FIBROGEN INC
Form 10-K
March 26, 2015
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2014

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: 001-36740

FIBROGEN, INC.

(Exact name of registrant as specified in its charter)

Delaware	**77-0357827**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
409 Illinois Street	
San Francisco, CA	**94158**
(Address of principal executive offices)	**(zip code)**

Registrant s telephone number, including area code:

(415) 978-1200

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

Title of Each Class	**Name of Exchange on Which Registered**
Common Stock, $0.01 par value	**The NASDAQ Global Select Market**

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

None

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

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T 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 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. x

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 the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act:

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

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

As of June 30, 2014, the last business day of the registrant s most recently completed second fiscal quarter, there was no established public market for the registrant s common stock. The registrant s common stock began trading on The NASDAQ Global Select Market on November 14, 2014.

The number of shares of common stock outstanding as of February 28, 2015 was 59,137,591.

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FORWARD-LOOKING STATEMENTS

This Annual Report filed on Form 10-K and the information incorporated herein by reference, particularly in the sections captioned Risk Factors, Management s Discussion and Analysis of Financial Condition and Results of Operations and Business, contains forward-looking statements, which involve substantial risks and uncertainties. In this Annual Report, all statements other than statements of historical or present facts contained in this Annual Report, including statements regarding our future financial condition, business strategy and plans and objectives of management for future operations, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as believe, will, may, estimate, continue, anticipate, contemplate, intend, target, project, should, plan, expect, predict, could, potentially or the negative of these terms or other similar terms or expressions that concern our expectations, strategy, plans or intentions. Forward-looking statements appear in a number of places throughout this Annual Report and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned preclinical development and clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for roxadustat, FG-3019 and our other product candidates, our intellectual property position, the potential safety, efficacy, reimbursement, convenience clinical and pharmaco-economic benefits of our product candidates, the potential markets for any of our product candidates, our ability to develop commercial functions, our ability to operate in China, expectations regarding clinical trial data, our results of operations, cash needs, spending of the proceeds from our initial public offering and the concurrent private placement, financial condition, liquidity, prospects, growth and strategies, the industry in which we operate and the trends that may affect the industry or us. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions described in the section of this Annual Report captioned Risk Factors and elsewhere in this Annual Report.

These risks are not exhaustive. Other sections of this Annual Report may include additional factors that could adversely impact our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. We cannot assure you that the events and circumstances reflected in the forward-looking statements will be achieved or occur. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. The forward-looking statements made in this Annual Report are based on circumstances as of the date on which the statements are made. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this Annual Report or to conform these statements to actual results or to changes in our expectations.

This Annual Report also contains market data, research, industry forecasts and other similar information obtained from or based on industry reports and publications, including information concerning our industry, our business, and the potential markets for our product candidates, including data regarding the estimated size and patient populations of those and related markets, their projected growth rates and the incidence of certain medical conditions, as well as physician and patient practices within the related markets. Such data and information involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates.

You should read this Annual Report with the understanding that our actual future results, levels of activity, performance and achievements may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

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ITEM 1. BUSINESS

OVERVIEW

We are a research-based, biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutic agents to treat serious unmet medical needs. We have capitalized on our extensive experience in fibrosis and hypoxia inducible factor, or HIF, biology to generate multiple programs targeting various therapeutic areas. Our most advanced product candidate, roxadustat, or FG-4592, is an oral small molecule inhibitor of HIF prolyl hydroxylases, or HIF-PHs, in Phase 3 clinical development for the treatment of anemia in chronic kidney disease, or CKD. Our second product candidate, FG-3019, is a monoclonal antibody in Phase 2 clinical development for the treatment of idiopathic pulmonary fibrosis, or IPF, pancreatic cancer and liver fibrosis. We have taken a global approach to the development and future commercialization of our product candidates, and this includes development and commercialization in the People s Republic of China, or China.

We intend to leverage our extensive experience in fibrosis and HIF biology to build a successful biopharmaceutical company with a strong pipeline of products and product candidates for the treatment of anemia, fibrosis, cancer, corneal blindness and other serious unmet medical needs. The chart below is a summary of our most advanced product candidates:

ROXADUSTAT FOR THE TREATMENT OF ANEMIA IN CHRONIC KIDNEY DISEASE

Roxadustat is an internally discovered HIF-PH inhibitor that acts by stimulating the body s natural pathway of erythropoiesis, or red blood cell production. Roxadustat, the first HIF-PH inhibitor to enter Phase 3 clinical development, represents a new paradigm for the treatment of anemia in CKD patients, with the potential to offer a safer, more effective, more convenient and more accessible therapy than the current therapies available for anemia in CKD, such as injectable erythropoiesis stimulating agents, or ESAs.

Roxadustat is currently in Phase 3 global development for the treatment of anemia in patients with chronic kidney disease, or CKD. Over 1,400 subjects have participated in 26 completed Phase 1 and 2 clinical studies for

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roxadustat in North America, Europe and Asia. These studies have demonstrated roxadustat s potential for a favorable safety and efficacy profile in anemic CKD patients, both those who are dialysis-dependent, or DD-CKD, including hyporesponsive patients, and those who are not dialysis-dependent, or NDD-CKD. According to IMS Health, 2013 global ESA sales in all anemia indications totaled $8.6 billion. While the use of ESAs to treat anemia in CKD has largely been limited to use in DD-CKD patients, we and our partners believe that, as an oral agent with a potentially more favorable safety profile, roxadustat could increase accessibility and expand the market for anemia treatment by penetrating the NDD-CKD market. In the longer term, we believe roxadustat has the potential to address non-CKD anemia markets, including chemotherapy-induced anemia, anemia related to inflammation (such as inflammatory bowel disease, lupus and rheumatoid arthritis), myelodysplastic syndrome, or MDS, and surgical procedures requiring transfusions.

We, along with our collaboration partners Astellas Pharma Inc., or Astellas, and AstraZeneca AB, or Astra Zeneca, have designed a global Phase 3 program to support regulatory approval of roxadustat in both NDD-CKD and DD-CKD patients in the United States, the European Union, Japan and China. Our US and EU Phase 3 program has an aggregate target enrollment of approximately 7,000 to 8,000 patients worldwide and is the largest Phase 3 clinical program ever conducted for an anemia product candidate. Our Phase 3 program is also designed and sized for, and will incorporate major adverse cardiac events, or MACE, composite safety endpoints that we believe will be required for approval in the United States for all new anemia therapies. Our Phase 3 program will study multiple patient populations, including patients within the first four months of initiating dialysis, or incident dialysis, and non-incident, or stable, dialysis patients and will include multiple NDD-CKD studies comparing roxadustat against placebo control.

Background of Anemia in CKD

Anemia is a serious medical condition in which patients have insufficient red blood cells and low levels of hemoglobin, or Hb, a protein in red blood cells that carries oxygen to cells throughout the body. Anemia is associated with increased risks of hospitalization, cardiovascular complications, need for blood transfusion, exacerbation of other serious medical conditions and death. In addition, anemia frequently leads to significant fatigue, cognitive dysfunction, and decreased quality of life. The more severe the anemia, as measured in lower Hb levels, the greater the health impact on patients. Severe anemia is common in patients with CKD, cancer, MDS, inflammatory diseases, and other serious illnesses. Even when it accompanies prevalent and serious diseases, anemia is often not effectively treated.

Anemia is particularly prevalent in patients with CKD, which is a critical healthcare problem and is most commonly caused by diabetes and hypertension in the United States and Europe. CKD affects over 200 million people worldwide and anemia significantly increases healthcare costs for those patients. CKD is generally a progressive disease characterized by the gradual loss of kidney function that may eventually lead to kidney failure, also known as end stage renal disease, or ESRD. Patients with ESRD require renal replacement therapy either dialysis treatment or kidney transplantation. CKD accompanied by anemia is associated with worse health outcomes than CKD alone, including more rapid progression of CKD and increased death rate. There are 5 stages of CKD which are primarily defined by a measure of the filtration function of the kidney (GFR).

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Stages of CKD and Prevalence in the United States

* US prevalence is estimated for adults 20 years of age or older
GFR: Glomerular Filtration Rate (ml/min/1.73m^2)
Sources: The prevalence of stage 1 through stage 4 CKD was calculated based on 2012 estimates by the U.S. Renal Data System (USRDS) using data from the National Health and Nutrition Examination Survey (NHANES) 2007-2012 and 2012 data from the U.S. Census Bureau. The prevalence of stage 5 CKD was calculated based on 2012 data from the USRDS using data from NHANES 2007-2012 and 2012 data from the U.S. Census Bureau.

The prevalence rate of anemia in patients with Hb<12 g/dL is set forth below.

Sources: The prevalence of anemia in stage 1 through stage 4 CKD and stage 5 NDD-CKD were derived from Stauffer and Fan, Prevalence of Anemia in Chronic Kidney Disease in the United States, PLoS ONE (2014). The prevalence of anemia in patients undergoing dialysis was derived from Goodkin et al, Naturally Occurring Higher Hemoglobin Concentration Does Not Increase Mortality among Hemodialysis Patients, J Am Soc Nephrol (2011).

In the United States, according to the USRDS, a majority of dialysis eligible CKD patients are currently on dialysis. According to USRDS data as of 2012, approximately 450,000 patients were receiving dialysis in the United States, of whom approximately 80% were being treated with ESAs for anemia. Despite the presence of anemia in stages 3 and 4 CKD patients, in clinical practice, patients typically do not receive ESA treatment for their anemia until they initiate dialysis. Approximately 15% of U.S. NDD-CKD patients were being treated with ESAs prior to initiation of dialysis as of 2012 (USRDS Annual Data Report (2014)). In many CKD patients, the disease progresses gradually over decades and, therefore, patients can spend years suffering from the symptoms and negative health impacts of anemia before they receive treatment. Many of these patients die from cardiovascular events before they initiate dialysis.

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Limitations of the Current Standard of Care for Anemia in CKD

Current therapies to treat anemia in CKD include injectable ESAs, intravenous iron, or IV iron, oral iron and blood transfusions. ESAs have been used in the treatment of anemia in CKD for over 20 years and are administered intravenously or subcutaneously, typically in conjunction with IV iron. NDD-CKD patients who are not under the care of nephrologists, including those with diabetes and hypertension, do not typically receive ESAs and are often left untreated. ESAs currently on the market are all synthetic recombinant versions of human erythropoietin, or EPO, a hormone that stimulates erythropoiesis and increases Hb levels by binding to receptors on red blood cell precursors in the bone marrow.

The introduction of the first ESA in 1989 was viewed as a major advance in the treatment of anemia in CKD because it significantly decreased the need for blood transfusions. Since then, ESAs have become one of the most commercially successful drug classes. However, because ESAs were never studied relative to placebo in large randomized clinical trials prior to approval, it was not until years later that their safety profile became better elucidated. Studies published in 2006 to 2009 demonstrated the safety risks of higher ESA doses used to target Hb levels of 13 to 15 g/dL, prompting physicians to balance serious safety concerns against the efficacy of ESAs. The safety concerns observed with injectable ESAs in these studies included an increased risk of cardiovascular adverse events and death as well as a potentially increased rate of tumor recurrence in patients with cancer.

The emergence of the safety issues resulted in several changes to ESA drug labeling. This combination of safety concerns and labeling changes, in addition to the subsequent reimbursement changes, described below, was followed by a decline in ESA sales revenues beginning in 2007. While we believe this decline in ESA sales is primarily due to complete suspension of the label for use of ESAs in anemias associated with cancer, and restrictions on use in chemotherapy induced anemia, we believe the decline in sales is also partly due to the progressive decline in ESA dose administered to CKD patients. Compared to the average ESA dose at the end of 2006, the mean monthly ESA dose in patients on hemodialysis dropped by 18%, 36% and 45% by the end of 2010, 2011 and 2012 respectively (USRDS Annual Data Report 2014).

Safety Issues of ESAs

Several large clinical trials were designed to demonstrate that targeting higher as opposed to lower Hb levels results in better outcomes. However, they instead generated data showing that targeting higher Hb levels with ESAs resulted in an increase in adverse events, including cardiovascular adverse events. These adverse events were initially observed in 1998 in the NHCT (Normal Hematocrit Cardiac Trial) in CKD patients on dialysis, where the high Hb level treatment arm targeted Hb levels of 13 to 15 g/dL. Additional safety concerns emerged following the CHOIR (Correction of Hemoglobin in Outcomes and Renal Insufficiency), CREATE (Cardiovascular Risk Reduction by Early Anemia Treatment with Epoetin Beta), and TREAT (Trial to Reduce Cardiovascular Events with Aranesp Therapy) studies in NDD-CKD patients, which were published between 2006 and 2009.

Secondary analyses of NHCT, CHOIR and TREAT, as well as subsequent observational studies in dialysis patients, suggest that these safety concerns, particularly the increased cardiovascular risk associated with ESAs, may result from the high ESA doses used to target higher Hb levels rather than the achieved Hb levels themselves. For example, a secondary analysis of CHOIR showed that patients who achieved the desired Hb level with the lowest amounts of ESA have the lowest risk of adverse cardiovascular outcomes as measured by composite endpoints consisting of hospitalization for heart failure, heart attack, stroke, and death. Patients who were treated with the highest ESA doses and, particularly those who achieved the lowest Hb levels, had the greatest risk for these events. In addition, observational studies in patients undergoing dialysis highlighted these risks with high ESA doses and also indicated that higher Hb levels achieved with lower ESA doses were associated with better outcomes.

For example, in an analysis of data from the USRDS of 94,569 hemodialysis patients, increased mortality was found in patients with increased epoetin alfa dose. Patients who achieved the highest hematocrit level (which is a

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measure of the percentage of volume of whole blood made up of red blood cells; under typical conditions, Hb level can be estimated as one-third the hematocrit level) and received the lowest ESA doses (lowest dose quartile, Q1) had the lowest mortality rate, and, at any particular ESA dose quartile, patients with higher hematocrit levels tended to have lower mortality levels, according to Zhang et al (Am J Kidney Dis 44:866-876) as illustrated in the chart below.

Unadjusted 1-Year Mortality Rates (per 1000)

by Hematocrit and ESA dosing quartile

Warnings about these risks have been incorporated into guidelines and position papers from major kidney societies and thought leaders. Kidney Disease: Improving Global Outcomes, or KDIGO, a non-profit foundation established in 2003 and operated by the National Kidney Foundation, committed to improving global clinical guidelines for kidney patients, for example, states that, [t]here may be toxicity from high doses of ESA, as suggested, though not proven, by recent post-hoc analyses of major ESA randomized controlled trials, especially in conjunction with the achievement of high Hb levels. Therefore, in general ESA dose escalation should be avoided. In addition, the European Renal Best Practices Group specified in a recent position statement that caution should be used in ESA therapy in patients with specific risk factors.

Limited Effectiveness of ESAs in Certain Patient Populations

Hb responses to ESA doses are on a continuum with some patients responding with a satisfactory Hb increase to a small ESA dose and others responding very poorly to very high doses. In addition, patients responsiveness to ESAs can change over time and as a result of circumstances such as acute illness or surgery. In an attempt to reach target Hb level, ESA doses are increased in treatment-resistant patients, or hyporesponders, which can result in up to a 40-fold difference in ESA doses between the most ESA-resistant and the most ESA-responsive DD-CKD patients. Even with high doses of ESAs and concomitant IV iron, some of these hyporesponders are unable to reach target Hb levels.

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Hyporesponsiveness is a significant problem in incident dialysis patients, for whom ESA doses are typically high, and is associated with a combination of critically low kidney function and accompanying illnesses, such as infections and chronic inflammation. Incident dialysis patients are generally more anemic, and have a higher risk of death, than patients who have been on dialysis for many months.

