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. On July 9, 2015, the FASB voted to delay the effective date of the new standard by one year. The standard would become effective for us beginning in the first quarter of 2018. Early application would be permitted in 2017. Entities would have the option of using either a full retrospective or a modified retrospective approach to adopt this new guidance. We are currently evaluating the impact of our adoption of this standard on our financial statements.

## **Item 7A. Quantitative and Qualitative Disclosures About Market Risk**

The primary objectives of our investment activities are to ensure liquidity and to preserve principal while at the same time maximizing the income we receive from our marketable securities without significantly increasing risk. Some of the securities that we invest in may have market risk. This means that a change in prevailing interest rates may cause the principal amount of the marketable securities to fluctuate. To minimize the risk in the future, we intend to maintain our portfolio of cash equivalents and short-term investments in a variety of securities, including commercial paper, money market funds, government and non-government debt securities and corporate obligations. Because of the short-term maturities of our cash equivalents and marketable securities, we do not believe that an increase in market rates would have any significant impact on the realized value of our marketable securities.

## **Item 8. Financial Statements and Supplementary Data**

Our consolidated financial statements and the reports of our independent registered public accounting firm are included in this Annual Report on Form 10-K on pages F-1 through F-23.

## **Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure**

None.

## **Item 9A. Controls and Procedures**

### **Conclusions Regarding the Effectiveness of Disclosure Controls and Procedures**

As of December 31, 2015, management, with the participation of our Disclosure Committee, performed an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms, and that such information is accumulated and communicated to our management, including the Chief Executive Officer and the Chief Financial Officer, to allow timely decisions regarding required disclosures.

Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that, as of December 31, 2015, the design and operation of our disclosure controls and procedures were effective.

## **Management's Annual Report on Internal Control Over Financial Reporting**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as such term is defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act. Our internal control over

financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with U.S. generally accepted accounting principles, or GAAP. Our internal control over financial reporting includes those policies and procedures that: (i) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets, (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with GAAP, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors, and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2015 based on the criteria established in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO (the 2013 Framework). Based on our evaluation under the criteria set forth in Internal Control — Integrated Framework issued by the COSO, our management concluded our internal control over financial reporting was effective as of December 31, 2015.

#### **Attestation Report of the Registered Public Accounting Firm**

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm due to an exemption established by the JOBS Act for “emerging growth companies”.

#### **Changes in Internal Control Over Financial Reporting**

There has been no change in our internal control over financial reporting during the quarter ended December 31, 2015, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

#### **Item 9B. Other Information**

None.

## PART III

### **Item 10. Directors, Executive Officers and Corporate Governance**

Information required by this item will be contained in our Definitive Proxy Statement, or the Definitive Proxy Statement, to be filed with the Securities and Exchange Commission in connection with our 2016 Annual Meeting of Stockholders, which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2015, under the headings “Election of Directors,” “Corporate Governance,” “Our Executive Officers,” and “Section 16(a) Beneficial Ownership Reporting Compliance,” and is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics that applies to our officers, directors and employees which is available on our website at [www.chemocentryx.com](http://www.chemocentryx.com). The Code of Business Conduct and Ethics contains general guidelines for conducting the business of our company consistent with the highest standards of business ethics, and is intended to qualify as a “code of ethics” within the meaning of Section 406 of the Sarbanes-Oxley Act of 2002 and Item 406 of Regulation S-K. In addition, we intend to promptly disclose (1) the nature of any amendment to our Code of Business Conduct and Ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions and (2) the nature of any waiver, including an implicit waiver, from a provision of our code of ethics that is granted to one of these specified officers, the name of such person who is granted the waiver and the date of the waiver on our website in the future.

### **Item 11. Executive Compensation**

Information required by this item will be contained in our Definitive Proxy Statement under the heading “Executive Compensation and Other Information,” and is incorporated herein by reference.

### **Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters**

Information required by this item will be contained in our Definitive Proxy Statement under the headings “Security Ownership of Certain Beneficial Owners and Management,” and is incorporated herein by reference.

### **Item 13. Certain Relationships, Related Transactions and Director Independence**

Information required by this item will be contained in our Definitive Proxy Statement under the headings “Certain Relationships and Related Party Transactions,” “Board Independence” and “Committees of the Board of Directors” and is incorporated herein by reference.

### **Item 14. Principal Accounting Fees and Services**

Information required by this item will be contained in our Definitive Proxy Statement under the heading “Independent Registered Public Accountants’ Fees,” and is incorporated herein by reference.



## PART IV

### Item 15. Exhibits, Financial Statement Schedules

#### (a) Documents filed as part of this Annual Report on Form 10-K:

##### 1. Financial Statements.

The following consolidated financial statements of ChemoCentryx, Inc., together with the report thereon of Ernst & Young LLP, an independent registered public accounting firm, are included in this Annual Report on Form 10-K:

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##### 2. Financial Statement Schedules.

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

##### 3. Exhibits.

A list of exhibits is set forth on the Exhibit Index immediately following the signature page of this Annual Report on Form 10-K, and is incorporated herein by reference.

**ChemoCentryx, Inc.**

**Consolidated Financial Statements  
As of December 31, 2015 and 2014  
and for each of the three years in the period ended December 31, 2015**

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## **Report of Independent Registered Public Accounting Firm**

The Board of Directors and Stockholders of ChemoCentryx, Inc.

We have audited the accompanying consolidated balance sheets of ChemoCentryx, Inc. as of December 31, 2015 and 2014, and the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2015. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of ChemoCentryx, Inc. at December 31, 2015 and 2014, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2015, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Redwood City, California  
March 14, 2016

**CHEMOCENTRYX, INC.**  
**Consolidated Balance Sheets**  
(In thousands, except share data)

	<u>December 31,</u> <u>2015</u>	<u>December 31,</u> <u>2014</u>
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 12,823	\$ 16,075
Short-term investments	58,455	57,282
Prepaid expenses and other current assets	757	972
Total current assets	<u>72,035</u>	<u>74,329</u>
Property and equipment, net	949	1,208
Long-term investments	5,011	41,263
Other assets	160	181
Total assets	<u>\$ 78,155</u>	<u>\$ 116,981</u>
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 675	\$ 748
Accrued liabilities	4,819	7,442
Total current liabilities	<u>5,494</u>	<u>8,190</u>
Other non-current liabilities	154	185
Total liabilities	<u>5,648</u>	<u>8,375</u>
Stockholders' equity:		
Preferred stock:		
Preferred stock, \$0.001 par value, 10,000,000 shares authorized; no shares issued and outstanding;	—	—
Common stock, \$0.001 par value, 200,000,000 shares authorized at December 31, 2015 and December 31, 2014; 44,185,506 shares and 43,446,096 shares issued and outstanding at December 31, 2015 and December 31, 2014, respectively.	44	43
Additional paid-in capital	339,615	328,440
Note receivable	(16)	(16)
Accumulated other comprehensive income	(40)	(70)
Accumulated deficit	<u>(267,096)</u>	<u>(219,791)</u>
Total stockholders' equity	<u>72,507</u>	<u>108,606</u>
Total liabilities and stockholders' equity	<u>\$ 78,155</u>	<u>\$ 116,981</u>

See accompanying notes.