A major cause of ESA hyporesponsiveness is an underlying chronic inflammatory state that exists in many CKD patients. Chronic inflammation has a suppressive effect on erythropoiesis in CKD via two main mechanisms. Firstly, pro-inflammatory cytokines such as tumor necrosis factor alpha, or TNF-alpha, and interleukin-6, or IL-6, have been implicated in the suppression of erythropoiesis through inhibition of the response of erythroid progenitor cells to EPO. Secondly, pro-inflammatory cytokines such as IL-6 elevate the levels of hepcidin, the major hormone that regulates iron metabolism. The consequence of elevated hepcidin levels is a reduction in iron absorption from the gastrointestinal tract, or GI tract, and the trapping of iron in cellular stores. Together this leads to inadequate availability of iron to keep pace with the demands of the bone marrow for erythropoiesis, despite adequate total body iron stores. This condition is referred to as functional iron deficiency.

In the presence of inflammation, even high doses of ESAs may be ineffective to achieve target Hb levels, and to the extent Hb levels are raised, the risks associated with the higher ESA doses required may outweigh the benefits of any increased Hb levels.

Requirement for IV Iron to Support ESA Activity and Associated Safety Risks

IV iron supplementation is used to support anemia correction in a majority of hemodialysis patients treated with ESAs in the United States. ESA labeling indicates that physicians should evaluate the iron status in all patients before and during CKD anemia treatment and maintain iron repletion. Many CKD patients have deficient iron stores, or absolute iron deficiency, and cannot absorb enough iron from diet or oral iron supplements to correct this deficiency. Physicians administer IV iron to ensure patients are iron replete prior to initiating ESA treatment and continue IV iron to mitigate iron depletion caused by ESA-mediated erythropoiesis.

Additionally, many CKD patients who have adequate iron stores suffer from functional iron deficiency. IV iron is administered in an attempt to address this shortage of available iron in these CKD patients, resulting in many patients having elevated body iron stores. While IV iron can help correct anemia when used with ESAs, published studies have suggested acute and chronic risks of both morbidity and mortality associated with the use of IV iron. The acute risks of IV iron supplementation include hypersensitivity reactions (which can be life-threatening and the warning of anaphylaxis risk appears in every IV iron product package insert in the United States), infection, as well as less severe but more common side-effects, such as skin problems, hypotension and GI tract symptoms. In addition to acute side-effects, there may also be chronic adverse effects on organ systems related to the cumulative deposits of iron resulting from the volume of iron administered.

Increased use of IV iron has been associated with increased risk of hospitalization and death. Using data from 12 countries obtained over the past twelve years, Bailie et al. demonstrated a direct dose risk relationship between the amount of IV iron administered per month to dialysis patients and the risk of hospitalization and death (Kidney International (2014)). The study identified that, even after controlling for other risk factors and adjusting for different practice patterns globally, dialysis patients receiving greater than 300 mg of IV iron per month had a greater risk of hospitalization or death than those receiving less than 300 mg. Mortality was 13% greater among those receiving between 300 and 400 mg of IV iron per month and 18% greater among those receiving greater than 400 mg of IV iron per month. Furthermore, hospitalization risk was 12% greater among those who received greater than 300 mg per month. The current paradigm of administrating greater doses of IV iron to decrease ESA doses in light of this recently described associated risk underscores the significant unmet need in the treatment of anemia. However, new and

purportedly safer and more effective iron supplementation therapies are being developed and introduced, and if such new therapies are accepted by patients and physicians as a superior alternative to traditional IV iron supplementation therapies, they may help maintain or increase the attractiveness of ESA therapy.

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Elevated Blood Pressure

ESAs have long been associated with increased blood pressure, including new onset hypertension and exacerbation of pre-existing hypertension. As a result, ESA labeling carries a warning for the potential for increased blood pressure with ESA usage. Hypertension has been shown to accelerate CKD progression and significantly increase the risk of death in CKD patients due to the increased risk of heart attack or stroke.

Increased Thromboembolism and Vascular Access Thrombosis

ESA use has been associated with thromboembolic events, including stroke, vascular access thrombosis (where the dialysis access shunt is blocked due to blood-clotting), blood clots in the leg, which may in part be due to increases in circulating platelet levels. As a result, ESA labeling carries a warning for an increased risk of thromboembolic events.

FDA Restrictions on ESA Usage

In response to safety concerns elucidated in the large clinical studies described above, the US Food and Drug Administration, or the FDA, steadily increased restrictions on the use of injectable ESAs from 2007 through 2011. During 2007, following the NHCT, CHOIR and CREATE studies and several oncology studies, the FDA mandated the inclusion of a boxed warning, or Black Box warning, in the package insert for ESAs. A Black Box warning is the strongest warning that the FDA can require in the package insert of prescription drugs. In June 2011, the FDA required further modification to the package insert for ESAs. The current boxed warning states that ESAs increase the risk of death, myocardial infarction, or heart attack, stroke, venous thromboembolism, thrombosis of vascular access and tumor progression or recurrence. In addition, the package insert changes include more conservative dosing guidelines for the use of injectable ESAs in anemic CKD patients. Specifically, the FDA removed the prior target Hb range of 10 to 12 g/dL and recommends that physicians initiate treatment of CKD patients when the Hb level is less than 10 g/dL and reduce or interrupt ESA dosing if the Hb level approaches or exceeds 10 g/dL for NDD-CKD patients and 11 g/dL for DD-CKD patients. In addition, physicians are advised to use only the lowest dose needed to avoid red blood cell transfusions.

Reimbursement Challenges Associated with ESAs

In addition to the safety concerns and labeling changes for ESAs, the reimbursement applicable to dialysis, including associated drugs such as ESAs, has also changed significantly in recent years, which made ESAs less economically attractive for providers to administer. Prior to January 2011, CMS reimbursed dialysis centers and other healthcare providers for use of ESAs at average selling price plus a premium to their cost, which enabled providers to realize a profit on the administration of ESAs, regardless of the quantity dosed. Under the Medicare Improvements for Patients and Providers Act, or MIPPA, a basic case-mix adjusted composite, or bundled, payment system commenced in January 2011 and transitioned fully by January 2014 to a single reimbursement rate for drugs and all services furnished by renal dialysis centers for Medicare beneficiaries with end-stage renal disease. Specifically, under MIPPA the bundle now covers drugs, services, lab tests and supplies under a single treatment base rate for reimbursement by CMS based on the average cost per treatment, including the cost of ESAs and IV iron doses, typically without adjustment for usage.

ESAs administered to NDD-CKD patients have long been reimbursed under Medicare Part B, which requires providers to purchase and store ESAs in advance of being reimbursed, and in many healthcare practices, the amount reimbursed does not cover the cost of ESA administration. For many of these providers, including in nephrology practices where purchase and storing is most common, due to label changes and related reduction in patients available for treatment, ESA administration in NDD-CKD has become economically unattractive. Furthermore,

non-nephrologists generally have elected not to provide ESAs. Accordingly, ESA treatment has been limited outside of dialysis centers.

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Inconvenience of ESAs

In addition to safety, labeling, reimbursement and efficacy limitations, ESAs must be administered intravenously or subcutaneously, often with IV iron in order for ESAs to be effective at treating to target Hb levels. ESAs are therefore inconvenient for the NDD-CKD population, the peritoneal dialysis population, for whom treatment is often administered at home, and other non-CKD anemia patients who are not already regularly visiting a hospital or dialysis center.

Our Solution

We believe that there is a significant need for a safer, more effective, more convenient and more accessible alternative to injectable ESAs for the treatment of anemia in CKD patients. In addition, we believe there is a significant opportunity for treatment of anemia in markets not effectively addressed by ESAs, such as in the NDD-CKD population, DD-CKD in the presence of inflammation, and non-CKD anemia markets.

Roxadustat A Novel, Orally Administered Treatment for Anemia

Roxadustat is an orally administered small molecule that corrects anemia by a different mechanism of action from that of ESAs. As a HIF-PH inhibitor, roxadustat activates a response that is naturally activated when the body responds to reduced oxygen levels in the blood, such as when a person adapts to high altitude. The response activated by roxadustat involves the regulation of multiple, complementary processes to promote erythropoiesis and increase the blood s oxygen carrying capacity. This coordinated erythropoietic response includes both the stimulation of red blood cell progenitors, by increasing the body s production of EPO, and an increase in iron availability for Hb synthesis. Patients taking roxadustat typically have circulating endogenous EPO levels at peak concentration within or near the physiologic range naturally experienced by people adapting to hypoxic conditions such as at high altitude, following blood donation or impaired lung function, such as pulmonary edema. By contrast, ESAs act only to stimulate red blood cell progenitors without a corresponding increase in iron availability, and are typically dosed at well above the natural physiologic range of EPO. The sudden demand for iron stimulated by ESA-induced erythropoiesis can lead to functional or absolute iron deficiency. We believe these high doses of ESAs are a main cause of the significant safety issues that have been attributed to this class of drugs. In contrast, the differentiated mechanism of action of roxadustat, which involves induction of the body s own natural pathways to achieve a more complete erythropoiesis, has the potential to provide a safer and more effective treatment of anemia, including in the presence of inflammation, which normally limits iron availability.

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Our HIF-PH inhibitor technology relies on the natural mechanism by which the body responds to low oxygen levels. HIF is a transcription factor comprised of a HIF-alpha and a HIF-beta subunit, both of which are required to stimulate erythropoiesis. Under normal oxygen conditions, the HIF-alpha subunit is targeted for rapid degradation through the activity of a family of HIF-PH enzymes. However, under low oxygen conditions, the HIF-PH enzymes cannot function and HIF-alpha accumulates. HIF-alpha then combines with HIF-beta, and the newly formed HIF complex initiates transcription of a number of genes involved in the erythropoietic process, which ultimately leads to increased oxygen delivery to tissues. Roxadustat works by reversibly inhibiting the HIF-PH enzymes, thus mimicking this coordinated natural erythropoietic response through genes transcribing the proteins shown below involved in iron absorption, mobilization and transport as well as stimulation of red blood cell progenitors.

Our discovery and development of roxadustat resulted from years of experience working with prolyl hydroxylase enzymes, such as those that regulate HIF, and a deep understanding of the complexities of HIF biology. We have explored therapeutic activation of HIF to treat anemia from an integrated perspective with a focus on applying our HIF-PH inhibitor technology to produce coordinated effects on erythropoiesis and iron homeostasis and metabolism. As part of these progressive efforts, we have explored the ability of our HIF-PH inhibitor technology to increase sensitivity to endogenous EPO by increasing EPO receptor expression on red blood cell progenitors. We have investigated multiple effects of HIF-PH inhibitors on iron metabolism, including their ability to regulate genes that can increase iron bioavailability. We have also shown that administration of HIF-PH inhibitors can decrease expression of hepcidin, the key hormone that regulates iron metabolism. Hepcidin is elevated under conditions of chronic inflammation, leading to reduced iron availability for erythropoiesis. Based on our gene expression and hepcidin data, we believe HIF-PH inhibitors can increase intestinal iron absorption and enhance the mobilization and uptake of iron. In addition, we have shown that HIF-PH inhibitors can improve

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transferrin saturation (a measure of circulating iron available for erythropoiesis) and can correct anemia associated with chronic inflammation by overcoming the hepcidin-mediated sequestration of iron that cannot be overcome by ESA therapy.

We selected roxadustat from our extensive library of compounds from various chemical classes of HIF-PH inhibitors, including heterocyclic carboxamides and 2-oxoglutarate mimetics. Roxadustat was selected based on our belief that stabilizing the two main forms of HIF in the cell, HIF-1 and HIF-2, leads to a more complete erythropoietic response.

Although HIF-PH inhibitor programs have been subsequently initiated at several other companies, we expect to remain the leader in the development of HIF-PH inhibitors for anemia, with more patients dosed and more studies conducted with roxadustat than with any other HIF-PH inhibitor.

Potential Advantages of Roxadustat for Treatment of Anemia in CKD

We believe that roxadustat has the potential to offer several safety, efficacy, reimbursement, and convenience advantages over ESAs.

Potential Safety and Efficacy Advantages

Our clinical trials to date have shown that roxadustat can treat anemia in CKD with much lower circulating EPO levels than with treatment by ESAs, mitigate the need for IV iron and treat anemia in the presence of inflammation, thereby offering potential safety and efficacy benefits over ESAs. We have incorporated several endpoints into our Phase 3 studies to further elucidate and demonstrate these and other potential clinical benefits of roxadustat.

Potential Cardiovascular Benefits

The CKD patient population is at high risk for cardiovascular events such as heart attacks and strokes. One known side effect of ESAs is elevation of blood pressure, which is particularly dangerous in this high risk patient population. In contrast, we did not observe increases in blood pressure in patients treated with roxadustat beyond the background levels observed for the comparable placebo-treated patients in a NDD-CKD Phase 2 trial. However, these data should be cautiously assessed due to the limited number of patients exposed. In Study 041, the NDD-CKD patients treated with roxadustat three times weekly for more than 12 weeks had a modest decrease in blood pressure in a subgroup analysis of our Phase 2 NDD-CKD study.

In our Phase 2 studies, we did not observe a safety signal for thromboembolic risk. In contrast to the platelet increase with ESA treatment, platelet counts reported in roxadustat-treated patients did not increase, as those with platelet levels in the top 25th percentile at baseline saw their platelet levels decrease towards normal levels while those with platelet levels in the lower 75th percentile at baseline saw their platelet levels remain stable. This finding supports our belief in a potential safety benefit over ESAs since the platelet increase with ESAs could be a contributing factor in the thromboembolic risk associated with ESAs.

In addition, in our Phase 2 clinical trials, we observed reductions in total cholesterol and an improvement in average HDL / LDL ratio. Since many CKD patients have high cholesterol levels, which contribute to cardiovascular-related morbidity and mortality, the improvement in the average HDL / LDL ratio observed with roxadustat treatment could confer a benefit to patients.

Based on our preclinical and clinical data generated to date, we believe roxadustat could offer cardiovascular benefits to a CKD patient population that typically has cardiovascular-related co-morbidities and is at a high risk for

cardiovascular events.

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Potential for Anemia Correction with Moderate EPO Levels

Randomized trials have suggested that high doses of ESAs administered in an attempt to achieve a target Hb level may cause the safety issues associated with ESA therapy. These high doses result in serum EPO levels much higher than physiological range. In contrast, the level of endogenous EPO elevation among patients treated with roxadustat is typically within or near the range observed when ascending to a higher elevation or giving blood. Treating anemia while maintaining lower circulating EPO levels may mitigate, or even avoid, the risks from ESA therapy, including cardiovascular events and death.

The following graph depicts:

1) the circulating endogenous EPO levels in natural physiologic adaptations, such as adjustment to high altitude, blood loss, or pulmonary edema [left,];

2) transient peak endogenous EPO levels estimated for CKD patients who achieved a Hb response to therapeutic doses of roxadustat in our phase 2 clinical studies [middle,];

3) the estimated peak circulating recombinant EPO levels resulting from IV ESA doses in distributions reported by the Dialysis Outcomes and Practice Patterns Study, or DOPPS, for the fourth quarter of 2011 in the United States (after bundling was initiated and when the Hb target in ESA labeling was in the range of 10-11 g/dL [right,]).

[1]Milledge & Cotes (1985) J Appl Physiol 59:360; [2]Goldberg et al. (1993), Clin Biochem 26:183, Maeda et al. (1992) Int J Hematol 55:111; [3]Kato et al. (1994) Ren Fail 16:645; [4]The transient peak endogenous EPO concentrations, or Cmax, data for roxadustat was derived from a subset of 243 patients who achieved a Hb response to roxadustat in our Phase 2 studies for whom we believe doses depicted approximated therapeutic doses. Hb target ranges for these patients were above the Hb levels specified in the current ESA package insert

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for CKD patients. Only doses in those patients whose Hb responded in Phase 2 studies are reflected in the figure. The subset of patients included 134 NDD-CKD patients treated to thrice-weekly, twice-weekly, or weekly doses of roxadustat for >16 weeks. The subset also included 109 DD-CKD patients, including incident dialysis patients whose anemia was corrected with therapeutic doses, and stable dialysis patients who received maintenance doses. Cmax of endogenous EPO levels were not measured in all patients; instead the range of EPO Cmax levels were estimated based on data derived from a more limited number of patients in whom EPO levels were measured at various roxadustat doses and among whom there was substantial variation in measured EPO levels. Accordingly, individual patients who received roxadustat may have realized EPO Cmax levels significantly above or below these estimated levels. Moreover, the estimates reflected in the graph may not be reflective or predictive of actual EPO Cmax levels or ranges that will be realized in larger populations of patients receiving roxadustat in our Phase 3 clinical trials. [5]EPO C_{max} was computed from ESA dose distributions based on Flaherty et al. (1990) Clin Pharmacol Ther 47:557.

Potential for Anemia Correction for Patient Populations that are Hyporesponsive to ESAs

Incident dialysis patients and patients who have chronic inflammation are often hyporesponsive to ESAs, which necessitates the use of higher doses of ESAs to increase Hb levels, thus increasing both safety risk and treatment cost. In contrast, the dose of roxadustat may not need to be increased in incident dialysis patients or to overcome the suppressive effects of inflammation on erythropoiesis, which we believe may confer significant safety and efficacy benefits.

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As a result of roxadustat s different mechanism of action, the ability of roxadustat to stimulate erythropoiesis does not appear to be impaired by chronic inflammation. In a preclinical model of inflammation induced by peptidoglycan-polysaccharide (PG-PS) polymers, roxadustat increased Hb levels and mean corpuscular volume (MCV), whereas Aranesp®, an ESA, and IV iron did not increase Hb or MCV. In contrast, the same doses of roxadustat and Aranesp® were both effective at raising Hb levels in the unchallenged rats (without inflammation). In addition, the ESA actually decreased MCV in the unchallenged rats, as compared to the control.

Our preclinical studies indicate that roxadustat can overcome the direct suppressive effects of inflammatory cytokines on erythropoiesis. In addition, roxadustat can reduce hepcidin levels, thus increasing absorption of iron from the GI tract and the release of iron from intracellular stores and mitigating the functional iron deficiency associated with chronic inflammation.

Furthermore, in our Phase 2 studies, patients Hb response to roxadustat was independent of the degree of underlying inflammation, as assessed by circulating levels of C-reactive protein, or CRP, a well-recognized marker of inflammation. Incident dialysis patients have the highest levels of mortality of all dialysis patients. The incident dialysis period is also the period during which mean ESA doses are generally highest. To the extent the increased levels of mortality are associated with high ESA doses, roxadustat may offer a benefit to incident dialysis patients. The median roxadustat dose in our dialysis Study 053 was 1.3 mg/kg; the Cmax of endogenous EPO levels usually associated with this dose level are comparable to the physiologic range naturally experienced by people adapting to high altitude or following blood donation. See additional information on endogenous EPO levels under the heading Potential for Anemia Correction with Moderate EPO Levels .

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Potential for Reduced Hepcidin Levels and Anemia Correction Without IV Iron

An important differentiator of roxadustat from ESAs is that roxadustat is expected to correct anemia and maintain Hb without IV iron supplementation. Patients with chronic illness, such as CKD, often suffer from absolute iron deficiency or functional iron deficiency. We believe that elevated levels of hepcidin, the major hormone that regulates iron metabolism, contributes to both absolute and functional iron deficiency.

Our Phase 2 clinical trials have shown that roxadustat can significantly reduce hepcidin levels in patients with DD-CKD and NDD-CKD. The following figure shows a reduction in serum hepcidin level of approximately two thirds, observed at week 5, in 52 incident dialysis patients treated with roxadustat.

Reduction of Serum Hepcidin Levels (Study 053) in Incident Dialysis Patients

In addition, we believe roxadustat increases the levels of proteins involved in iron uptake, release and transport. Data from our Phase 2 clinical trials indicate that oral iron supplementation alone is adequate to correct anemia during treatment with roxadustat, in contrast to ESAs which typically require IV iron supplementation. Additionally, our data indicate that unlike ESAs, roxadustat treatment does not require that patients be iron replete before initiating therapy.

Avoiding IV iron helps to avoid the significant safety risks associated with IV iron described above, and, because the cost of oral iron is significantly less than the cost of IV iron, could also confer significant costs savings.

Potential Reimbursement and Convenience Advantages

Potentially Differentiated Reimbursement Framework

ESAs are included in the MIPPA bundled payment system in the DD-CKD setting and reimbursed under Medicare Part B in the NDD-CKD setting. Based on our roxadustat data to date, we believe roxadustat has the potential to correct anemia through a differentiated mechanism of action and different therapeutic effects that create the potential to displace multiple drugs in current use (such as ESAs and IV iron), or those in development (such as agents for suppression of hepcidin). Although the bundle currently covers ESAs or oral equivalents of ESAs or other IV products encompassed by the bundle, due to the differentiated nature of roxadustat and a lack of definition in the regulations on oral equivalency, for which there may be a CMS determination later this year, it is unclear whether roxadustat will be included in or excluded from the bundle. Under MIPPA, agents that have no IV equivalent in the bundle are currently expected to be excluded from the bundle until 2024. We believe that there may be commercial benefits in either event but are unable to predict the potential benefits until further guidance from CMS becomes available.

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In the NDD-CKD setting, we expect that roxadustat, an oral treatment, should be subject to Medicare Part D, which would allow physicians to prescribe roxadustat without the financial and reimbursement risk associated with purchasing and storing injectable ESAs. We believe that this should encourage significantly greater usage outside of the dialysis setting.

Potential Reduction of Other Medications

In addition to potentially eliminating the need for IV iron, based on our Phase 2 clinical trial results to date, we believe that roxadustat has the potential to reduce the use of other medications frequently required in some CKD anemia patients, such as anti-hypertensives, anti-coagulants, and statins.

Oral Administration

Many physicians that treat CKD patients, particularly cardiologists, endocrinologists, and internists, do not typically stock or administer ESAs. An easily accessible oral agent that is dispensed by pharmacies could significantly increase the number of physicians treating anemia in patients with CKD and therefore the number of patients receiving treatment.

In addition, the oral administration of roxadustat potentially offers a significant convenience advantage for CKD patients who have yet to initiate dialysis and are therefore not regularly visiting a dialysis center. Patients can more easily self-administer medicine in any setting, rather than being subject to the inconvenience and restrictions of regular visits to physicians offices or infusion centers for treatment with ESAs.

Potential Pharmacoeconomic Advantages

Based on our Phase 2 clinical trial results to date, we believe that roxadustat s potential pharmacoeconomic advantages over ESA therapy may include safety (with a potential decrease in cardiovascular events and consequently lower associated treatment costs), lower administrative cost, reduction or elimination of IV iron and potentially other medications. If we can demonstrate any of these pharmacoeconomic advantages in our Phase 3 studies, they may help support reimbursement worldwide, including Europe and China.

The Market Opportunity for Roxadustat

We believe that there is a significant opportunity for roxadustat to address markets currently served by injectable ESAs. According to IMS Health, 2013 global ESA sales in all indications totaled $8.6 billion, driven primarily by $6.2 billion in the United States and Europe. We believe that a substantial portion of ESA sales are for CKD anemia. For example, in the U.S., EPOGEN, which is primarily used in the DD-CKD patient population, had 2014 sales of approximately $2 billion. We further believe that the number of patients requiring anemia therapy will grow steadily as the global CKD population and access to dialysis care continue to expand, particularly in China and other emerging markets including the rest of Asia, Latin America, Eastern Europe, the Middle East and the Commonwealth of Independent States.

Furthermore, we believe that there is a significant opportunity for roxadustat to address patient segments that are currently not effectively served by ESAs, such as anemia in the NDD-CKD patient population, which is substantially larger than the DD-CKD patient population. Diabetes and hypertension are the leading causes of secondary CKD. Although we estimate approximately 36% of diabetic and 20% of hypertensive CKD patients are anemic (Hb<12g/dL), we believe the majority of these patients are currently untreated for anemia since they are under the care of non-nephrology specialists, such as endocrinologists, diabetologists, cardiologists and internists, where ESA

therapies are not readily available.

We also believe that roxadustat may provide a safer option to re-establish the chemotherapy induced anemia market, which was once a market of comparable size to the DD-CKD anemia market. Other non-CKD anemias, including anemia related to inflammatory diseases, MDS and surgical procedures requiring transfusions, which are not addressed adequately with currently available therapies, could form another opportunity.

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OUR DEVELOPMENT PROGRAM FOR ROXADUSTAT

Over 1,500 subjects have been exposed to roxadustat in clinical studies, including treatment of some patients for 24 weeks in Phase 2 studies and several patients for approximately 3 years in a safety extension study.

We along with our partners, Astellas and AstraZeneca, have designed our global Phase 3 program to support regulatory approval of roxadustat in both NDD-CKD and DD-CKD patients in the United States, the European Union, Japan and China. Our US and EU Phase 3 program has an aggregate target enrollment of approximately 7,000 to 8,000 patients worldwide and is the largest Phase 3 clinical program ever conducted for an anemia product candidate. Our U.S. Phase 3 program is also designed and sized for demonstrating non-inferiority to comparators for the MACE composite safety endpoints in two separate patient pools, NDD-CKD and DD-CKD. We believe this will be required for approval in the United States for all new anemia therapies. Our Phase 3 program will study multiple patient populations, including incident dialysis patients and stable dialysis patients and will include multiple NDD-CKD studies comparing roxadustat against placebo controls. Five of the six Phase 3 studies supporting approval in the EU use the same patients that are intended to support approval in the United States. However, the EU requires shorter treatment duration and less overall patient exposure. We currently expect to complete patient enrollment in our U.S. studies by or in the first half of 2016, and that data for U.S. Phase 3 NDD-CKD studies will be reported in 2017. We currently anticipate filing for approval for roxadustat in the United States in 2018.

We have a separate roxadustat clinical development program for China and we currently plan to initiate Phase 3 studies in the second half of 2015 through our subsidiary FibroGen China. We currently anticipate filing for approval for roxadustat in China in 2016. In addition, Astellas is developing roxadustat in Japan as part of a Japan-specific development program and is currently conducting Phase 2 studies there.

Our Phase 2 Program

We have completed and analyzed six roxadustat Phase 2 studies, three in NDD-CKD patients and three in DD-CKD patients, to assess the efficacy of roxadustat to both correct anemia (correction) and maintain the Hb response (maintenance). Data from these studies have been published and presented at various medical conferences. Two of the six completed Phase 2 studies were conducted in China. The efficacy and safety data generated from our China studies were consistent with our U.S. Phase 2 studies and further contributed to the promising efficacy and safety results to date. Our collaboration partner Astellas Japan Phase 2 dialysis study in patients with CKD anemia has been completed, and data reconciliation and analysis are in process.

The data from our completed Phase 2 studies demonstrated that roxadustat achieved a clinically meaningful increase in Hb levels in anemic NDD-CKD and DD-CKD patients and maintained Hb levels in DD-CKD patients who were converted from ESA therapy. Roxadustat corrected anemia without the need for IV iron supplementation and exhibited an acceptable safety profile. Specifically, our Phase 2 studies achieved the following objectives:

- Identified optimal roxadustat dosing regimens for anemia correction and maintenance of Hb response.

- Demonstrated roxadustat s potential to treat anemia in both NDD-CKD and DD-CKD patients, including incident dialysis patients, the most unstable and high risk CKD patient population.

Generated substantial safety data, indicating that roxadustat is well tolerated, appears safe and could offer an improved cardiovascular profile relative to ESAs. Including our Phase 1, 2 and 3 studies over 1,500 subjects have been exposed to roxadustat.

Demonstrated that roxadustat may be able to treat anemia without the need for IV iron supplementation.

Demonstrated that roxadustat can reduce hepcidin levels and potentially treat anemia in a significant subset of patients with inflammation.

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The following chart summarizes the design of our completed studies in DD-CKD and NDD-CKD patients and indicates the primary objectives of each study.

Completed Phase 2 Studies

Study Number, Study Location	CKD Patient Population	Study Objective	Number of Roxadustat Patients	Number of Comparator Patients Placebo	Number of Comparator Patients ESA	Total Number of Patients in Study	Treatment Duration (Weeks)	Dose Frequencies
FGCL-4592-017 US	Non-dialysis	Correction, PK	88	28		117	4	TIW, BIW
FGCL-4592-041 US	Non-dialysis	Correction & Maintenance	145			145	16;24	TIW, BIW, QW
FGCL-4592-047 China	Non-dialysis	Correction	61	30		91	8	TIW
FGCL-4592-040 US	Stable Dialysis	Conversion & Maintenance	117	4	40	161	6;19	TIW
FGCL-4592-053 Russia, US, Hong Kong	Incident Dialysis	Correction	60			60	12	TIW
FGCL-4592-048 China	Stable Dialysis	Conversion, PK	74		22	96	6	TIW
Total			**545**			**669**		

QW = weekly; BIW = twice weekly; TIW = three times weekly

The following chart summarizes the design of our ongoing Phase 2 studies and indicates the primary objectives of each study.

Ongoing Phase 2 Studies

Study Number, Location	CKD Patient Population	Study Objective	Number of Roxadustat Patients	Number of Comparator Patients Placebo	Number of Comparator Patients ESA	Total Target Number of Patients in Study	Treatment Duration (weeks)	Dose Frequencies
1517-CL-0303* Japan	Non-dialysis	Correction	75	25		100	24	TIW, QW
1517-CL-0304* Japan	Dialysis	Maintenance	90		30	120	24	TIW
FGCL- 4592-059 US	Non-dialysis & Dialysis	Long Term Safety &	15			15	260+	TIW, BIW, QW

	Maintenance

*Studies 1517-CL-303 and -304 are being conducted by Astellas
QW = weekly; BIW = twice weekly; TIW = three times weekly

Study 017: Dose Escalating Study in NDD-CKD patients

Study 017 established proof of concept for roxadustat by showing a significant increase in Hb in a dose-dependent manner, and provided data on the relationship between roxadustat dose and Hb response. This formed the basis for the dosing rules that we applied in subsequent studies of longer duration and in a larger number of patients.

This study, a randomized, single-blind, placebo-controlled, dose-escalation study, was the first Phase 2 study to assess the safety and efficacy of a range of roxadustat doses in the correction of anemia in NDD-CKD stage 3 and 4 patients, over four weeks of treatment, and a 12-week safety follow-up period. A total of 117 patients

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(of which 96 were evaluable) were randomized sequentially into four weight-based dose cohorts: 1 mg/kg, 1.5 mg/kg, 2 mg/kg, and 0.7 mg/kg, respectively. Roxadustat was administered either twice weekly or three times weekly.

Weight Based, Three Times Weekly and Twice Weekly Dosing Leads to Hb Improvement. We tested 4 different roxadustat weight-based doses administered for four weeks with Hb measurements over a six week period. As shown in the table below, all of the patients in the highest weight-based dose cohort met the criteria for response in that they achieved Hb rise ≥ 1 g/dL in four weeks. As roxadustat achieved 100% Hb response at the 2 mg/kg dose, higher doses were not pursued in this study despite the absence of dose limiting toxicity. Roxadustat was well tolerated without any safety concerns.

Significant, Dose Dependent Increases in Hb. As shown in the table below, the dose-dependent change in Hb from baseline in roxadustat patients was statistically significant from placebo by Day 8 ($p=0.025$) and remained so at each assessment through Week 6 ($p=0.0001$ at Day 22; $p<0.0001$ at Day 26 29/end of treatment).

A p-value is a statistical measure of the probability that the difference in two values could have occurred by chance. The smaller the p-value, the greater the statistical significance and confidence in the result. Typically, results are considered statistically significant if they have a p-value less than 0.05, meaning that there is less than a one-in-20 likelihood that the observed results occurred by chance. The FDA requires that sponsors demonstrate the effectiveness and safety of their product candidates through the conduct of adequate and well-controlled studies in order to obtain marketing approval. Typically, the FDA requires a p-value of less than 0.05 to establish the statistical significance of a clinical trial, although there are no laws or regulations requiring that clinical data be statistically significant, or that require a specific p-value, in order for the FDA to grant approval.