**CHEMOCENTRYX, INC.**  
**Consolidated Statements of Operations**  
(In thousands, except share data)

	Year Ended December 31,		
	2015	2014	2013
Revenues:			
Collaborative research and development revenue from related party	\$ —	\$ —	\$ 6,060
Operating expenses:			
Research and development	33,183	33,815	33,541
General and administrative	14,506	13,584	11,634
Total operating expenses	47,689	47,399	45,175
Loss from operations	(47,689)	(47,399)	(39,115)
Other income (expense):			
Interest income	384	494	501
Interest expense	—	(24)	(59)
Total other income, net	384	470	442
<b>Net loss</b>	<b>\$(47,305)</b>	<b>\$(46,929)</b>	<b>\$(38,673)</b>
Basic and diluted net loss per common share	\$ (1.08)	\$ (1.08)	\$ (0.95)
Shares used to compute basic and diluted net loss per common share	43,890	43,275	40,916

See accompanying notes.



**CHEMOCENTRYX, INC.**  
**Consolidated Statements of Comprehensive Loss**  
(In thousands)

	Year Ended December 31,		
	2015	2014	2013
Net loss	\$(47,305)	\$(46,929)	\$(38,673)
Unrealized (loss) gain on available-for-sale securities	30	(110)	38
Comprehensive loss	\$(47,275)	\$(47,039)	\$(38,635)

See accompanying notes.

**CHEMOCENTRYX, INC.**

**Consolidated Statements of Stockholders' Equity**  
(in thousands, except share data)

	Common Stock		Additional Paid-In Capital	Note Receivable	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount					
	(In thousands, except share and per share data)						
Balance as of December 31, 2012	36,354,547	\$ 36	\$244,513	\$ (16)	\$ 2	\$(134,189)	\$110,346
Net loss	—	—	—	—	—	(38,673)	(38,673)
Unrealized gain / (loss) on investments	—	—	—	—	38	—	38
Issuance of common stock upon follow-on offering, net of issuance costs	5,750,000	6	64,359	—	—	—	64,365
Issuance of common stock upon exercise of warrant	60,000	—	312	—	—	—	312
Issuance of common stock upon net exercise of warrant	48,611	—	—	—	—	—	—
Issuance of common stock upon exercise of stock options and under employee stock purchase plan	675,010	1	2,677	—	—	—	2,678
Employee stock-based compensation	—	—	6,092	—	—	—	6,092
Compensation expense related to options granted to consultants	—	—	150	—	—	—	150
Balance as of December 31, 2013	42,888,168	43	318,103	(16)	40	(172,862)	145,308
Net loss	—	—	—	—	—	(46,929)	(46,929)
Unrealized gain / (loss) on investments	—	—	—	—	(110)	—	(110)
Issuance of common stock upon exercise of stock options and under employee stock purchase plan	557,928	—	2,123	—	—	—	2,123
Employee stock-based compensation	—	—	7,960	—	—	—	7,960
Compensation expense related to options granted to consultants	—	—	254	—	—	—	254
Balance as of December 31, 2014	43,446,096	\$ 43	\$328,440	\$ (16)	\$ (70)	\$(219,791)	\$108,606
Net loss	—	—	—	—	—	(47,305)	(47,305)
Unrealized gain / (loss) on investments	—	—	—	—	30	—	30
Issuance of common stock upon exercise of stock options and under employee stock purchase plan	739,410	1	2,190	—	—	—	2,191
Employee stock-based compensation	—	—	8,860	—	—	—	8,860
Compensation expense related to options granted to consultants	—	—	125	—	—	—	125
Balance as of December 31, 2015	<u>44,185,506</u>	<u>\$ 44</u>	<u>\$339,615</u>	<u>\$ (16)</u>	<u>\$ (40)</u>	<u>\$(267,096)</u>	<u>\$ 72,507</u>

See accompanying notes.

**CHEMOCENTRYX, INC.**  
**Consolidated Statements of Cash Flows**  
(In thousands)

	Year Ended December 31,		
	2015	2014	2013
<b>Operating activities</b>			
Net loss	\$(47,305)	\$ (46,929)	\$ (38,673)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:			
Depreciation of property and equipment	477	543	576
Stock-based compensation	8,985	8,214	6,242
Noncash interest expense, net	1,007	2,157	2,065
Changes in assets and liabilities:			
Accounts receivable due from related party	—	393	763
Prepays and other current assets	236	(376)	34
Other assets	—	(21)	—
Accounts payable	(73)	(161)	159
Other liabilities	(2,654)	1,865	(723)
Deferred revenue from related party	—	—	(3,761)
Net cash used in operating activities	(39,327)	(34,315)	(33,318)
<b>Investing activities</b>			
Purchases of property and equipment, net	(218)	(352)	(554)
Purchases of investments	(24,372)	(100,837)	(136,600)
Sales of investments	4,051	—	5,142
Maturities of investments	54,423	139,528	100,344
Net cash provided by (used in) investing activities	33,884	38,339	(31,668)
<b>Financing activities</b>			
Proceeds from issuance of common stock	—	—	64,365
Proceeds from exercise of stock options and employee stock purchase plan	2,191	2,123	2,678
Proceeds from exercise of warrants	—	—	312
Payments on equipment financing obligations	—	(330)	(571)
Net cash provided by financing activities	2,191	1,793	66,784
Net increase (decrease) in cash and cash equivalents	(3,252)	5,817	1,798
Cash and cash equivalents at beginning of period	16,075	10,258	8,460
Cash and cash equivalents at end of period	\$ 12,823	\$ 16,075	\$ 10,258
<b>Supplemental disclosures of cash flow information</b>			
Cash paid for interest	\$ —	\$ 137	\$ 26

See accompanying notes.

**CHEMOCENTRYX, INC.**  
**Notes to Consolidated Financial Statements**  
**December 31, 2015**

**1. Description of Business**

ChemoCentryx, Inc. (the Company) commenced operations in 1997. The Company is a clinical-stage biopharmaceutical company focused on discovering, developing and commercializing orally-administered therapeutics to treat orphan and rare diseases, autoimmune diseases, inflammatory disorders and cancer. The Company's principal operations are in the United States and it operates in one segment.

**2. Summary of Significant Accounting Policies**

**Consolidation**

The consolidated financial statements include the Company's accounts and those of its wholly owned subsidiary, ChemoCentryx Limited. The operations of ChemoCentryx Limited have been immaterial to date. All intercompany amounts have been eliminated in consolidation.

**Use of Estimates**

The preparation of financial statements in conformity with accounting principles generally accepted in the United States (GAAP) requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Actual results could differ from these estimates.

**Basis of Presentation**

The financial statements are prepared in conformity with GAAP. The Company has made estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

**Cash Equivalents and Investments**

The Company considers all highly liquid investments with an original maturity at the date of purchase of three months or less to be cash equivalents. The Company limits its concentration of risk by diversifying its investments among a variety of issuers. All investments are classified as available for sale and are recorded at fair value based on quoted prices in active markets or based upon other observable inputs, with unrealized gains and losses excluded from earnings and reported in other comprehensive income (loss). Purchase premiums and discounts are recognized in interest income using the interest method over the terms of the securities. Realized gains and losses and declines in fair value that are deemed to be other than temporary are reflected in the statement of operations. The cost of securities sold is based on the specific-identification method.

**Fair Value of Financial Instruments**

The carrying amounts of certain of the Company's financial instruments, including cash and cash equivalents, short-term investments, accounts receivable from related party and accounts payable, approximate their fair value due to their short maturities.

Fair value is considered to be the price at which an asset could be exchanged or a liability transferred (an exit price) in an orderly transaction between knowledgeable, willing parties in the principal or most advantageous market for the asset or liability. Where available, fair value is based on or derived from observable market prices or other observable inputs. Where observable prices or inputs are not available, valuation models are applied. The valuation techniques involve management estimation and judgment, the degree of which is dependent on the price transparency for the instruments or market and the instruments' complexity.

## CHEMOCENTRYX, INC.

### Notes to Consolidated Financial Statements (continued)

#### 2. Summary of Significant Accounting Policies (continued)

##### Concentration of Credit Risk

The Company invests in a variety of financial instruments and, by its policy, limits the amount of credit exposure with any one issuer, industry or geographic area.

During the year ended December 31, 2013, 100% of the Company's total revenues were derived from contract revenue, up-front payments and development milestone payments earned under the Company's former collaboration with Glaxo Group Limited (GSK). The Company did not generate any revenue in 2014 and 2015.

##### Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets, which range from five to seven years. Tenant improvements are depreciated over the lesser of the estimated useful life or the remaining life of the lease at the time the asset is placed into service.

##### Impairment of Long-Lived Assets

The Company reviews long-lived assets, including property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset over its respective fair value. To date, the Company has not recorded any impairment losses.

##### Revenue Recognition

The Company recognizes revenue in accordance with the criteria outlined in the Securities and Exchange Commission's (the SEC) Topic 13 and Accounting Standards Codification (ASC) 605-25. The Company generates revenue from collaborative research and development agreements with pharmaceutical companies. Collaboration agreements may include nonrefundable up-front fees, research and development funding, milestone payments for the achievement of defined collaboration objectives, license fees and royalties on potential sales of commercialized products. In multiple arrangements, the Company evaluates the selling price used for each deliverable based on vendor-specific objective evidence, if available, third-party evidence if vendor-specific objective evidence is not available, or estimated selling price if neither vendor-specific nor third-party evidence is available. For multiple element arrangements entered into prior to January 1, 2011, the Company determined whether the elements had value on a stand-alone basis and whether there was objective and reliable evidence of fair value. When the delivered element did not have stand-alone value or there was insufficient evidence of fair value for the undelivered element(s), the Company recognized the consideration for the combined unit of accounting in the same manner as the revenue was recognized for the final deliverable, which was generally ratably over the longest period of involvement. For example, up-front payments received upon execution of collaborative agreements are recorded as deferred revenue and recognized as collaborative research and development revenue based on a straight-line basis over the period of the Company's continuing involvement with the third-party collaborator pursuant to the applicable agreement. Such period generally represents the longer of the estimated research and development period or other continuing obligation period defined in the respective agreements between the Company and its third-party collaborators. The Company periodically reviews the estimated performance periods of its contracts based on the progress of the related programs.

## CHEMOCENTRYX, INC.

### Notes to Consolidated Financial Statements (continued)

#### 2. Summary of Significant Accounting Policies (continued)

Research and development funding related to collaborative research and development efforts is recognized as revenue as the related services are performed or delivered, in accordance with contract terms. Such payments generally are made based on the number of full-time equivalent researchers assigned to the collaboration project and the related research and development expenses incurred, or as other deliverables under the contracts are fulfilled.

In addition to up-front payments and research and development funding, the Company may also be entitled to milestone or option payments that are contingent upon achieving a predefined objective. The Company follows the milestone method of recognizing revenue from milestones and milestone payments are recorded as revenue in full upon achievement of the milestone if there is substantive uncertainty at the date the arrangement is entered into that the event will be achieved, the event is based on the vendor's performance, and the amount of the payment was negotiated as part of the collaboration agreement.

#### Research and Development Expenses

All research and development expenses, including those funded by third parties, are expensed as incurred. Research and development expenses include, but not limited to, salaries and related benefits, including stock-based compensation, third-party contract costs relating to research, formulation, manufacturing, preclinical study and clinical trial activities, laboratory consumables, allocated facility costs.

Research and development expenses under collaborative agreements approximated the revenue recognized, excluding milestone, up-front and option fees.

#### Clinical Trial Accruals

Clinical trial costs are a component of research and development expenses. The Company accrues and expenses clinical trial activities performed by third parties based upon estimates of the percentage of work completed over the life of the individual study in accordance with agreements established with clinical research organizations and clinical trial sites. The Company determines the estimates through discussions with internal clinical personnel and external service providers as to the progress or stage of completion of trials or services and the agreed-upon fee to be paid for such services.

Nonrefundable advance payments for goods and services that will be used or rendered in future research and development activities, are deferred and recognized as expense in the period that the related goods are delivered or services are performed.

#### Income Taxes

The Company uses the liability method for income taxes, whereby deferred tax assets and liabilities are determined based on the differences between the financial reporting and tax reporting bases of assets and liabilities and are measured using enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. Valuation allowances are provided when the expected realization for the deferred tax assets does not meet the more-likely-than-not criteria.

The Company accounts for uncertain tax positions in the financial statements when it is more likely than not that the position will be sustained upon examination by the tax authorities. Such tax positions must initially and



## CHEMOCENTRYX, INC.

### Notes to Consolidated Financial Statements (continued)

#### 2. Summary of Significant Accounting Policies (continued)

subsequently be measured as the largest amount of tax benefit that has a greater than 50% likelihood of being realized upon ultimate settlement with the tax authority assuming full knowledge of the position and relevant facts. The Company's policy is to recognize any interest and penalties related to unrecognized tax benefits in income tax expense.

#### Comprehensive Loss

Comprehensive loss comprises net loss and other comprehensive income (loss). For the periods presented, other comprehensive income (loss) consists of unrealized gains and losses on the Company's available-for-sale securities. For the years ended December 31, 2015 and 2013, amounts reclassified from accumulated other income to net loss for unrealized gains (losses) on available-for-sale securities were not significant, and were recorded as part of other income (expense), net in the Consolidated Statements of Operations. For the year ended December 31, 2014, there were no sales of investments, and therefore there were no reclassifications.