Hb Responses to a Range of Roxadustat Doses in FGCL-4592-017

		0.7 mg/kg		1 mg/kg		1.5 mg/kg		2 mg/kg	
	Placebo	**BIW**	**TIW**	**BIW**	**TIW**	**BIW**	**TIW**	**BIW**	**TIW**
N	23	10	12	5	5	10	11	9	11
Mean Maximum Change in Hb	0.44	0.82	1.22	1.12	0.81	1.74	2.03	1.93	2.16
Standard Error of the Mean	0.11	0.28	0.37	0.26	0.45	0.32	0.26	0.22	0.25
% Hb Responder	13%	30%	58%	60%	40%	80%	91%	100%	100%
Median Time to Response (Days)	NA	NA	26.5	42	NA	24.5	14	21	14

BIW = twice weekly; TIW = three times weekly

Standard error of the mean, or SE, is a statistical measure of the amount that an observed mean may be expected to differ by chance from the true mean. For a population that follows a normal distribution, 68% of observed means will be within one standard error of the mean.

Dose-Dependent Reduction in Hepcidin Levels. Roxadustat reduced serum hepcidin levels in a dose-dependent fashion.

Study 041: Study for Optimization of Starting Dose and Dose Titration in NDD-CKD Patients

Study 041 demonstrated that both tier-weight and fixed starting doses can initiate anemia correction. In tier-weight based dosing for this study, we used starting doses based on the patient s body weight category: high, middle or low. This randomized, open-label Phase 2 study was designed to evaluate the efficacy and safety of roxadustat over 16 to 24 weeks in 145 NDD-CKD patients (of which 143 were efficacy evaluable), and to evaluate the effects of dosing regimens in order to determine an optimized approach to anemia correction. In this trial, we tested six different starting dose regimens: three fixed doses, and three tier-weight doses. In fixed dosing, all patients in the same cohort were given the same starting dose.

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We tested both three times weekly and twice weekly dosing frequencies for anemia correction, similar to Study 017, and further demonstrated that Hb levels can be maintained using 3 dosing frequencies (three times weekly, twice weekly and weekly) once target Hb ³ 11 g/dL was achieved. We also studied various dose adjustment rules, with dose adjustment decisions made from 5 weeks onward, and every 4 weeks thereafter, to seek the best dose titration scheme.

Hb Correction. We met the primary efficacy endpoint of cumulative number (%) of patients with a Hb response, defined as an increase in Hb ³ 1.0 g/dL from baseline and Hb ³ 11.0 g/dL at the end of treatment. Regardless of the starting dose or dose titration scheme, 92% of patients collectively from all cohorts achieved an Hb increase of at least 1 g/dL from baseline. These data suggest the doses studied are of adequate range for anemia correction. The following figure shows mean Hb levels for the six dose groups.

FGCL-4592-041 Hb Response Over Various Dosing Regimens

*** n at baseline**
TIW = three times weekly; BIW = twice weekly; QW= once weekly

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Hb Correction was Independent of Inflammation Status. In this study, in a post-hoc analysis, we observed that the magnitude of increases in Hb in response to roxadustat treatment was comparable for both patients with inflammation (elevated CRP levels) and without inflammation (normal CRP levels).

FGCL-4592-041 Mean (± SE) Maximum Change in Hb (g/dL) in 12 Weeks

This stands in contrast to treatments with ESAs, where elevated CRP is frequently associated with lower Hb response to ESAs. We observed a 30% reduction in mean hepcidin level from baseline with eight weeks of roxadustat treatment (p=0.0003), which supports our belief in roxadustat s ability to overcome inflammation and to maintain iron availability for erythropoiesis.

FGCL-4592-041 Mean (± SE) Serum Hepcidin Level (ng/mL)

Hb Correction Without IV Iron and in Patients Who Have Low Iron Levels at Study Initiation. In connection with the conduct of the study, we also evaluated several iron parameters to assess roxadustat s ability to improve Hb without the use of IV iron. At baseline, 49% of the efficacy evaluable patients did not have sufficient iron levels in the body to qualify for initiation of ESA treatment under current practice guidelines and would have been excluded from participation in all prior ESA Phase 3 trials. These patients would not be considered iron replete and are typically first treated with IV iron prior to ESA treatment initiation in an effort to ensure an

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adequate response to ESA and to minimize the risk of iron depletion. Of all patients in this study receiving roxadustat, only 38% were taking oral iron supplements. A mean Hb increase of 1.8 g/dL was achieved in the first 16 weeks of treatment without IV iron supplementation. There was no evidence for iron depletion as CHr, reticulocyte hemoglobin content or the amount of Hb in newly formed red blood cells, was maintained. Furthermore, there was evidence for improved iron utilization with increases in the MCV and increase in mean corpuscular hemoglobin concentration (MCHC) over the first 16 weeks of treatment with roxadustat from baseline ($p=0.0018$ and $p<0.0001$, respectively); both MCV and MCHC typically decrease when there is iron deficiency.

Despite the minimal use of oral iron and lack of IV iron usage, patients who were not iron replete had similar Hb responses at Week 16 as patients who were iron replete.

Reduction in Cholesterol Levels. In a post-hoc analysis of all cohorts, total cholesterol decreased during treatment with roxadustat. Mean reductions in total cholesterol were greater for patients with abnormally high cholesterol levels (> 200mg/dL). Decreases in cholesterol levels were independent of whether patients were taking statins or other lipid lowering agents. Furthermore, the HDL/LDL ratio improved with roxadustat treatment in the subgroup of patients in whom lipid profiles were conducted.

Improvement in Quality of Life. Finally, in an analysis of exploratory endpoints we observed improved quality of life in patients treated with roxadustat using a standard questionnaire called the SF-36 HRQOL. The largest positive changes from baseline occurred in the Vitality subscale (>4 points, $p<0.0001$) and Physical Component (>1.6 points, $p<0.005$) subscales of the questionnaire. We believe these data demonstrate that by correcting patients anemia, roxadustat may improve quality of life.

Study 040: ESA Conversion Study in DD-CKD Patients

Study 040 was designed to evaluate the short- and long-term dosing of roxadustat in patients on hemodialysis, or HD, treatment. These results established a conversion dose relationship between ESAs and roxadustat that will be used for Phase 3 trials. Roxadustat maintained Hb without the use of IV iron, which is generally required for the treatment of anemia by ESAs.

This randomized, single-blind study was the first roxadustat study in patients on HD treatment. Part 1 was a six week open-label Phase 2 dose ranging study in 54 patients (of which 42 were efficacy evaluable) to evaluate the impact of 4 sequential doses of roxadustat on dialysis patients Hb levels over six weeks upon switching from epoetin alfa, in comparison to those continuing prior epoetin alfa doses. Part 2 was a 19 week treatment study in 90 patients (of which 83 were efficacy evaluable) to establish optimal conversion doses and dose adjustments. Patients included had previously demonstrated a wide range of ESA-responsiveness. Study 040 met its primary endpoint in Part 1 of maintaining Hb in patients previously treated with epoetin alfa at Week 6, indicating that roxadustat can replace ESAs in DD-CKD. Study 040 also met its primary endpoint in Part 2 of maintaining Hb at Week 19, indicating that roxadustat may be effective at long-term maintenance of Hb. IV iron was prohibited in both roxadustat treated patients and ESA treated control patients during this study.

Maintenance of Hb Levels Following Conversion from ESAs. In Part 1 of this study (six week treatment), 41 patients were randomized to one of four roxadustat dose cohorts, and 13 were randomized to continue on epoetin alfa treatment. The primary endpoint was maintaining an Hb level equal to or above 0.5 g/dL below baseline Hb by the end of six weeks. As shown in the figure below, roxadustat had a dose-response effect for maintaining Hb levels. The lowest roxadustat dose cohort of 1.0 mg/kg was comparable to epoetin alfa with maintenance in 44% of roxadustat patients and 33% of the control arm, patients who continued treatment with epoetin alfa (but who were required to stop concomitant treatment with IV iron). Roxadustat doses of 1.5 mg/kg or higher were better than epoetin alfa at

maintaining Hb, with 79.2% overall maintenance and with 80% maintenance at the 1.5 mg/kg roxadustat dose, 80% maintenance at the 1.8 mg/kg roxadustat dose and 77.8% maintenance at 2 mg/kg roxadustat dose.

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In Part 2 of the study (19 week treatment), 67 patients (with baseline ESA dose requirements ranging from 7 to 164.5 U/kg three times weekly) were randomized to seven cohorts of roxadustat (with various starting doses) and 23 patients were randomized to continue on epoetin alfa. Hb correction in the roxadustat treated patients pooled across all treatment cohorts was maintained over the 19 week treatment period and was comparable to epoetin alfa. The average roxadustat dose requirement for Hb maintenance was approximately 1.70 mg/kg three times weekly.

In Part 1, which was dose ranging, we observed an increase in Hb level at doses of 1.5 to 2.0 mg/kg TIW as shown in the figures below. In Part 2, which was to establish the optimal conversion dose, we observed similar Hb maintenance between roxadustat and epoetin alfa.

FGCL-4592-040 Mean: (± SE) Hemoglobin Over Time During Anemia Treatment with Roxadustat or Epoetin Alfa in Dialysis Patients

Part 1 (6 Weeks Dosing) **Part 2 (19 Weeks Dosing)**

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In addition, in an exploratory analysis of this study we observed a dose dependent decrease in hepcidin in Part 1 of this study.

FGCL-4592-040: Change in Hepcidin Level from Baseline (ng/mL)

* n at baseline

** $p<0.05$ (comparing hepcidin change from baseline between the 2.0 mg/kg roxadustat group and the epoetin alfa group).

DD-CKD patients who switched from ESA treatment to treatment with 2.0 mg/kg roxadustat had significantly greater reduction in serum hepcidin level than those who continued ESA treatment ($p=0.038$).

FGCL-4592-040 Mean (± SE) Serum Hepcidin Level (ng/mL)

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Roxadustat Doses are Associated with Lower Circulating EPO Levels than Epoetin Alfa. The following chart shows the result of six patients who were highly responsive to epoetin alfa and participated in a substudy in which their EPO levels during treatment with roxadustat were compared to EPO levels when the patients were receiving epoetin alfa prior to randomization. Their mean peak EPO concentration after an average dose of 44 U/kg was significantly higher when patients were receiving epoetin alfa relative to when they were receiving a mean roxadustat dose of 1.3 mg/kg as illustrated below. This observation is consistent with the mechanisms of action of ESA and roxadustat, respectively, and we believe the lower EPO exposure observed with roxadustat offers potential safety benefits.

FGCL-4592-040: Mean (+SE) Plasma Erythropoietin Levels During Treatment With Roxadustat Compared With Prior Epoetin Alfa Dosing In the Same Patients (n=6)

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Maintenance of Adequate Iron Supply. The concentrations of Hb within newly formed red blood cells, or CHr, is a measure of iron availability for erythropoiesis. In an exploratory analysis of this study, without IV iron supplementation (which was prohibited in this study), CHr was maintained during roxadustat treatment but declined in patients who continued treatment with epoetin alfa. This finding indicates that unlike epoetin alfa, roxadustat allows endogenous stores of iron to provide an adequate supply to newly forming red blood cells without any IV iron supplementation.

FGCL-4592-040: Mean Reticulocyte Hb Content (CHr) Over Time in Subjects Treated with Roxadustat and Epoetin Alfa

* n at baseline

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Reduction in Total Cholesterol. Consistent with our Phase 2 studies in NDD-CKD patients, we observed in a post-hoc analysis that roxadustat reduced total cholesterol levels in stable dialysis patients, and this effect appeared durable throughout the 19 week treatment period as depicted below.

FGCL-4592-040: Mean (±SE) Total Cholesterol Over Time During Treatment of Dialysis Patients with Roxadustat or epoetin alfa-Treated

Study 053: Correction of Anemia in Incident Dialysis Patients

Incident dialysis patients are at increased risk of serious cardiovascular events and death as compared to stable dialysis patients. The mortality rate among dialysis patients is highest during the first few months of dialysis initiation, and on average, patients also require the highest doses of ESA in this period. These patients typically have high levels of systemic inflammation and require IV iron supplementation for ESA to be effective.

This randomized, open-label study was designed to evaluate the safety and efficacy of roxadustat for correction of anemia in 60 incident dialysis patients (of which 55 were efficacy evaluable) who were on dialysis for at least two weeks and not more than four months and had not been treated with ESAs, and to compare the treatment responses to roxadustat under the different iron supplementation conditions. All treatment groups in Study 053 met their primary endpoint in increasing Hb level during treatment: each cohort achieved maximum mean Hb increases from baseline, ranging between 2.8 g/dL to 3.5 g/dL, resulting from 12 weeks of roxadustat treatment. We observed that at week 12 in excess of 90% of the patients achieved a greater than 1 g/dL increase in Hb from baseline. In addition, while roxadustat corrected anemia without iron supplementation, oral iron enabled an optimal Hb response. More importantly, oral iron was as effective as IV iron for Hb correction by roxadustat. In contrast, ESA therapy requires IV iron supplementation in this patient population.

This study also showed that roxadustat can correct anemia regardless of the patient s level of inflammation as measured by CRP. At Week 12, the median weekly dose of roxadustat was 4.0 mg/kg in this trial of incident dialysis patients and is similar to the median weekly dose of 4.45 mg/kg at Week 12 in Study 040, our trial of roxadustat in stable dialysis patients. In contrast, ESA therapy typically involves higher doses at the time of dialysis initiation.

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The 48 HD patients were randomized to one of the three iron supplementation options: oral iron, IV iron or no iron. Included in the 60 patients were 12 peritoneal dialysis, or PD, patients who received oral iron. This study incorporated the same tier-weight based dosing regimen utilized in Study 041.

Hb Correction in Incident Dialysis Patients Without IV Iron Administration. All three cohorts of roxadustat treated HD patients (no iron, oral iron or IV iron supplementation) and PD patients (oral iron) achieved a significant increase in the maximum Hb change from baseline, the primary efficacy endpoint. Most importantly, the maximum increase in Hb was not significantly different between roxadustat treated HD patients supplemented with oral iron (3.5 g/dL) and those supplemented with IV iron (3.5 g/dL). In contrast, a published study of ESAs in this patient population showed that patients supplemented with oral iron achieved a Hb response comparable to no iron supplementation and significantly lower Hb response than those supplemented with IV iron. These Phase 2 data demonstrate that roxadustat, unlike ESAs, may eliminate the need for IV iron and thus avoid the side effects of IV iron in DD-CKD patients.

FGCL-4592-053: Hemoglobin Over Time During Anemia Correction with Roxadustat in Incident Dialysis Patients, with No Iron, Oral Iron, or IV Iron Supplementation

Note: Hb = hemoglobin; HD = hemodialysis; PD = peritoneal dialysis; n= number of patients

Note: *p<0.05 compared to IV iron and oral iron

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Maintenance of Iron Stores. In an exploratory analysis of this study, transferrin saturation, or TSAT, a marker of iron stores, was well maintained during this period of intensive production of red blood cells with oral iron alone, indicating that iron stores can be maintained without IV iron.

FGCL-4592-053: TSAT Over Time During Anemia Correction With Roxadustat In Incident Dialysis Patients, With No Iron, Oral Iron, or IV Iron Supplementation

Hb Correction Independent of Inflammation Status. As is typical of incident dialysis patients, about half of all patients had elevated CRP levels at baseline. In a post-hoc analysis of this study, we observed that Hb responses following roxadustat treatment were independent of baseline CRP levels. These data demonstrate that, unlike the ESAs, roxadustat has the potential to overcome the suppressive effects of inflammation on Hb responsiveness to treatment.