#### Stock-Based Compensation

The Company accounts for employee stock-based compensation using a fair-value-based method, which measures stock-based compensation cost at the grant date based on the fair value of the award, and recognizes as an expense over the award's vesting periods on a straight-line basis. Because stock compensation expense is based on awards ultimately expected to vest, it has been reduced by an estimate for future forfeitures. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

The Company accounts for stock-based compensation arrangements with nonemployees using a fair-value approach. For stock options granted to nonemployees, the fair value of the stock options is estimated using the Black-Scholes valuation model. This model utilizes the estimated fair value of common stock and requires that, at the date of grant, assumptions are made with respect to the remaining contractual term of the option, the volatility of the fair value of its common stock, the risk-free interest rates and the expected dividend yields of its common stock. The measurement of nonemployee stock-based compensation is subject to periodic adjustment as the underlying equity instruments vest.

The Company accounts for restricted stock compensation arrangements with nonemployee directors using a fair-value approach. For restricted stock units (RSUs) granted to nonemployee directors, the fair value of a RSU is valued at the closing price of the Company's common stock on the date of the grant. The Company recognizes stock-based compensation expense associated with these RSUs over the requisite service period, with no adjustment in future periods based on the Company's actual stock price over the vesting period.

#### Net Loss Per Share

Basic net loss per common share is computed by dividing net loss attributable to common stockholders by the weighted-average number of common shares outstanding during the period, without consideration for common stock equivalents.

Diluted net loss per share is computed by dividing net loss attributable to common stockholders by the sum of the weighted-average number of common shares outstanding and dilutive common stock equivalent shares outstanding for the period. The Company's potentially dilutive common stock equivalent shares, which include incremental common shares issuable upon (i) the exercise of outstanding stock options and warrants, (ii) vesting

**CHEMOCENTRYX, INC.**

**Notes to Consolidated Financial Statements (continued)**

**2. Summary of Significant Accounting Policies (continued)**

of RSUs, and (iii) the purchase from contributions to the 2012 Employee Stock Purchase Plan (the ESPP) (calculated based on the treasury stock method), are only included in the calculation of diluted net loss per share when their effect is dilutive.

The following potentially dilutive securities were excluded from the calculation of diluted net loss per share due to their anti-dilutive effect:

	Year Ended December 31,		
	2015	2014	2013
Options to purchase common stock, including purchases from contributions to ESPP	7,861,953	6,849,607	5,324,876
Restricted stock units	67,481	135,135	—
Warrants to purchase common stock	150,000	150,000	150,000
	8,079,434	7,134,742	5,474,876

**Recent Accounting Pronouncements**

In May 2015, the Financial Accounting Standards Boards (FASB) issued a comprehensive new standard on revenue from contracts with customers. The standard's core principle is that a reporting entity will recognize revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. On July 9, 2015, the FASB voted to delay the effective date of the new standard by one year. The standard would become effective for the Company beginning in the first quarter of 2018. Early application would be permitted in 2017. Entities would have the option of using either a full retrospective or a modified retrospective approach to adopt this new guidance. The Company is currently evaluating the impact of its adoption of this standard on its financial statements.

**3. Cash Equivalents and Investments**

The amortized cost and fair value of cash equivalents and investments at December 31, 2015 were as follows (in thousands):

	December 31, 2015			Fair Value
	Amortized Cost	Gross Unrealized		
		Gains	Losses	
Money market fund	\$11,340	—	—	\$11,340
U.S. treasury securities	14,027	1	(2)	14,026
Government-sponsored agencies	30,959	—	(25)	30,934
Commercial paper	3,992	—	—	3,992
Corporate debt securities	14,528	—	(14)	14,514
Total available-for-sale securities	\$74,846	\$ 1	\$(41)	\$74,806
Classified as:				
Cash equivalents				\$11,340
Short-term investments				58,455
Long-term investments				5,011
Total available-for-sale securities				\$74,806

**CHEMOCENTRYX, INC.**

**Notes to Consolidated Financial Statements (continued)**

**3. Cash Equivalents and Investments (continued)**

The amortized cost and fair value of cash equivalents and investments, with gross unrealized gains and losses, at December 31, 2014 were as follows (in thousands):

	December 31, 2014			Fair Value
	Amortized Cost	Gross Unrealized		
		Gains	Losses	
Money market fund	\$ 15,922	\$—	\$—	\$ 15,922
U.S. treasury securities	19,117	5	(2)	19,120
Government-sponsored agencies	29,772	4	(13)	29,763
Commercial paper	1,500	—	—	1,500
Corporate debt securities	48,226	4	(68)	48,162
Total available-for-sale securities	<u>\$114,537</u>	<u>\$ 13</u>	<u>\$(83)</u>	<u>\$114,467</u>
Classified as:				
Cash equivalents				\$ 15,922
Short-term investments				57,282
Long-term investments				<u>41,263</u>
Total available-for-sale securities				<u>\$114,467</u>

Cash equivalents in the tables above exclude cash of \$1.5 million and \$0.2 million as of December 31, 2015 and 2014, respectively. All available-for-sale securities held as of December 31, 2015, had contractual maturities of less than two years. There have been no significant realized gains or losses on available-for-sale securities for the periods presented. No available-for-sale securities held as of December 31, 2015, have been in a continuous unrealized loss position for more than 12 months. As of December 31, 2015, unrealized losses on available-for-sale investments are not attributed to credit risk and are considered to be temporary. The Company believes that it is more-likely-than-not that investments in an unrealized loss position will be held until maturity or the recovery of the cost basis of the investment. The Company believes it has no other-than-temporary impairments on its securities because it does not intend to sell these securities and it believes it is not more likely than not that it will be required to sell these securities before the recovery of their amortized cost basis. To date, the Company has not recorded any impairment charges on marketable securities related to other-than-temporary declines in market value.

**4. Fair Value Measurements**

The Company determines the fair value of financial assets and liabilities using three levels of inputs as follows:

Level 1—Inputs which include quoted prices in active markets for identical assets and liabilities.

Level 2—Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

**CHEMOCENTRYX, INC.**

**Notes to Consolidated Financial Statements (continued)**

**4. Fair Value Measurements (continued)**

The Company's financial assets and liabilities subject to fair value measurements on a recurring basis and the level of inputs used in such measurements are as follows as of December 31, 2015 and 2014 (in thousands):

	<b>December 31, 2015</b>			
	<u>Level 1</u>	<u>Level 2</u>	<u>Level 3</u>	<u>Total</u>
<b>Description</b>				
Money market fund	\$11,340	\$ —	\$—	\$11,340
U.S. treasury securities	—	14,026	—	14,026
Government-sponsored agencies	—	30,934	—	30,934
Commercial paper	—	3,992	—	3,992
Corporate debt securities	—	14,514	—	14,514
Total assets	<u>\$11,340</u>	<u>\$63,466</u>	<u>\$—</u>	<u>\$74,806</u>
	<b>December 31, 2014</b>			
	<u>Level 1</u>	<u>Level 2</u>	<u>Level 3</u>	<u>Total</u>
<b>Description</b>				
Money market fund	\$15,922	\$ —	\$—	\$ 15,922
U.S. treasury securities	—	19,120	—	19,120
Government-sponsored agencies	—	29,763	—	29,763
Commercial paper	—	1,500	—	1,500
Corporate debt securities	—	48,162	—	48,162
Total assets	<u>\$15,922</u>	<u>\$98,545</u>	<u>\$—</u>	<u>\$114,467</u>

During the year ended December 31, 2015, there were no transfers between Level 1 and Level 2 financial assets. When the Company uses observable market prices for identical securities that are traded in less active markets, the Company classifies its marketable debt instruments as Level 2. When observable market prices for identical securities are not available, the Company prices its marketable debt instruments using non-binding market consensus prices that are corroborated with observable market data; quoted market prices for similar instruments; or pricing models, such as a discounted cash flow model, with all significant inputs derived from or corroborated with observable market data. Non-binding market consensus prices are based on the proprietary valuation models of pricing providers or brokers. These valuation models incorporate a number of inputs, including non-binding and binding broker quotes; observable market prices for identical or similar securities; and the internal assumptions of pricing providers or brokers that use observable market inputs and, to a lesser degree, unobservable market inputs. The Company corroborates non-binding market consensus prices with observable market data using statistical models when observable market data exists. The discounted cash flow model uses observable market inputs, such as LIBOR-based yield curves, currency spot and forward rates, and credit ratings.

**CHEMOCENTRYX, INC.**

**Notes to Consolidated Financial Statements (continued)**

**5. Property and Equipment**

Property and equipment consist of the following (in thousands):

	December 31,	
	2015	2014
Lab equipment	\$ 5,740	\$ 5,744
Computer equipment and software	1,458	1,481
Furniture and fixtures	530	524
Tenant improvements	832	783
	8,560	8,532
Less: accumulated depreciation	(7,611)	(7,324)
	\$ 949	\$ 1,208

**6. Accrued Liabilities**

Accrued liabilities consist of the following (in thousands):

	December 31,	
	2015	2014
Research and development related	\$2,223	\$4,982
Compensation related	1,908	1,956
Consulting and professional services	454	254
Other	234	250
	\$4,819	\$7,442

**7. Commitments**

**Operating Leases**

In May 2004, the Company entered into a noncancelable operating lease for its current office and primary research facility located in Mountain View, California. The Company received a discounted lease rate during the first year of the agreement. In August 2012, the Company entered into an amendment to the lease agreement for the same facility to extend the term through April 2019. The total rent obligation is being expensed ratably over the term of the agreement, as amended. Rental expenses for the years ended December 31, 2015, 2014, and 2013 were \$1,120,800, \$993,700, and \$942,000, respectively.

Future minimum lease payments under all noncancelable operating leases as of December 31, 2015, are as follows (in thousands):

Year ending December 31:	
2016	\$ 894
2017	915
2018	937
2019	315
2020	—
Total minimum lease payments	\$3,061

## CHEMOCENTRYX, INC.

### Notes to Consolidated Financial Statements (continued)

#### 8. Common Stock and Warrants

##### Follow On Public Offering

In April 2013, the Company completed an underwritten public offering of 5,750,000 shares of its common stock at \$12.00 per share. The Company received net proceeds of \$64.4 million, after deducting underwriting discounts, commissions and offering expenses.

##### Warrants

In February 2012, in connection with the Company's initial public offering (IPO), the outstanding warrants to purchase the Company's Series B convertible preferred stock converted into warrants to purchase 159,500 shares of common stock at \$5.20 per share, with expiration dates from 2012 through 2014. In addition, Bio-Techne received a warrant with a ten-year term to purchase 150,000 shares of the Company's common stock at an exercise price per share equal to \$20.00. During the year ended December 31, 2013, warrants to purchase 150,000 shares of common stock were exercised, and 1,672 warrants expired. During the years ended December 31, 2014 and 2015, no warrants were exercised. As of December 31, 2015 and December 31, 2014, warrants to purchase 150,000 shares of common stock were outstanding with a weighted-average exercise price of \$20.00. All other warrants were either expired or exercised.

#### 9. Related-Party Transactions

##### Glaxo Group Limited

In August 2006, the Company entered into a product development and commercialization agreement with GSK (the GSK Agreement), which ended in November 2013. Concurrent with entering into the GSK Agreement, the Company issued 6,493,506 shares of Series D convertible preferred stock at \$3.85 per share, for gross proceeds of \$25.0 million, which was converted into common stock upon the completion of the Company's IPO in February 2012. No revenue associated with GSK was recognized for years ending December 31, 2015 and 2014. During the year ended December 31, 2013, the Company recognized total revenues of \$6.1 million, of which \$3.8 million was related to recognition of up-front payments and \$2.3 million was related to contract revenue under the GSK Agreement. Research and development costs for the year ended December 31, 2013 under the GSK Agreement were partially offset by contract revenue.

In the event the Company elects to continue to develop and commercialize drug candidates covered under the GSK Agreement, including vercirnon, CCX168, and CCX832, the Company would be subject to the following future royalties to GSK: (i) with respect to vercirnon, the Company would be subject to a reverse royalty to GSK of 3% on annual worldwide net sales only if a regulatory agency were to deem one of GSK's SHIELD trials to be a pivotal Phase III clinical trial and (ii) with respect to CCX168 and CCX832, the Company would be subject to reverse royalties to GSK of 3% on annual worldwide net sales not to exceed \$50.0 million in royalties for each.

##### Bio-Techne

As of December 31, 2015, Bio-Techne held 6,385,056 shares of the Company's common stock. For the years ended December 31, 2015, 2014, and 2013, the Company paid Bio-Techne \$62,000, \$93,000, and \$95,000, respectively, for research materials. As of December 31, 2015 and 2014, the Company had an accounts payable balance due to Bio-Techne for the purchase of research materials of zero and \$1,150, respectively. In September 2011, the Company entered into a convertible note loan agreement with Bio-Techne, pursuant to which the Company issued a convertible note to Bio-Techne with a principal amount of \$10.0 million. Following the



## CHEMOCENTRYX, INC.

### Notes to Consolidated Financial Statements (continued)

#### 9. Related-Party Transactions (continued)

completion of the Company's IPO, all outstanding principal and accrued interest automatically converted into 1,021,490 shares of common stock. In addition, pursuant to the terms of the convertible note loan agreement, Bio-Techne purchased \$5.0 million of the Company's common stock in a private placement concurrent with the offering at \$10.00 per share.