Significant Reduction in Hepcidin. Consistent with our other studies, in an exploratory analysis of this study we observed that patients hepcidin levels were significantly reduced, most notably in the no iron and oral iron cohorts, by $\geq$ 50% from baseline, and to a lesser extent in the IV iron cohort. At follow-up (4 weeks after stopping roxadustat), hepcidin levels returned towards baseline values. Hepcidin reduction may be one of the mechanisms for overcoming the Hb suppressive effects of inflammation by making iron more available for roxadustat-induced erythropoiesis.

China Phase 2 Studies

In China, roxadustat is known as FG-4592. We performed two Phase 2 studies in China, one trial in NDD-CKD patients, and another trial in DD-CKD patients. In these trials, Hb correction in NDD-CKD patients and Hb maintenance in DD-CKD patients replicated the results seen in the US trials.

Study 047: 8 Week Placebo-Controlled NDD-CKD

In this multi-center, double-blind, placebo-controlled study, 91 anemic CKD patients were randomized 2:1 to roxadustat or placebo treatment groups, respectively, in two sequential dose cohorts or placebo. Iron repletion at baseline was not required and IV iron supplementation was prohibited during the trial; oral iron supplementation was allowed during the trial, similar to the corresponding US Study 041. The study used tier-weight starting dose for four weeks after which the roxadustat dose was adjusted, depending upon the initial response to treatment. Study 047 met its primary endpoint of a mean maximum increase from baseline Hb at the end of Week 8. The

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mean Hb increases at the end of eight weeks of treatment were 1.6 g/dL and 2.4 g/dL in the low-dose and the high dose cohort, respectively, compared to 0.4 g/dL for placebo, $p < 0.0001$ for each cohort compared to placebo.

FGCL-4592-047: Hb Over Time (g/dL) in Chinese NDD-CKD Patients

* n at baseline

Study 048: Stable Dialysis Conversion in China

In this multi-center, open-label, ESA-controlled study, 87 HD patients (of which 82 were efficacy evaluable) with Hb 9 to 12 g/dL previously maintained with ESAs were randomized 3:1 to roxadustat or epoetin alfa treatment groups, respectively, in three sequential dose cohorts of increasing starting doses of roxadustat. This study design was similar to Part 1 of Study 040. Study 048, an exploratory study, achieved its objective of number (%) of patients with successful dose conversion whose Hb levels are maintained at no lower than 0.5 g/dL below their mean baseline value at the end of Weeks 5 and 6 (59.1% for the low-dose, 88.9% for the mid-dose, and 100% for the high dose). The Hb responses to the roxadustat treatment of Chinese dialysis patients, with the low dose cohort were numerically similar to epoetin alfa, while the mid-dose and the high-dose cohorts each had a statistically significantly higher Hb response rate than epoetin alfa. Hb responses to the roxadustat treatment of Chinese dialysis patients (as shown in the figure below) were similar to Part 1 of Study 040 in the United States.

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FGCL-4592-048: Hb Over Time in Chinese Stable Dialysis Patients

Safety Summary

A range of roxadustat doses, up to 3.0 mg/kg in DD-CKD patients and up to 5.0 mg/kg in healthy volunteers, have been administered and all roxadustat doses have been well-tolerated. The following summarizes the safety findings of our preclinical, Phase 1 and Phase 2 studies:

No Overall Safety Signals. An independent data monitoring committee consisting of external experts in nephrology, hepatology, and biostatistics reviewed safety data from all US and Europe Phase 2 studies, and determined there were no safety signals. The overall frequency and type of treatment-emergent adverse events and serious adverse events, or SAEs, observed in these clinical studies reflect events that would be expected to occur in each of the NDD-CKD and DD-CKD patient populations. Safety analyses did not reveal any association between the rates of occurrence of cardiovascular events with roxadustat dose, rate of Hb rise or Hb level. The SAEs experienced in our studies identified by the principal investigator as possibly related to roxadustat were a stroke in a patient with a prior history of multiple strokes, one incident of vomiting, and one incident of deep venous thrombosis. The most commonly reported treatment emergent adverse events in the Phase 2 studies were diarrhea, nausea, urinary tract infection, nasopharyngitis, peripheral edema, hyperkalemia, headache, hypertension and upper respiratory tract infection.

Of our completed Phase 2 clinical studies, four (Studies 017, 047, 040 and 048) were controlled, two with placebo and two with ESA.

For Study 017, which had a treatment period of 4 weeks, for 88 subjects on roxadustat, and 28 subjects on placebo, we observed treatment emergent SAEs, or TSAEs, in 4 patients (4.5%) on roxadustat, with 0 cardiovascular SAEs and 0 SAEs for the composite safety endpoint. There were also TSAEs in 1 patient (3.6%) in the placebo arm of the study, including 1 cardiovascular SAE and 0 SAEs for the composite safety endpoint. The composite safety endpoint (exploratory analysis) includes death, myocardial infarction, congestive heart failure, subendocardial ischaemia, cerebrovascular accident, thrombosis (fistula), arteriovenous fistula occlusion, angina pectoris, and vascular graft thrombosis. A patient may experience more than one SAE, in which case a patient is only counted once in this

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analysis. TSAEs observed in patients treated with roxadustat were arteriovenous fistula site complications, dyspnea, femoral neck fracture and non-cardiac chest pain. SAEs observed in patients treated with placebo were acute renal failure and pericarditis.

For Study 047, which had a treatment period of 8 weeks, for 61 subjects on roxadustat, and 30 subjects on placebo, we observed TSAEs in 8 patients on roxadustat (13.1%), with 0 cardiovascular SAEs, and 0 SAEs for the composite safety endpoint, and TSAEs in 4 patients on placebo (13.3%), including 1 cardiovascular SAE (3.3%), and 1 SAE (3.3%) for the composite safety endpoint. TSAEs observed in patients treated with roxadustat were chronic renal failure (4), upper respiratory tract infection (1), hyperkalaemia (2) and urinary tract infection (1). TSAEs observed in patients treated with placebo were unstable angina (1), anemia (1), retinal detachment (1), pneumonia (1) and gastritis (1).

For Study 040, for those who had a treatment period of 19 weeks, for 66 subjects on roxadustat, and 23 subjects on ESAs, we observed TSAEs in 15 patients on roxadustat (22.7%), including 1 cardiovascular SAEs (1.5%), and 8 SAEs for the composite safety endpoint (12.1%), and TSAEs in 4 patients on ESAs (17.4%), including 2 cardiovascular SAEs (8.7%), and 4 SAEs (17.4%) for the composite safety endpoint. TSAEs categorized by System Organ Class, a standard event classification, observed in patients treated with roxadustat were infections and infestations (5), metabolism and nutrition disorders (2), cardiac disorders (1), gastrointestinal disorders (1), nervous system disorders (2), respiratory, thoracic and mediastinal disorders (2), skin and subcutaneous tissue disorders (1), injury, poisoning and procedural complications (2), and psychiatric disorders (1). TSAEs categorized by System Organ Class observed in patients treated with ESA were infections and infestations (3), metabolism and nutrition disorders (3), cardiac disorders (1), respiratory, thoracic and mediastinal disorders (1), blood and lymphatic system disorders (1) and vascular disorders (1).

For Study 048 which had a treatment period of 6 weeks, for 74 subjects on roxadustat, and 22 subjects on ESAs, we observed 0 TSAEs in patients on roxadustat, including cardiovascular SAEs and for the composite safety endpoint. There were also 0 TSAEs in the patients taking ESAs.

The differences in the SAE percentages described are not considered statistically significant.

The three SAEs described above that were considered by the principal investigator to be possibly related to roxadustat did not occur in these four studies.

No Liver Enzyme Safety Signal. Liver enzymes were monitored closely in the roxadustat Phase 2 clinical development program. No evidence of hepatotoxicity was observed in any of the roxadustat clinical trials, and the independent data monitoring committee concluded that there was no concern for hepatotoxicity to date. Liver enzymes are being monitored in Phase 3 according to current FDA guidelines, without any special requirements.

Extensive Evaluation of Cancer Risk. Furthermore, to assess the potential cancer risk of roxadustat, we conducted 12 tumor studies in rodents. These studies included xenograft, syngeneic, or spontaneous tumors of lung, colon, breast, pancreas, melanoma, ovarian, renal, prostate and leukemic origin, several of which are reported to be dependent on vascular endothelial growth factor, or VEGF, a protein that can be regulated by HIF for which increased levels have potentially been linked to increased tumor growth. No effect on tumor promotion was observed with roxadustat in any of the studies. In addition, roxadustat had no effect on tumor

initiation or metastasis in the studies in which these end-points were also measured. Five other HIF-PH inhibitors from our library have been evaluated in many of the same rodent tumor models as roxadustat, as well as some additional ones (35 studies of six HIF-PH inhibitors in 18 models total), with no observed effect on tumor initiation, promotion or metastasis. Finally, no significant increases in plasma VEGF levels have been observed in any of our nonclinical studies at clinically relevant erythropoietic doses of roxadustat. In March 2015, we received final reports for two-year rat and mouse carcinogenicity studies of roxadustat. Roxadustat treatment had no adverse effect on survival and did not cause carcinogenic effects in either species. Two-year rodent carcinogenicity studies that were conducted with one of the other HIF-PH inhibitors evaluated in the tumor models showed no effect on mortality or incidence of tumors.

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In clinical studies to date, we and our independent data monitoring committee have not identified any evidence to suggest tumor risk in the use of roxadustat.

No QT Prolongation. We conducted a Thorough QT study evaluating roxadustat doses up to 5 mg/kg (approximately four times the average maintenance dose studied in the NDD-CKD patient population). A lengthened QT interval is a biomarker for certain ventricular arrhythmias and a risk factor for sudden death. Our results demonstrate that roxadustat did not affect the QT interval in this study. Based on the extensive safety data collected to date, we believe that roxadustat has a favorable safety profile that supports its further development in Phase 3 clinical studies.

Our Global Phase 3 Program for Roxadustat

In support of our efforts for regulatory approval in the United States and Europe, we have initiated with our partners our global Phase 3 clinical program for roxadustat in North America, South America, Europe, Russia and Asia Pacific, with plans for expanding to other regions. FibroGen China will begin a separate Phase 3 program in China in the second half of 2015, and Astellas is responsible for Phase 3 studies upon completion of Phase 2 studies in Japan. Roxadustat is the first HIF-PH inhibitor to enter Phase 3 clinical trials. We believe that our ongoing global Phase 3 program will be the largest Phase 3 program ever conducted for an anemia agent. This broad Phase 3 program is designed to meet regulatory approval requirements of multiple regions, and is being jointly implemented with our partners, Astellas and AstraZeneca. The below chart summarizes our ongoing and planned Phase 3 clinical trials, all of which include Hb level maintenance as a study objective once correction or conversion is achieved.

Ongoing and Planned Roxadustat Phase 3 Clinical Trials

Study Number, Enrollment Start Date for Ongoing Trials	**Company Sponsor**	**Dose Frequencies for Ongoing Trials**	**Comparator**	**Estimated # of Patients to be Enrolled**	**Randomization**	**Study Objective**
United States and Europe Trials						
NON-DIALYSIS						
FGCL-4592-060, November 2012	FibroGen	TIW, BIW, QW	Placebo	Up to 600	2:1	Correction
1517- CL-0608, October 2013	Astellas	TIW, BIW, QW	Placebo	450 to 600	2:1	Correction
D5740C00001, July 2014	AstraZeneca	TIW	Placebo	2,600	1:1	Correction
1517-CL-0610, April 2014	Astellas	TIW, BIW, QW	Darbepoetin alfa	570	2:1	Correction
		NDD-CKD Sub Total		**4,000 to 4,500**		
DIALYSIS						

Stable and Incident Dialysis						
* FGCL-4592-063, February 2014	FibroGen	TIW	Epoetin alfa	Up to 750	1:1	Correction
1517- CL-0613 December 2014	Astellas	TIW	Epoetin alfa or Darbepoetin alfa	750	376:200:174	Conversion
FGCL-4592-064 January 2015	FibroGen	TIW	Epoetin alfa	750	1:1	Conversion
* D5740C00002, July 2014	AstraZeneca	TIW	Epoetin alfa	1,425	1:1	Correction & Conversion
			DD-CKD Sub Total	**3,000 to 3,700**		
NDD and DD-CKD Total for the U.S. and EU				**7,000 to 8,000**		
			China Trials			
Non- Dialysis						
FGCL-4592-808	FibroGen	TIW	Placebo	150	2:1	Correction
Stable Dialysis						
FGCL-4592-806	FibroGen	TIW	Epoetin alfa	300	2:1	Correction & Conversion
			China Total	**450****		

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TIW = three times weekly; BIW = twice weekly; QW = weekly

* Study 063 consists of only incident dialysis patients, Study 002 consists of both incident dialysis patients and conversion of stable dialysis patients. All other dialysis studies consist of only conversion of stable dialysis patients.

** Mandatory post-approval safety study of approximately 2,000 patients expected to be required in China.

The below chart summarizes the planned and ongoing Phase 3 clinical trials by regulatory approval region, emphasizing the differences in estimated patients enrolled, minimum and average treatment durations, and resulting patient years (the product of estimated number of patients and average patient treatment duration). The studies supporting both U.S. and EU approval have extended treatment durations in the U.S. (52+ weeks) as compared with the EU (36+ weeks).

Regional Differences in Estimated Approval Requirements

Roxadustat Phase 3 Clinical Trials

			Estimated # of Patients to be Enrolled		
	Study Sponsor	**Study Number**	**United States**	**Europe**	**China**
Non-Dialysis					
	FibroGen	FGCL-4592-060	Up to 600*	Up to 600*	
	Astellas	1517-CL-0608	450-600*	450-600*	
	AstraZeneca	D5740C00001	2,600		
	Astellas	1517-CL-0610		570	
	FibroGen	FGCL-4592-808			150
NDD-CKD Sub Total by Region			Up to 3,800	Up to 1,770	150
Stable and Incident Dialysis					
	FibroGen	FGCL-4592-063**	Up to 750*	Up to 750*	
	Astellas	1517-CL-0613	750*	750*	
	FibroGen	FGCL-4592-064	750*	750*	
	AstraZeneca	D5740C00002**	1,425		
	FibroGen	FGCL-4592-806			300
DD-CKD Sub Total by Region			Up to 3,675	Up to 2,250	300
Total by Approval Region			**~7,500**	**~4,000**	**450*****
Combined U.S. and EU total			**~7,000**	**8,000**	
Minimum Treatment Duration			52 Weeks	36 Weeks	26-52 Weeks
Average Patient Treatment Duration			~1.3-1.5 years	~1 year	~32 Weeks****
Patient Years by Approval Region			**~10,000+**	**~4,000**	**~275**
Estimated Time to Complete Patient Enrollment			1H 2016		1H 2016

* Same patients used for U.S. approval and Europe approval, with extended treatment durations for U.S. approval.

**

Study 063 consists of only incident dialysis patients, Study 002 consists of both incident dialysis patients and conversion of stable dialysis patients. All other dialysis studies consist of only conversion of stable dialysis patients.

*** Mandatory post-approval safety study of approximately 2,000 patients expected to be required in China.

**** 350 patients will be treated for a minimum of 26 weeks and 100 patients will be treated for a minimum of 52 weeks.

To maximize the commercial potential for roxadustat, we have incorporated several unique elements into our Phase 3 program. We are performing the first placebo-controlled Phase 3 studies in NDD-CKD patients to potentially demonstrate the benefits of anemia therapy and safety of roxadustat compared to placebo. We are also

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performing the largest Phase 3 study in incident dialysis anemia patients, who have the highest risk for death, and are the most difficult patients to stabilize and treat for anemia in CKD. Based on data from our Phase 2 studies, we believe that roxadustat may offer a safer alternative to ESAs for this particularly vulnerable patient population. We are also evaluating the cardiovascular safety of roxadustat compared to placebo in NDD-CKD patients to first demonstrate a lack of increased risk to qualify for marketing approval by the FDA, and in these patients we will have an opportunity to measure improvements in patient outcomes with anemia therapy. Separately, we are evaluating cardiovascular safety of roxadustat compared to ESA in DD-CKD patients.