#### 10. Equity Incentive Plans

In May 2002, the stockholders approved the Amended and Restated 1997 Stock Option/Stock Issuance Plan (the 1997 Plan) and in September 2002, the stockholders approved the 2002 Equity Incentive Plan (the 2002 Plan). In February 2012, the stockholders approved the 2012 Equity Incentive Award Plan (the 2012 Plan). As of December 31, 2015, a total of 7,850,000 shares of the Company's common stock were reserved for issuance under the 2012 Plan. In addition, the number of shares available for issuance under the 2012 Plan will be annually increased by an amount equal to the lesser of: 2,000,000 shares; 4% of the outstanding shares of the Company's common stock as of the last day of the Company's immediately preceding fiscal year; or an amount determined by the Company's Board of Directors. In October 2015, the Board of Directors approved an increase to the number of shares reserved for issuance under the 2012 Plan by 1,750,000 shares effective January 1, 2016. Collectively, the 1997 Plan, the 2002 Plan and the 2012 Plan are known as the Stock Plans.

#### Restricted Stock Units

The Company began issuing RSUs in 2014 to its nonemployee directors pursuant to the Company's Non-Employee Director Compensation Policy (Directors Plan) under its 2012 Plan. RSUs are independent of stock option grants and are not transferrable, and are subject to forfeiture if recipients terminate their service to the Company prior to the release of the vesting restrictions. The RSUs awarded under the Directors Plan vest on the earlier of the first anniversary of the grant date or upon a change in control. The RSUs are valued at the closing price of the Company's common stock on the date of grant.

The activity for RSUs is summarized as follows:

	<u>Shares</u>	<u>Weighted Average Grant-Date Fair Value</u>
Balance at December 31, 2014	135,135	\$4.81
Granted	79,276	7.88
Vested	(135,135)	4.81
Canceled	(11,795)	7.63
Outstanding at December 31, 2015	<u>67,481</u>	\$7.93

As of December 31, 2015, there was \$0.3 million of unrecognized compensation expense associated with unvested RSUs, which is expected to be recognized over a weighted-average period of 1.05 years.

#### Stock Options

Under the Stock Plans, incentive stock options may be granted by the Board of Directors to employees at exercise prices of not less than 100% of the fair value at the date of grant. Nonstatutory options may be granted by the Board of Directors to employees, officers, and directors of the Company or consultants at exercise prices of not less than 85% of the fair value of the common stock on the date of grant. The fair value at the date of grant

**CHEMOCENTRYX, INC.**

**Notes to Consolidated Financial Statements (continued)**

**10. Equity Incentive Plans (continued)**

is determined by the Board of Directors. Under the Stock Plans, options may be granted with different vesting terms from time to time, but not to exceed 10 years from the date of grant. Outstanding options generally vest over four years, with 25% of the total grant vesting on the first anniversary of the option grant date and 1/36th of the remaining grant vesting each month thereafter.

The following table summarizes stock option activity and related information under the Company's Stock Plans:

	<u>Available for Grant</u>	<u>Shares</u>	<u>Weighted Average Exercise Price</u>	<u>Weighted Average Remaining Contractual Term</u>	<u>Aggregate Intrinsic Value</u>
Balance at December 31, 2014	2,010,735	6,831,532	\$8.29		\$4,765,642
Shares authorized	1,700,000				
Granted <sup>(1)</sup>	(1,890,076)	1,810,800	8.15		
Exercised		(469,696)	3.32		
Forfeited and expired <sup>(1)</sup>	336,982	(325,187)	9.07		
Outstanding at December 31, 2015	<u>2,157,641</u>	<u>7,847,449</u>	8.52	6.74	8,103,675
Vested at December 31, 2015		<u>4,766,766</u>	8.61	5.55	6,374,684
Exercisable at December 31, 2015		<u>4,768,069</u>	8.61	5.55	6,379,260
Vested and expected to vest, net of estimated forfeiture at December 31, 2015		<u>7,669,903</u>	\$8.53	6.69	\$8,001,079

(1) The difference between the number of shares available for grant and shares outstanding represents the RSUs granted and forfeited for the period.

The aggregate intrinsic value represents the value of the Company's closing stock price on the last trading day of the period in excess of the weighted-average exercise price multiplied by the number of options outstanding or exercisable. Total intrinsic value of options exercised was \$2.1 million, \$1.1 million, and \$5.6 million during 2015, 2014, and 2013, respectively. As of December 31, 2015, there was \$12.6 million of unrecognized compensation expense, net of estimated forfeitures, associated with outstanding stock options, which is expected to be recognized over an estimated weighted-average period of 2.36 years.

**Early Exercise of Stock Options**

Certain equity incentive plans allow for the granting of options that may be exercised before the options have vested. The difference between the number of shares vested and exercisable as of December 31, 2015 in the table above represents such shares that are exercisable before they are vested. Shares issued as a result of early exercise that have not vested are subject to repurchase by the Company upon termination of the purchaser's employment or services, at the price paid by the purchaser.

For the years ended December 31, 2015 and 2014, there were no shares of common stock issued related to the early exercise of stock options subject to repurchase by the Company.

**CHEMOCENTRYX, INC.**

**Notes to Consolidated Financial Statements (continued)**

**10. Equity Incentive Plans (continued)**

As of December 31, 2015, stock options outstanding were as follows:

<u>Exercise Price Range</u>	<u>Options Outstanding</u>	
	<u>Shares</u>	<u>Weighted-Average Contractual Life</u>
\$0.88-\$5.94	424,491	4.57
\$6.00	1,198,975	3.14
\$6.05-\$6.30	1,327,260	6.60
\$6.60-\$6.90	234,183	5.56
\$7.10	988,500	8.13
\$7.12-\$8.14	84,100	9.64
\$8.19	1,431,700	9.15
\$8.22-\$14.28	1,174,841	7.43
\$14.31	908,399	6.56
\$14.42-\$15.90	75,000	6.42
	<u>7,847,449</u>	<u>6.74</u>

**Employee Stock Purchase Plan**

In February 2012, the stockholders approved the ESPP. As of December 31, 2015, a total of 500,000 shares of the Company's common stock were reserved for issuance under the ESPP. In addition, the number of shares available for issuance under the ESPP may be annually increased on the first day of each fiscal year during the term of the ESPP, beginning with the 2012 fiscal year, by an amount equal to the lesser of: 300,000 shares; 1% of outstanding shares of the Company's common stock; or an amount determined by the Company's Board of Directors. The ESPP provides for an aggregate limit of 3,000,000 shares of common stock that may be issued under the ESPP during the term of the ESPP. In October 2015, the Board of Directors approved an increase to the number of shares reserved for issuance under the ESPP by 250,000 shares effective January 1, 2016.

The Company issued 134,579 shares, 149,788 shares and 49,912 shares under the ESPP in 2015, 2014 and 2013, respectively. As of December 31, 2015, 134,449 shares were available for issuance under the ESPP. As of December 31, 2015, there was \$0.1 million of unrecognized compensation expense, net of estimated forfeitures, associated with the ESPP, which is expected to be recognized over an estimated weighted-average period of 0.4 years.

**Stock Awards Granted to Employees**

Employee stock-based compensation expense recognized is calculated based on awards ultimately expected to vest and reduced for estimated forfeitures. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

Total employee stock-based compensation expense recognized associated with RSUs, stock options, and the ESPP, was as follows (in thousands):

	<u>Year Ended December 31,</u>		
	<u>2015</u>	<u>2014</u>	<u>2013</u>
Research and development	\$3,240	\$2,756	\$1,832
General and administrative	5,620	5,204	4,260
Total	<u>\$8,860</u>	<u>\$7,960</u>	<u>\$6,092</u>

**CHEMOCENTRYX, INC.**

**Notes to Consolidated Financial Statements (continued)**

**10. Equity Incentive Plans (continued)**

***Valuation Assumptions***

Fair value of options granted under the Stock Plans and purchases under the Company's ESPP were estimated at grant or purchase dates using a Black-Scholes option valuation model. The Black-Scholes valuation model requires that assumptions are made with respect to various factors, including the expected volatility of the fair value of the Company's common stock. The Company has based its expected volatility on the average historical volatilities of public entities having similar characteristics including: industry, stage of life cycle, size, and financial leverage. The fair values of the employee stock options granted under the Company's Stock Plans and the option component of the shares purchased under the ESPP during 2015, 2014, and 2013 were estimated at the date of grant using the Black-Scholes option-pricing model with the following assumptions:

	<u>Employee Stock Options</u>			<u>Employee Stock Purchase Plan</u>		
	<u>2015</u>	<u>2014</u>	<u>2013</u>	<u>2015</u>	<u>2014</u>	<u>2013</u>
Dividend yield	0%	0%	0%	0%	0%	0%
Volatility	67.6%	74.1%	77.8%	60.1%	55.5%	67.3%
Weighted-average expected life (in years)	6.0	6.0	5.9	0.5	0.5	0.5
Risk-free interest rate	1.70%	1.96%	1.54%	0.21%	0.06%	0.11%
Weighted average grant date fair value	\$5.00	\$4.29	\$9.41	\$2.22	\$1.49	\$1.71

**Stock Options Granted to Nonemployees**

During 2015, 2014 and 2013, the Company granted to consultants options to purchase 90,300, 150,000 and 85,000 shares of common stock, respectively. The stock-based compensation expense related to nonemployees will fluctuate as the fair value of the Company's common stock fluctuates. In connection with grants of stock options to nonemployees, the Company recorded stock-based compensation expense as follows (in thousands):

	<u>Year Ended December 31,</u>		
	<u>2015</u>	<u>2014</u>	<u>2013</u>
Research and development	\$105	\$254	\$150
General and administrative	20	—	—
Total	<u>\$125</u>	<u>\$254</u>	<u>\$150</u>

***Valuation Assumptions***

Stock-based compensation expense associated with stock options granted to nonemployees is recognized as the stock options vest. The estimated fair values of the stock options granted are calculated at each reporting date using the Black-Scholes option-pricing model, with the following assumptions:

	<u>Year Ended December 31,</u>		
	<u>2015</u>	<u>2014</u>	<u>2013</u>
Dividend yield	0%	0%	0%
Volatility	65-66%	68-76%	77-79%
Weighted-average expected life (in years)	5.6-9.9	6.6-9.8	7.6-9.9
Risk-free interest rate	1.7-2.4%	2.0-2.7%	1.5-2.9%

**CHEMOCENTRYX, INC.**

**Notes to Consolidated Financial Statements (continued)**

**11. 401(k) Plan**

In October 1997, the Company established the ChemoCentryx 401(k) Plan and Trust (the 401(k) Plan). Employees may contribute, up to the percentage limit imposed by the Internal Revenue Code of 1986, as amended, an amount of their salary each calendar year until termination of their employment with the Company. The Company may elect to make matching contributions, as per the Plan; however, no matching contributions were made in the years ended December 31, 2015, 2014, and 2013.

**12. Income Taxes**

The Company's loss before tax is only attributable to U.S. operations. A reconciliation of the federal statutory income tax rate to the Company's effective income tax rate is as follows:

	<b>Year Ended December 31,</b>		
	<b>2015</b>	<b>2014</b>	<b>2013</b>
Federal statutory income tax rate	(34.0%)	(34.0%)	(34.0%)
State income taxes, net of federal benefit	(5.80)	(5.80)	(5.80)
Permanent items	1.90	2.60	1.10
Research and development credits	(2.10)	(1.80)	(3.90)
Change in valuation allowance	40.0	39.0	43.10
Other	—	—	(0.50)
(Benefit from) provisions for income taxes	— %	— %	— %

The tax effects of temporary differences and carryforwards that give rise to significant portions of the deferred tax assets consist of the following (in thousands):

	<b>2015</b>	<b>2014</b>
Net operating loss carryforwards	\$ 90,813	\$ 74,699
Research and development credit	7,583	6,712
Amortization of deferred stock compensation - non-qualified	8,603	6,041
Reserves and accruals	1,125	1,419
Depreciation and amortization	420	408
Net deferred tax asset	108,544	89,279
Less: valuation allowance	(108,544)	(89,279)
Net deferred tax assets	\$ —	\$ —

In November 2015, the FASB issued ASU 2015-17, "Balance Sheet Classification of Deferred Taxes", which simplifies the presentation of deferred income taxes. This ASU requires that deferred tax assets and liabilities be classified as non-current in a statement of financial position. We early adopted ASU 2015-17 effective December 31, 2015 on a prospective basis. No prior periods were retrospectively adjusted.

The Company has concluded that its deferred tax assets are not more likely than not to be realized. Accordingly, the total deferred tax assets have been fully offset by a valuation allowance. The Company's valuation allowance increased by approximately \$19.3 million, \$18.3 million, and \$16.7 million during 2015, 2014, and 2013 respectively.

At December 31, 2015, the Company had federal and state net operating loss carryforwards of approximately \$233.4 million and \$234.0 million, respectively. The federal net operating loss carryforwards begin to expire in 2025 and the state net operating loss carryforwards begin to expire in 2016, if not utilized.

## CHEMOCENTRYX, INC.

### Notes to Consolidated Financial Statements (continued)

#### 12. Income Taxes (continued)

The Company has federal and state research and development credit carryforwards of \$8.8 million and \$4.6 million, respectively. The federal research and development credits will begin to expire in 2019, if not utilized. California research and development credits can be carried forward indefinitely. The American Taxpayer Relief Act of 2012, which was enacted on January 2, 2013, extends the Federal research tax credit retroactively for two years from January 1, 2012 through December 31, 2013. The tax benefit from the extension of the Federal research tax credit has been reflected in the income tax provision for the year ended December 31, 2014 with an offsetting increase in valuation allowance.