Primary and Secondary Endpoints of Our Phase 3 Program

With our partners, we have designed our Phase 3 studies to evaluate the following endpoints, most of which were evaluated in our Phase 2 studies.

Primary efficacy endpoints for anemia correction studies:

U.S.: Hb change from baseline to the average Hb level during weeks 28-52.

EU: Cumulative % patients with Hb response by week 24. Hb response is defined as Hb of 11 g/dL and an increase of at least 1 g/dL from baseline.

Primary efficacy endpoints for conversion and maintenance studies:

U.S.: Hb change from baseline to the average Hb level during weeks 28-52.

EU: Hb change from baseline to the average Hb level during weeks 28-36.

The primary safety endpoints for U.S. approval will be major adverse cardiac events, commonly referred to as MACE, which is a composite endpoint designed to identify major safety concerns, in particular relating to cardiovascular events such as cardiovascular death, myocardial infarction and stroke, and will be pooled across multiple studies and evaluated separately in our NDD-CKD trials and our DD-CKD trials.

We expect that our Phase 3 clinical trials supporting approval in Europe will be required to include MACE+ as a safety endpoint which, in addition to the MACE endpoints, also incorporates measurements of hospitalization rates due to heart failure or unstable angina.

We also plan to evaluate secondary endpoints, including the following:

IV iron usage in roxadustat-treated patients relative to ESA-treated patients with DD-CKD.

Red blood cell transfusion rate in roxadustat-treated relative to placebo treated patients with NDD-CKD.

Hypertension adverse events in roxadustat-treated patients relative to ESA-treated patients with DD-CKD, and blood pressure in roxadustat-treated patients relative to placebo-treated patients with NDD-CKD.

Total cholesterol, LDL-cholesterol and VLDL-cholesterol levels in roxadustat-treated patients relative to placebo-treated patients with NDD-CKD and relative to ESA-treated patients in all three anemic CKD patient populations.

Quality of life in roxadustat-treated patients relative to placebo-treated patients with NDD-CKD.

CKD progression in roxadustat-treated patients relative to placebo-treated patients with NDD-CKD.

Hospitalization rate in roxadustat-treated patients relative to placebo-treated patients with NDD-CKD and relative to ESA-treated patients in all three anemic CKD patient populations.

Rate of vascular access thrombosis in roxadustat-treated patients relative to ESA-treated patients in DD-CKD.

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Dosing Regimen

Our Phase 3 studies incorporate dosing regimens that were extensively tested in our six Phase 2 studies.

Identified Dosing Regimen. The dosing regimens for our Phase 3 studies are designed to achieve an appropriate rate and magnitude of Hb rise. In our Phase 2 studies, we explored ranges of therapeutic doses under several dosing regimens, including both tier-weight and fixed starting doses and conversion doses. Our Phase 3 program will use two tier-weight starting doses for ESA-naive patients (70 mg for patients between 45 and 70 kg and 100 mg for patients between 70 and 160 kg). Our Phase 3 dosing strategies are based on our understanding of effective approaches, derived from our Phase 2 studies, tested in modeling and simulation, and were designed to achieve Hb correction for patients with varying dose requirements in a manner that is optimal for both patients and physicians.

Dose Titration. Our Phase 3 program will use a pre-determined sequence of dose steps to titrate to a patient s particular response to roxadustat, which we found to be simple to use and sufficient to correct anemia in our Phase 2 studies. In our Phase 2 anemia correction studies, only one or two cycles of dose titration were necessary to achieve Hb correction in at least 80% of patients on average.

Dose Conversion for Dialysis Patients Previously Treated with ESAs. In our Phase 2 conversion studies, we tested a variety of starting doses and developed a mathematical relationship between baseline ESA dose and roxadustat dose required to maintain Hb levels. We use dose conversion tables derived from these Phase 2 studies to formulate starting roxadustat doses in our Phase 3 trials for patients who switch to roxadustat from ESAs.

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Dose Frequency. In preclinical and Phase 1 studies, we observed that intermittent dosing yielded optimal responses to roxadustat. Our Phase 2 studies indicated that three times weekly, twice weekly and weekly dosing regimens achieved Hb maintenance. Our Phase 3 program will dose three times weekly for all studies except two (060 and 0608) which will dose some patients twice per week and some patients once per week. We believe that intermittent dosing may help ensure a consistent and durable treatment effect for several reasons:

Greater Hb Response While Minimizing Total Drug Exposure. Early preclinical studies in rodents with a HIF-PH inhibitor (that was not FG-4592) indicated that a greater Hb response could be achieved using a lower total weekly dose with intermittent dosing compared to daily dosing. In the studies shown below, rats were dosed with HIF-PH inhibitor using either a twice weekly dosing regimen. Both a higher Hb response and a better dose response were observed in animals dosed with HIF-PH inhibitor twice weekly compared to animals that were dosed daily. Furthermore, the total weekly dose required to achieve this greater Hb response was lower.

In addition, our previous preclinical studies suggested that a wider therapeutic window was achieved with intermittent dosing compared with daily dosing. Preclinical observations such as these led us to conclude that intermittent dosing could enable a better Hb response with a lower overall drug exposure and offer a potentially wider therapeutic window.

Reduce the Risk of Changing the HIF Set Point. The HIF system has a built-in negative feedback mechanism. Genes for two of the PHD enzymes that are responsible for degrading HIF under normal oxygen conditions are actually HIF target genes. Thus, while these PHD enzymes are inhibited by hypoxia (or by a HIF-PHI), the resulting HIF activation leads to an increase in the very enzymes that are responsible for its degradation following the re-oxygenation (or potentially removal of the HIF-PHI). This negative feedback mechanism is important in enabling the HIF system to reset. However, under chronically hypoxic conditions, it has been shown that the elevation in PHD enzyme levels is maintained, leading to a change in the HIF set-point. Based on this knowledge of HIF biology, it is our belief that prolonged HIF activation by a HIF-PHI drug could similarly lead to a change in the HIF set-point, which we believe may then require an

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increased HIF-PHI dose to elicit the same HIF response. In an effort to avoid this potential risk, and to potentially prolong drug effectiveness, we have undertaken an intermittent dosing regimen.

Increase Intervals Between HIF Activation. The kinetics of HIF target gene induction (including genes encoding PHD enzymes) are variable, with some HIF target genes being induced very quickly after HIF activation and others requiring longer periods of HIF activation for significant induction. We believe that increasing the intervals between HIF activation using an intermittent dosing regimen has the potential to limit the HIF target gene response.

Potential Commercial Advantages. We expect that a dosing regimen that enables dosing concurrently with hemodialysis treatment, typically administered on a thrice weekly basis, will be more commercially attractive in the dialysis market.

Our Phase 2 studies indicated that intermittent dosing enabled anemia correction up to 24 weeks and Hb maintenance up to 19 weeks when converting a patient from ESA.

Clinical Trial Eligibility, Iron Status, and Iron Supplementation During Treatment

Unlike ESA clinical trials where patient study eligibility criteria included a requirement of adequate iron availability (measured by ferritin ³ 100 ng/mL and TSAT ³ 20%) and encouraged IV iron use, roxadustat Phase 2 studies included anemic NDD-CKD patients with ferritin ³ 30 ng/mL and TSAT³ 5% and anemic DD-CKD patients with ferritin ³ 50 ng/mL and TSAT ³10%, which permits the inclusion of patients who are iron deficient. Hemoglobin response was generally achieved in iron deficient NDD-CKD and DD-CKD patients (ferritin <100 ng/mL and TSAT< 20%) despite the fact that IV iron was not allowed during roxadustat treatment.

Our placebo-controlled Phase 3 NDD-CKD studies will use iron eligibility criteria employed in our Phase 2 studies, allow oral iron, but prohibit the use of IV iron (except as a rescue medication). In our Phase 3 DD-CKD studies, since ESA serves as the comparator and similar treatment conditions are required for roxadustat and ESA, study eligibility criteria include ferritin ³ 100 ng/mL and TSAT ³ 20%. Patients will be randomized to roxadustat or ESA, and will be encouraged to take oral iron as a first line supplemental agent. IV iron is permitted if there is inadequate Hb response to treatment and if the patient is iron deficient (ferritin <100 ng/mL and TSAT< 20%).

Status with Regulatory Agencies

In the last two years, we and our collaboration partners have had interactions with regulatory agencies in multiple territories regarding the planned development and potential path to approval of roxadustat.

Most recently, we met with the FDA in May, June and July of 2014 to discuss the overall scope of our Phase 3 development program. In order to comply with FDA s recommendation, we have designed and sized our Phase 3 program for, and will incorporate MACE composite safety endpoints that we believe will be required for approval in the United States for all new anemia therapies.

We have also discussed our Phase 3 clinical development program with three National Health Authorities in the EU and obtained scientific advice from the European Medicines Agency, which was confirmed in writing in January 2014 with respect to the adequacy of our current clinical development program to support the indication for the treatment of anemia in NDD-CKD and DD-CKD patients. We expect the MAA submission in Europe to precede our NDA filing in the United States.

Investigational New Drug and Clinical Trial Applications

Roxadustat is being studied under one Investigational New Drug Application, or IND, and several Clinical Trial Applications, or CTAs, all with a specified indication of treatment of anemia in CKD. We originally submitted the IND in the United States to the FDA in April 2006. Our collaboration partner, Astellas, submitted the CTA in

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Japan to the Pharmaceuticals and Medical Devices Agency in June 2009. We and our collaboration partners Astellas and AstraZeneca have also submitted CTAs in Europe, Latin America, Canada, Russia, and Asia, beginning in 2013.

Opportunities in Other Anemia Indications

Based on roxadustat s safety and efficacy profile to date and other potential advantages over ESAs, we believe that in addition to treating anemia in CKD, roxadustat has the potential to treat anemia associated with many other conditions, such as chemotherapy-induced anemia, anemia related to inflammatory diseases, MDS and surgical procedure requiring transfusions. We think that roxadustat, if successful, could potentially address the significant unmet need in these anemia markets.

HIF-PH Inhibitor Platform

We have been a world leader in prolyl hydroxylase inhibition since the mid-nineties. Over the past two decades, we have built a robust drug discovery platform based on our deep understanding of the inhibition of prolyl hydroxylase enzymes using small molecules. Our platform is supported not only by internal research but also by numerous academic collaborations, including a long-standing funded collaboration with a research group at the University of Oulu, Finland, headed for many years by our scientific co-founder, Dr. Kari I. Kivirikko. Dr. Kivirikko is one of the world s leading experts in collagen prolyl hydroxylases, and he remains an advisor to us.

Prior to the discovery of HIF regulation by prolyl hydroxylase activity, we had acquired compound collections from several pharmaceutical companies and assembled a diverse library of prolyl hydroxylase inhibitors to target collagen prolyl hydroxylase enzymes for fibrosis. Consequently, we were particularly well positioned to rapidly generate proof-of-concept for a number of aspects of HIF biology, and to direct medicinal chemistry efforts towards increasing potency and selectivity for the newly identified HIF-PH enzymes.

We have applied our expertise in the field of HIF-PH inhibition to develop an understanding, not only of the role of HIF in erythropoiesis, but also of other areas of HIF biology with important therapeutic implications. This consistent progression of discovery has led to findings relating to HIF-mediated effects associated with inflammatory pathways, various aspects of iron metabolism, insulin sensitivity and glucose and fat metabolism, neurological disease, and stroke. The extensive patent portfolio covering our discoveries represents an important competitive advantage.

The strength of our platform capitalizes on these internal discoveries, as well as some of the complexities of HIF biology that we and the scientific community have uncovered over the past decade. There are at least three different HIF-PH enzymes that are known to regulate the stability of HIF these enzymes are commonly referred to in the scientific literature as PHD1, PHD2 and PHD3. Studies of genetically modified mice, in which the individual HIF-PH enzymes have been deleted, have revealed that PHD2 plays a major role in the regulation of erythropoiesis by HIF. In contrast, PHD1 and PHD3 appear to play less important roles in HIF-mediated erythropoiesis, but instead have been implicated in other important biological pathways.

We believe that inhibitors selectively targeting PHD1 or PHD3 could have important therapeutic applications beyond anemia. For example, as PHD1 has been implicated in ischemic tissue injury, it has been proposed that PHD1 inhibitors may provide a novel therapeutic approach to protect organs and tissues from ischemic damage. PHD3 on the other hand has been implicated in insulin signaling, raising the possibility that PHD3 inhibitors may have therapeutic utility in the treatment of diabetes. Despite the challenges associated with selectively inhibiting just one enzyme from a closely related family, we have made important advances in the identification of selective HIF-PH inhibitors. We currently have active research programs focused on exploring the therapeutic utility of PHD1 selective inhibitors and PHD3 selective inhibitors. A lead candidate from our PHD1 inhibitor program, FG-8205, is currently in

preclinical evaluation for use as a cardioprotective agent to prevent the onset of heart failure following a heart attack.

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In addition, FG-6874, another novel HIF-PH inhibitor selected from our proprietary compound library, has recently completed Phase 1 single dose and multiple dose studies in which it was found to be well tolerated. We are planning on exploring FG-6874 for hematopoietic stem cell mobilization and certain other indications.

In September 2011, we submitted a CTA in Singapore for our HIF-PH inhibitor FG-6874; however, no indication was specified under this CTA as it was for a Phase 1 trial. While we have other HIF-PH inhibitors in preclinical evaluation, such as FG-8205, we have not submitted any INDs or CTAs with respect to such compounds at this time.

ROXADUSTAT FOR THE TREATMENT OF ANEMIA IN CHRONIC KIDNEY DISEASE IN CHINA

We believe there is a particularly significant unmet medical need for the treatment of anemia in CKD in China. Specifically, anemia is undertreated in the rapidly growing number of dialysis stage patients and anemia is not treated in non-dialysis patients including patients who are eligible for dialysis but are not treated due to a shortage of dialysis facilities, and cannot easily obtain anemia treatment outside of the dialysis system. In the context of the rapidly growing Chinese pharmaceutical market, we believe that the demand for anemia therapy will continue to grow as a result of an expanding CKD population, as well as the central government s mandate to make dialysis, which is still in the early stages of infrastructure development, more available through expansion of government reimbursement and build-out of dialysis facilities. We believe that roxadustat is a particularly promising product candidate for this market.

Addressable Patient Populations in China

Based on a cross-sectional survey performed between September 2009 and September 2010 published in the *Lancet* (Zhang, et al. *Lancet* (2012)), there are an estimated 119.5 million CKD patients in China. There were approximately 19 million patients in CKD stage 3, stage 4 and stage 5 which we have grouped into three categories: dialysis dependent CKD patients, or DD-CKD; Dialysis Eligible patients who need dialysis under treatment guidelines but are not dialyzed, or Dialysis Eligible NDD-CKD; and stages 3 and 4 patients as well as stage 5 patients who are not eligible for dialysis, or Other NDD-CKD.

DD-CKD (Dialysis)

Dialysis can be delivered in the form of hemodialysis, or HD, or peritoneal dialysis, or PD. In China, HD is mostly performed at dialysis clinics within hospitals, not at freestanding dialysis centers outside of hospitals which is the common practice in the United States. PD is self-administered at home by patients, and they visit their nephrologists on a monthly basis at the hospital for monitoring and follow-up.

Dialysis Eligible NDD-CKD

Dialysis Eligible NDD-CKD refers to patients who need dialysis under Chinese treatment guidelines but are not dialyzed. The Chinese treatment guidelines recommend initiation of dialysis at eGFR<10 mL/min/1.73 m^2 (and eGFR<15 mL/min/1.73m^2 for diabetic nephropathy patients). The Minister of Health estimated that one to two million people in China were eligible for dialysis in 2011, and of those we believe that only 300,000 to 400,000 are on dialysis. While the size of dialysis population is large and approaches that of the United States, it nevertheless falls far short of the number who require dialysis treatment. We believe that this Dialysis Eligible NDD-CKD population is characteristic of developing markets like China and is at risk for severe anemia.