Utilization of the net operating loss and credit carryforwards may be subject to annual limitation due to historical or future ownership percentage change rules provided by the Internal Revenue Code of 1986, as amended, and similar state provisions. The annual limitation may result in the expiration of certain net operating loss and credit carryforwards before their utilization.

The deferred tax asset balances as of December 31, 2015 and 2014 did not include excess tax benefits from stock option exercises. The amount excluded at December 31, 2015 and 2014 was \$5.5 million and \$4.2 million respectively. The use of tax benefits associated with the stock option related deductions will be credited directly to stockholders' equity upon ultimate realization.

A reconciliation of the Company's unrecognized tax benefits for the years ended December 31, 2015, 2014, and 2013, is as follows (in thousands):

	<b>Unrecognized Income Tax Benefits</b>
Balance as of December 31, 2013	\$ 4,956
Additions for current tax positions	434
Balance as of December 31, 2014	\$ 5,390
Additions for current tax positions	495
Releases	<u>(1,013)</u>
Balance as of December 31, 2015	<u>\$ 4,872</u>

As of December 31, 2015 and 2014, the Company had approximately \$4.9 million and \$5.4 million, respectively, of unrecognized tax benefits, none of which would currently affect the Company's effective tax rate if recognized due to the Company's deferred tax assets being fully offset by a valuation allowance. The Company is not aware of any items that will significantly increase or decrease its unrecognized tax benefits in the next 12 months.

For U.S. federal and California income tax purposes, the statute of limitations remains open for the years beginning 2012 and 2011, respectively, except for the carryforward of net operating losses and research and development credits generated in prior years.

If applicable, the Company would classify interest and penalties related to uncertain tax positions in income tax expense. Through December 31, 2015, there has been no interest expense or penalties related to unrecognized tax benefits.

The IRS has completed its audit for the years ended December 31, 2007 and 2008, and there have been no adjustments to the Company's attributes carryforwards; however, the research and development credit may be subject to re-examination.



## CHEMOCENTRYX, INC.

### Notes to Consolidated Financial Statements (continued)

#### 12. Income Taxes (continued)

The Company has completed the examination by the California Franchise Tax Board for the years ended December 31, 2008 and 2009. The examination resulted in an update to the Company's California net operating loss carryforwards and R&D credits. The Company is not currently under examination in any other jurisdictions.

#### 13. Selected Quarterly Financial Data (unaudited)

Selected quarterly results from operations for the years ended December 31, 2015 and 2014 are as follows (in thousands except per share amounts):

	2015 Quarter Ended			
	<u>March 31</u>	<u>June 30</u>	<u>September 30</u>	<u>December 31</u>
Revenue	\$ —	\$ —	\$ —	\$ —
Net loss	(12,006)	(12,078)	(11,647)	(11,574)
Basic and diluted net loss per share	(0.28)	(0.28)	(0.26)	(0.26)

	2014 Quarter Ended			
	<u>March 31</u>	<u>June 30</u>	<u>September 30</u>	<u>December 31</u>
Revenue	\$ —	\$ —	\$ —	\$ —
Net loss	(11,537)	(12,261)	(10,941)	(12,190)
Basic and diluted net loss per share	(0.27)	(0.28)	(0.25)	(0.28)

## SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

### CHEMOCENTRYX, INC.

Date: March 14, 2016

By: /s/ Thomas J. Schall, Ph.D.

Thomas J. Schall, Ph.D.  
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Annual Report on Form 10-K has been signed by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Thomas J. Schall, Ph.D.</u> Thomas J. Schall, Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	March 14, 2016
<u>/s/ Susan M. Kanaya</u> Susan M. Kanaya	Senior Vice President, Finance, Chief Financial Officer and Secretary (Principal Financial and Accounting Officer)	March 14, 2016
<u>/s/ Thomas A. Edwards</u> Thomas A. Edwards	Director	March 14, 2016
<u>/s/ Joseph M. Feczko, M.D.</u> Joseph M. Feczko, M.D.	Director	March 14, 2016
<u>/s/ Roger C. Lucas, Ph.D.</u> Roger C. Lucas, Ph.D.	Director	March 14, 2016
<u>/s/ Geoffrey M. Parker</u> Geoffrey M. Parker	Director	March 14, 2016
<u>/s/ James L. Tyree</u> James L. Tyree	Director	March 14, 2016

## CORPORATE INFORMATION .....

ChemoCentryx, Inc.  
850 Maude Avenue  
Mountain View, CA 94043  
650.210.2900 tel  
650.210.2910 fax  
<http://www.chemocentryx.com>

## CORPORATE COUNSEL .....

Latham & Watkins  
San Diego, CA

## TRANSFER AGENT .....

American Stock Transfer & Trust Company, LLC  
6201 15th Avenue  
Brooklyn, NY 11219  
888-444-0057  
[customerservice@astinvestor.com](mailto:customerservice@astinvestor.com)  
<http://www.amstock.com/new/InvestorServices/ShareholderServices.aspx>

## INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM .....

Ernst & Young LLP  
Redwood City, CA

## FORM 10-K .....

A copy of the ChemoCentryx annual report on Form 10-K filed with the Securities and Exchange Commission is available free of charge from the company's Corporate Communications Department by calling 650.210.2900.

## STOCK INFORMATION .....

The common stock of the company has traded on the Nasdaq Global Select Market under the symbol "CCXI" since February 8, 2012. No dividends have been paid on the common stock since the company's inception.

## BOARD OF DIRECTORS .....

Thomas J. Schall, PhD  
President, Chief Executive Officer and Chairman of the Board  
ChemoCentryx, Inc.

Roger C. Lucas, PhD  
Vice Chairman, Bio-Techne Corporation  
Lead Independent Director, ChemoCentryx, Inc.

Thomas A. Edwards  
Retired Partner, Latham & Watkins, LLP

Joseph M. Feczko, MD  
Former Senior Vice President and Chief Medical Officer, Pfizer Inc.

Geoffrey M. Parker  
Former Executive Vice President and Chief Financial Officer, Anacor  
Pharmaceuticals, Inc,  
Chairman of the Audit Committee, ChemoCentryx, Inc.

James L. Tyree  
Former Executive Vice President, Abbott Laboratories  
Chairman of the Compensation Committee, ChemoCentryx, Inc.

## MANAGEMENT .....

Thomas J. Schall, PhD  
President, Chief Executive Officer and Chairman of the Board

Markus J. Cappel, PhD  
Chief Business Officer and Treasurer

Susan M. Kanaya  
Senior Vice President, Finance, Chief Financial Officer and Secretary

Petrus (Pirow) Bekker, MD, PhD  
Chief Medical Officer

Israel F. Charo, MD, PhD  
Senior Vice President, Research

## CHEMOCENTRYX, INC.

850 Maude Avenue | Mountain View, CA 94043 | 650.210.2900 tel | 650.210.2910 fax

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<http://www.chemocentryx.com>