Other NDD-CKD

Other NDD-CKD refers to the other sub-groups of CKD patients within non-dialysis who are earlier stage: CKD patients in stage 3 and stage 4, as well as stage 5 who are not eligible for dialysis. Many of these patients receive medical care in endocrinology, cardiology or internal medicine clinics where they are treated for their primary disease.

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Unmet Medical Need

DD-CKD Patients are Under-Treated for Anemia

We believe there is chronic under-treatment for anemia within the DD-CKD patient population, as many patients do not reach target Hb levels despite ESA therapy. The consensus opinion of the expert panel assembled by the Chinese Journal of Nephrology in 2013 advocated treating to Hb 11.0 g/dL to 13.0 g/dL, whereas we believe, based on our key opinion leader Advisory Board Meeting in Shanghai in March 2013 that in clinical practice, nephrologists generally use Hb 10.0 g/dL to 12.0 g/dL as the target. However, according to the 2012 Shanghai Dialysis Registry, approximately 50% of patients in Shanghai did not exceed a Hb level of 10.0 g/dL and approximately 75% did not exceed Hb 11.0 g/dL. Over 19% of dialysis patients failed to reach a severely low Hb level of 8.0 g/dL. The Chinese Renal Data System reported that in 2011, the most recently reported data, the average Hb level of DD-CKD patients in the registry was approximately 9.1 g/dL and the percentage of patients who reached Hb levels greater than or equal to 11.0 g/dL was only about 21%.

We believe there are a number of factors that have led to under-treatment of anemia in the dialysis population, including:

- The ESA doses used are generally not sufficient to treat to target Hb levels for certain patient populations. We believe that the reasons include constraints on reimbursement for anemia treatment and fixed hospital pharmacy budgets, as well as safety and efficacy limitations of these drugs. Lower dose levels are particularly ineffective in the hypo-responsive patient population.

- The use of IV iron, which is often needed to correct Hb to target levels with ESAs, is limited due to limited reimbursement and perceived clinical risk. According to the Shanghai Dialysis Registry, in 2011, less than 9% of dialysis patients in Shanghai were treated with IV iron.

- For the PD population, where patients are not already visiting the hospital for HD and are receiving ESA treatment during dialysis, similar logistical and financial issues that impede ESA use in the NDD-CKD population discussed below apply to these patients.

Dialysis Eligible NDD-CKD and Other NDD-CKD Patients are Largely Un-Treated for Anemia

Apart from the ESAs used by the dialysis patients in China, we believe that there is a low level of use of ESAs in the non-dialysis population. Based on our clinical trial experience in China, we believe use of ESAs in this population is generally limited to CKD Clinics at major research hospitals in top cities where CKD patients are admitted into programs for academic research purposes. We believe there are a number of significant impediments that inhibit the use of ESAs in the outpatient setting, for patients who are not already visiting the hospital for dialysis treatment on a regular basis.

- Generally, under the Chinese healthcare system, patients do not have a personal physician but rather are seen by the physician on the schedule on the day of the visit. This limited continuity of care makes managing the potential risks of ESAs and the titration of ESA treatment needed to maintain Hb within target range

particularly difficult.

Hypertension and associated co-morbidities are top risk factors for the CKD population. Many physicians in China believe that for the outpatient NDD-CKD population, the risk of developing new or exacerbating existing hypertension from ESA with the attendant risk of worsening renal failure outweigh the benefits of treating anemia.

Injectable drugs like ESAs present a challenge in China because even subcutaneous administration is performed at hospitals and not in the home. Frequent hospital visits for injections, for the sole purpose of receiving ESA treatment, can present a substantial logistical and financial burden on patients.

Nephrologists are the primary prescribers of ESAs. Those CKD patients with hypertension or diabetes who are treated by other physicians, such as cardiologists and endocrinologists, are generally not treated with ESAs.

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Non-dialysis patients are covered under outpatient reimbursement, unlike dialysis patients who are covered under Severe Disease reimbursement, when available. The lower level of reimbursement coverage means a higher patient co-pay, which further limits ESA use and compliance.

We believe that these impediments have contributed to a low rate of ESA use in the NDD-CKD population in China, and that roxadustat, as an oral agent triggering the HIF mechanism of action, has the potential to make this population accessible for effective anemia treatment in CKD.

Growing Market Opportunity

Healthcare expenditures in China have more than doubled over the past five years, from $156 billion in 2006 to $357 billion in 2011. China is projected by IMS Health to become the world s second largest pharmaceutical market after the United States by 2016 (IMS Market Prognosis, May 2012). We believe several factors will continue to drive the growth of the overall pharmaceutical market in China as well as the market for the treatment of anemia in CKD. These factors include continuing urbanization, an aging population and the increasing prevalence of chronic diseases (particularly diabetes and hypertension which are common causes of CKD), and income growth. We also believe that the increasing standard of living will drive higher rates of disease awareness, leading to greater rates of diagnosis and treatment.

The strong growth in the China healthcare sector is a direct result of central government policy. In 2009, the Chinese government implemented healthcare reform that greatly expanded reimbursement coverage across population, scope, and level of coverage, and in 2011, the 12th Five Year Plan placed the biomedical industry and development of innovative medicines as a strategic priority for the country. The following table shows the growth and size of the China healthcare market:

	2006 ($US)	2011 ($US)
Total Healthcare Expenditures	$156 billion	$357 billion
Per Capita Healthcare Expenditures	$119	$261
Market Size for Pharmaceuticals	$27 billion	$71 billion
Percentage of Population with Health Insurance	43%	>95%
China in Global Ranking of Pharmaceutical Markets	9th	3rd

Source: Health care in China: Entering uncharted waters , McKinsey & Company, healthcare systems and services practice, November 2012

Current ESA Market Size and Drivers of Market Growth in China

Total ESA sales in China were approximately $145 million in 2013, and the ESA market in China has grown at a 25% compound annual growth rate between 2006 and 2013 based on data from IMS Health.

We believe that given the limited availability of dialysis in China, dialysis is still in the early stages of development relative to the United States, and has the potential for sustained long-term growth. We believe growth of dialysis will be driven by the expansion of reimbursement and expansion of dialysis facilities. We further believe that the growing pipeline of CKD patients and expansion of reimbursement will drive growth in demand for anemia treatment in CKD patients.

Expansion of Reimbursement. Reimbursement exists for the use of ESAs in the treatment of anemia in CKD and the coverage levels are expanding. Under Basic Medical Insurance, the reimbursement program for the urban population, coverage for healthcare and drugs is categorized into one of three categories: outpatient, inpatient, and Severe Disease. Both the Dialysis Eligible and Other NDD-CKD patients are reimbursed under outpatient coverage. As an example, coverage levels for outpatient are in the 60-85% range in Shanghai, depending on level of hospital visited and patient age. Dialysis patients,

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on the other hand, receive reimbursement under the more generous Severe Disease coverage, which is reimbursement for catastrophic healthcare expenditures. Coverage levels are set at a minimum level of 50% by policy and are as high as 85% for employees and 92% for retirees in Shanghai. We expect the availability of Severe Disease reimbursement to significantly drive the utilization of dialysis services and ESAs in the coming years.

Expansion of Dialysis Infrastructure. The number of DD-CKD patients increased from approximately 70,000 in 2007 to an estimated 300,000 to 400,000 in 2013 and has grown at a compound annual growth rate of 25% to 30% per year from 2007 to 2013. Despite this substantial rate of growth, the Ministry of Health and the Chinese Society of Nephrology have publicly recognized the need for further investment in dialysis infrastructure to accommodate the expected continued growth of the patient population requiring dialysis. PD is an alternative to HD and does not require the level of capital investment in facilities and equipment that is necessary to enable HD. At the end of 2012, PD was estimated to account for 10% of the current dialysis population.

Demographics-Driven Growth. Diabetes and hypertension are common causes of CKD, the rates of which have been growing in China over past two decades. China is experiencing epidemiological changes in metabolic diseases due to economic development, urbanization and an aging population. We believe the increase in diabetes and hypertension prevalence will result in increasing numbers of patients with CKD in the future.

Our China Solution

We believe that roxadustat, if approved, has the potential to address the unmet medical need for the treatment of anemia in each of the three categories of CKD patients in China. Several of the safety, efficacy, reimbursement and convenience advantages that roxadustat, our oral therapeutic, potentially offers over ESAs (see Our Solution Roxadustat A Novel, Orally Administered Treatment for Anemia) are particularly applicable in the China market.

Roxadustat May Address Chronic Under-Treatment in DD-CKD Patients

We expect roxadustat to be viewed as more attractive than ESAs, and particularly attractive within certain categories of the dialysis population patients who are not treated to target Hb levels for any reason, patients who are hyporesponsive to ESAs, patients on PD, which is home-based, and DD-CKD patients who have not previously received ESA treatment.

Roxadustat May Increase Rate of Successful Anemia Treatment. We believe that the level of ESA dosing generally used in China is not adequate to achieve target Hb levels for many dialysis patients, especially with minimal use of IV iron. The dose levels used are within a very narrow range due to clinical concerns over ESA safety at higher doses. Moreover, reimbursement limits may cap ESA dose. In contrast, assuming roxadustat is approved, we believe we can price roxadustat so that reimbursable doses of roxadustat will be sufficient to treat most patients to target Hb levels.

Roxadustat May Address Hyporesponsiveness. Hyporesponsive patients, who often fail to respond to ESA treatment, in particular are often inadequately treated due to need for significantly higher doses of ESAs. Our data suggest that roxadustat may be safe and effective in this patient population without the use of high doses.

Roxadustat May Reduce Requirements for IV Iron. ESAs generally require IV iron for effective anemia treatment, and IV iron use is limited in China due to limited reimbursement and perceived clinical risk. Roxadustat potentially eliminates the need for IV iron to reach treatment target.

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Roxadustat May Address Lack of Access of ESA Treatment in NDD-CKD Patients

We view NDD-CKD as the segment where roxadustat, with the benefits of the HIF mechanism of action and being an orally administered small molecule, could potentially represent the only viable treatment solution for this patient population.

Roxadustat May Make Treatment Accessible and Feasible. As an oral agent, roxadustat eliminates the need for frequent hospital visits which are needed for ESA administration, decreasing the overall cost and inconvenience of treatment, particularly for DD-CKD patients undergoing PD who are otherwise treated in the home, as well as Dialysis Eligible NDD-CKD and Other NDD-CKD patients.

Roxadustat May Have an Improved Safety Profile. ESA treatment is associated with an increased risk of severe adverse events including hypertension, stroke, myocardial infarction and death. Our data suggest that roxadustat may not increase the risk of these events and therefore may be safer than ESAs thereby potentially removing a significant deterrent to anemia therapy in China.

Roxadustat May Add Value in Both the NDD-CKD and DD-CKD Patient Populations

Roxadustat May Reduce Overall Cost of Treatment Associated With Anemia. For the equivalent reimbursement cost to the government, we believe that roxadustat may deliver a higher potential clinical benefit compared to ESAs. Roxadustat, if approved, could treat patients to target Hb level. Roxadustat could also potentially lower the use of IV iron and anti-hypertensives. Moreover, the total cost of care would be reduced by lowering loss of time and cost of hospital-based ESA injections, and eliminating the infrastructure costs necessary to store ESAs in a cold storage environment. Finally, patients would benefit by reducing the cost of travel to the hospital and the potential lost wages for hospital visits.

Commercialization

Regulatory Strategy

We plan to seek product approval from the China Food and Drug Administration, or CFDA, as a Domestic Class 1.1 drug through our China subsidiary, FibroGen China. FibroGen China submitted a CTA to the CFDA for roxadustat for the treatment of anemia in CKD in March 2013. This Domestic Class 1.1 designation allows us to use the green channel , which may facilitate expedited approval with access to the regulatory authorities for formal and informal dialogue about development plans. We believe the domestic pathway represents the fastest route for bringing roxadustat to market and providing patients with access to a potentially safer, more effective, more convenient and more accessible therapy.

We believe the development of roxadustat is aligned with the Chinese government s current policies. The Chinese government is building dialysis infrastructure to address the unmet need for dialysis. We believe that anemia treatment is a critical component of any national dialysis program, and the cost of anemia treatment is an important factor in the public health burden of CKD.

FibroGen China has completed Phase 1 and Phase 2 clinical trials in China and expects to start Phase 3 clinical trials in China in the second half of 2015, with Phase 3 data expected in the second half of 2016 and, assuming the Phase 3

clinical trial is successful, possible NDA approval in China in mid-2017. However, actual dates depend on a variety of factors and are subject to numerous risks and uncertainties, including with respect to patient enrollment, safety results, manufacturing, third party contractors and government regulators, some of which are out of our control (such as the recent backlog in CFDA review of pending clinical trial applications). See also Risk Factors beginning on page 100, and particularly those risk factors under the heading Risk Related to the Development and Commercialization of Our Product Candidates. These trials have been conducted, and will continue to be conducted, in parallel with but independently of the other trials conducted in the global roxadustat development program. All available safety data from the global program will be included in the China NDA submission.

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Manufacturing Certification

FibroGen China plans to secure all New Drug and Manufacturing Licenses (including a Drug Approval Code) required for commercialization of roxadustat in China. A Manufacturing License is fundamental for production and sale of drugs in China, and it is the Manufacturing License, not the New Drug License which is granted at NDA approval, that gives FibroGen China the right to market roxadustat. With the Manufacturing License, FibroGen China will have the right to sell roxadustat (issue fa-piaos , or invoices, for the sale) into the highly regulated pharmaceutical distribution system, and recognize revenues for such sale. FibroGen China will also have the right to negotiate pricing with the government and the right to apply for reimbursement for roxadustat.

FibroGen China has completed construction and validation of its manufacturing facility in Beijing. We received a Pharmaceutical Production Permit, which is a general manufacturing license, for the manufacturing facility in August 2014, and we expect to receive the Manufacturing Licenses that will be necessary to manufacture roxadustat in the next few years after successful completion of the registration and GMP validation campaigns. *(See Manufacture and Supply and Government Regulation Regulation in China).*

Market Segmentation

We believe DD-CKD market in China is readily addressable in the near term, and we believe roxadustat has the potential to deliver a compelling value proposition in particular to certain subgroups within DD-CKD: patients who are not treated to target Hb levels for any reason, patients who are hypo-responsive to ESAs, and patients on PD, which is performed at home. In addition, we believe that roxadustat, if approved, would have the potential to be the preferred anemia treatment for newly-initiated dialysis patients who have not been previously treated with ESA. With the expected expansion of Severe Disease reimbursement, we believe that the number of DD-CKD patients will increase steadily. We believe that it could require more than a decade for China to address the treatment gap between patients who need dialysis and those who are actually dialyzed.

If roxadustat is approved, we believe the Dialysis Eligible NDD-CKD population could represent another readily accessible and potentially new market segment for anemia therapy. There is an urgent and severe unmet medical need for these very sick patients, and the current low rate of treatment within this patient group could be addressed by an approved anemia treatment such as roxadustat. We view the Other NDD-CKD population as a longer term market opportunity where the potential number of patients could be substantial.

We believe the hospital-based nature of the China healthcare system is a very attractive feature of this market as it lends itself to rapid adoption of roxadustat within nephrology practices and across specialties, unlike in the United States where dialysis is performed separately at freestanding dialysis centers and CKD is treated at widely dispersed clinics and primary care offices across the country. In China, within nephrology, the same physicians care for dialysis, Dialysis Eligible NDD-CKD and Other NDD-CKD patients. Moreover, cardiologists and endocrinologists are located at the same hospitals as nephrologists, and prescriptions from all specialties are often filled at the same hospital pharmacy; as a result, the points of sale are highly concentrated.

Reimbursement

As roxadustat is potentially a chronic use drug that addresses an unmet medical need and is intended to benefit large numbers of Chinese patients, we intend to apply for reimbursement by the Chinese government. Pricing for drugs sold without reimbursement is determined by the drug manufacturer, whereas pricing for drugs under reimbursement is determined by the government. We believe the compelling pharmaco-economic value proposition will support fair pricing for roxadustat.

AstraZeneca

We have entered into an agreement with AstraZeneca relating to roxadustat in China. Under the agreement, FibroGen China will hold all of the regulatory licenses issued by China regulatory authorities and be primarily responsible for regulatory, clinical and manufacturing activities.

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AstraZeneca will conduct commercialization activities as well as serve as the national distributor for roxadustat, sourcing the distribution of roxadustat to a network of regional and local distributors. FibroGen China will be responsible for medical affairs and physician education.

We believe that the collaboration will not only help to accelerate market access and patient adoption, but also reduce our risks associated with roxadustat launch in China, as AstraZeneca has significant experience with the China market and will be paying for launch-related commercialization costs in advance and recouping 50% of these expenses from initial roxadustat profits.

Clinical Trials

Our clinical development plan is based upon an agreement with the CFDA that our NDA package will include Phase 1, 2 and 3 trials performed exclusively in China, as well as reference data from Phase 1 and Phase 2 trials performed outside of China.

Clinical Trials of Roxadustat in China

We have successfully completed Phase 1 and Phase 2 trials in China. A summary of our data and comparison to data from our trials performed outside of China is as follows:

Phase 1 Trials

We completed Phase 1 trials of single and multiple ascending doses of roxadustat. Key findings were:

- Roxadustat pharmacokinetic parameters in Chinese are similar to those in Caucasians and Japanese.
- Stimulation of endogenous erythropoietin, a marker of roxadustat pharmacodynamics, in Chinese is similar to stimulation in Caucasians and Japanese.
- Roxadustat was well tolerated and there were no negative safety signals.

Phase 2 Trials

We completed a Phase 2 double-blind placebo controlled trial in NDD-CKD patients and a Phase 2 randomized trial of roxadustat compared to epoetin alfa in DD-CKD patients. Results of these trials are very similar to results from comparable trials performed in the United States. See Business Our Development Program for Roxadustat. The results of the DD-CKD trial were presented at the 2013 World Congress of Nephrology and the results of the NDD-CKD trial were presented at the 2013 American Society of Nephrology meeting. Key findings of these trials are as follows:

DD-CKD Trial Results

- Roxadustat achieved Hb maintenance in DD-CKD patients who discontinued treatment with epoetin alfa.

In a post-hoc analysis, the data met the primary endpoint of our planned Phase 3 trial in China in this patient population.

There were no serious adverse events after starting roxadustat and most common adverse events were muscle spasms, abdominal discomfort, decreased appetite and infections which were typical of those expected for DD-CKD patients. There were no dose-related trends or imbalances in the nature of adverse events between roxadustat and epoetin alfa groups.

NDD-CKD Trial Results

By Week 9, roxadustat increased Hb levels significantly compared to placebo ($p<0.001$).

In a post-hoc analysis, the data met the primary endpoint of our planned Phase 3 trial in China in this patient population.

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Serious adverse events were progression of CKD, infection and high potassium levels and the most common adverse events were infections, high potassium levels, nausea and dizziness. The percentage of patients with adverse events was similar for patients treated with roxadustat compared to patients treated with placebo. There were no imbalances in the nature of adverse events between the patient groups.

Strategy for Continued Development of Roxadustat in China

We plan to perform two Phase 3 trials in China to support approval of roxadustat for treatment of anemia in DD-CKD and NDD-CKD patients. Based on discussions with the CFDA, our planned Phase 3 trials are designed to confirm Phase 2 results. Consequently, these Phase 3 trials are similar in design and endpoints to our Phase 2 trials in DD-CKD and NDD-CKD, except that our Phase 3 trials will include a larger number of patients and will study longer dosing durations. The overall designs of our planned Phase 3 trials are as follows:

Phase 3 Trial in DD-CKD (FGCL-4592-806):

Design: Randomized, multicenter, open-label, active control.

Patients: CKD on dialysis.

Number: 300.

Control treatment: epoetin alfa.

Randomization: 2:1 (roxadustat:epoetin alfa).

Dosing duration: 26 weeks with option for some patients to continue dosing to Week 52.

Primary endpoint: Hb mean change from baseline averaged over Weeks 23 to 27.

Phase 3 Trial in NDD-CKD (FGCL-4592-808):

Design: Randomized, multicenter, double-blind, placebo controlled.

Patients: CKD not on dialysis.

Number: 150.

Control treatment: placebo.

Randomization: 2:1 (roxadustat:placebo).

Dosing duration: 8 weeks followed by open-label treatment to week 26 and option for some patients to continue dosing to week 52.

Primary endpoint: Proportion of patients who achieve a confirmed Hb response at any time up to and including Week 9.

In designing these trials, we had several important considerations:

We had successful Phase 2 trials, and in post-hoc analyses our Phase 2 trial results met the primary endpoints of our planned Phase 3 trials.

The dosing regimens in our planned Phase 3 trials are based on the dosing regimens in our China Phase 2 trials doses that met the primary endpoints.

Dosing duration to meet the primary endpoint in the NDD-CKD Phase 3 trial is identical to the China Phase 2 trial dosing duration with additional dosing beyond eight weeks as part of this trial.

Dosing duration to meet the primary endpoint in the DD-CKD Phase 3 trial is longer than the China Phase 2 trial dosing duration but similar to U.S. Phase 2 trial dosing duration.

Increased number of patients in Phase 3 increases the trials power, or ability to detect the primary endpoint.

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The CFDA is currently reviewing our Phase 3 clinical trial application, and we expect to begin enrolling subjects in the second half of 2015.

Planned Phase 4 Studies

The CFDA imposes a five-year monitoring surveillance period after NDA approval on all Class 1.1 innovative drugs like roxadustat. Based on current CFDA guidelines, we believe we will need to conduct a 2,000 subject post-marketing observational study to demonstrate the long-term safety of roxadustat as well as provide additional information related to the quality and stability of the manufacturing process for roxadustat. The study design will be determined after Phase 3 data become available.

FG-5200 FOR THE TREATMENT OF CORNEAL BLINDNESS IN CHINA

Corneal blindness, defined as visual acuity of 3/60 or less, is caused by various factors, including scarring resulting from infections, such as herpes simplex, physical trauma, chemical injury and genetic diseases affecting the function of the cornea. In countries with sufficient tissue banks and skilled surgeons, the treatment for corneal blindness is the replacement of the damaged cornea with a corneal graft from donor corneas from human cadavers. Despite use of immunosuppressive drugs, graft rejection remains a serious problem, resulting in graft failure within five years in approximately 35% of cases in the United States. We are developing FG-5200 for the treatment of corneal blindness resulting from partial thickness corneal damage.

In China, there are ethical or religious beliefs, cultural norms and significant infrastructure barriers that limit organ donation or tissue banking possibilities, resulting in an extreme shortage of cadaver corneas. Alternatives to cadaver corneas, such as collagen derived from porcine tissue or fish scales, are experimental, and to our knowledge, have not yielded satisfactory results. In many cases of corneal blindness, infection and other factors lead to serious risks to the patient.

Market Opportunity

Approximately 40,000 corneal grafts were performed in the U.S. in 2011 using tissue from human cadavers. In contrast, while there are approximately 4 to 5 million patients in China with corneal blindness and an incidence of 100,000 cases of corneal blindness each year, there were only about 3,000 corneal grafts performed in China in 2007 using tissue from human cadavers. We believe the number of corneal grafts using cadaver tissue in China may decrease significantly due to recent changes in government policy.

FG-5200 as a Potential Solution to This Unmet Medical Need

FG-5200 Corneal Implant

Our expertise in fibrosis and extracellular matrix proteins has allowed us to develop processes for producing human collagen types I, II and III, as well as coordinate expression of several enzymes involved in assembly of collagen. We have successfully produced a proprietary version of recombinant human collagen III that is suitable for use in cornea repair.

FG-5200, a corneal implant that we intend to apply for approval as a medical device in China, is designed to serve as an immediately functional replacement cornea as well as a temporary scaffold to allow for regeneration of the native corneal tissue. In contrast, cadaver graft tissue is never turned over ; in fact, only limited integration occurs over the life of the graft. Our FG-5200 implant is made of recombinant human collagen that has been formed into a highly

concentrated fibrillar matrix to provide physical characteristics optimal for corneal implantation.

In animal models, FG-5200 persists for less than one year, at which time native tissue has completely regrown, including both epithelium (the outer cell layer of the cornea) and stroma. The stroma in these animal models is seen to be infiltrated with nerve fibers, leading to the reacquisition of the touch response critical to the avoidance of additional corneal damage.

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Corneal implants using human donor tissue are currently being reimbursed by the government, and similar to many other implantable Class III devices in China (including stents and bone grafts), we would expect that FG-5200 could be added to the reimbursement list for medical devices, if approved.

Clinical Testing of FG-5200

An initial clinical study outside of China has been conducted to test the safety and feasibility of using a biosynthetic implant composed of recombinant human collagen for the treatment of severe corneal damage as an alternative to human donor tissue. Ten patients with advanced keratoconus, or severe corneal scarring, were implanted with the recombinant collagen implants and have been followed for more than five years. Two-year follow-up data were reported in *Science Translational Medicine* (Fagerholm et al., (2010)) and four-year follow-up data were reported in *Biomaterials* (Fagerholm et al., *Biomaterials* (2014)). Key clinical findings include the following:

- Patients with biosynthetic implants had a 4-year mean corrected visual acuity of 20/54 and gained on average more than 5 Snellen lines of vision on an eye chart.
- Nerve re-growth and touch sensitivity was closer to that of healthy corneas and significantly better in corneas with biosynthetic implants than in human donor corneas.
- Corneas with biosynthetic implants maintained a stable shape and thickness without any need for a long course of immunosuppression therapy.
- There has been no recruitment of inflammatory dendritic cells into the biosynthetic implant area and no episodes of rejection, in contrast to the control arm of human donor cornea transplantation, where a rejection episode was observed.

Using our animal models, we tested FG-5200 against the original formulation of our implants used in the clinical study described above, which contained a lower collagen concentration. The animal studies showed no difference in safety but improved epithelialization with FG-5200 due to the less intrusive suturing technique possible with the new, higher collagen content formulation.

We plan to meet with the CFDA to reach agreement on design and patient size of our clinical program for FG-5200.

FG-5200 Strategy

FibroGen China has submitted a device classification application to the CFDA to designate FG-5200 corneal implants as a Domestic Class III medical device. We have also applied for Innovative Medical Device designation for FG-5200 with the CFDA. We have not submitted an investigational device exemption or similar application for FG-5200. We are currently focused on completing the build out and certification of our corneal implant manufacturing production facility in China prior to initiating a pivotal study.

Subject to CFDA designation, we currently plan to manufacture FG-5200 clinical trial material in an aseptic production suite built within the same Beijing manufacturing plant in which we will manufacture roxadustat for China.

We plan to develop FG-5200 in China first. If FG-5200 is successful in China, we believe there is a future opportunity to develop FG-5200 in other Asian countries where cadaver materials are in short supply, in part because cultural norms and infrastructure and other challenges in tissue banking limit tissue donations. We also believe there is an opportunity to obtain CE Marking to facilitate entry into other markets, such as Latin America. We may develop FG-5200 in the United States and Europe as well, where cadaver corneas are available but the required immunosuppressive therapy may make FG-5200 a potentially attractive alternative.

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FG-3019 FOR THE TREATMENT OF FIBROSIS AND CANCER

We were founded to discover and develop therapeutics for fibrosis. We began studying connective tissue growth factor, or CTGF, shortly after its discovery. Our ongoing internal research, efforts with collaboration partners and the work of other investigators have consistently demonstrated elevated CTGF levels in pathologic fibrotic conditions characterized by sustained production of extracellular matrix, or ECM, elements that are key molecular components of fibrosis. Our accumulated discovery research efforts indicate that CTGF is a critical common element in the progression of serious diseases associated with fibrosis.

From our library of fully-human monoclonal antibodies that bind to different parts of the CTGF protein and block various aspects of CTGF biological activity, we selected FG-3019, for which we have exclusive worldwide rights. We believe that FG-3019 blocks CTGF and inhibits its central role in causing diseases associated with fibrosis. Our data to date indicate that FG-3019 is a promising and highly differentiated product with broad potential to treat a number of fibrotic diseases and cancers. We are currently conducting Phase 2 trials in idiopathic pulmonary fibrosis, or IPF, pancreatic cancer and liver fibrosis. FG-3019 has received orphan drug designation in IPF in the United States.

Based on its ability to block CTGF, FG-3019 may be a treatment for a broad array of fibrotic disorders of nearly every organ system. In animal studies of FG-3019, such as radiation-induced pulmonary fibrosis in mice, we have demonstrated that FG-3019 is capable of reversing fibrosis. In clinical trials, we have used advanced medical imaging technology to quantify changes in fibrosis throughout the lungs. Our data to date using these measures demonstrate that FG-3019 may stabilize and in some instances reverse pulmonary fibrosis and improve pulmonary function in IPF patients.

Certain cancers have a prominent ECM component that contributes to metastasis and progressive disease. Specifically, ECM is the connective tissue framework of an organ or tissue; all tumors have ECM. In the case of fibrotic tumors, ECM is more pronounced and there is more fibrosis than in other tumor types. In mouse models of pancreatic cancer, FG-3019 treatment has demonstrated reduction of tumor mass, slowing of metastasis and improvement in survival. In an open-label Phase 2 study of FG-3019 plus gemcitabine and erlotinib, FG-3019 demonstrated a dose-dependent improvement in one year survival rate.

Results to date indicate that FG-3019 has broad potential to address unmet needs for the treatment of fibrotic diseases and cancers. Specifically, given the preclinical and clinical data in pulmonary fibrosis and pancreatic cancer, our primary focus for clinical development of FG-3019 is additional Phase 2 clinical trials in pancreatic cancer and IPF. We are also conducting exploratory clinical trials with FG-3019 in liver fibrosis secondary to viral infection.

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Overview of Fibrosis

Fibrosis is an aberrant response of the body to tissue injury that may be caused by trauma, inflammation, infection, cell injury, or cancer. The normal response to injury involves the activation of cells that produce collagen and other components of the ECM that are part of the healing process. This healing process helps to fill in tissue voids created by the injury or damage, segregate infections or cancer, and provide strength to the recovering tissue. Under normal circumstances, where the cause of the tissue injury is limited, the scarring process is self-limited and the scar resolves to approximate normal tissue architecture. However, in certain disease states, this process is prolonged and excessive and results in progressive tissue scarring, or fibrosis, which can cause organ dysfunction and failure as well as, in the case of certain cancers, promote cancer progression.

Excess CTGF Causes Fibrosis. FG-3019 Blocks CTGF and Reverses Fibrosis

Excess CTGF levels are associated with fibrosis. CTGF increases the abundance of myofibroblasts, a cell type that drives wound healing, and stimulates them to deposit ECM proteins such as collagen at the site of tissue injury. In the case of normal healing of a limited tissue injury, myofibroblasts eventually die by programmed cell death, or apoptosis, and the fibrous scarring process recedes. In fibrotic conditions, excess CTGF results in chronic activation of myofibroblasts, which leads to chronic ECM deposition and fibrosis (see figure above).

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Multiple biological agents and pathways have been implicated in the fibrotic process (Wynn J Pathol (2008)). Many fibrosis pathways converge on CTGF (see figure below), which the scientific literature demonstrates to be a central mediator of fibrosis (Oliver et al, J Inv Derm (2010)). In the case of cancer, the sustained tumor-associated fibrotic tissue promotes tumor cell survival and metastasis. The figure below shows the commonality of cellular mechanisms that may result in fibrosis and cancer.

Most Biological Factors Implicated in Fibrosis Work Through CTGF

CTGF is a secreted glycoprotein produced by fibroblasts, endothelium, mesangial cells and other cell types, including cancers, and is induced by a variety of regulatory modulators, including TGF-ß and vascular endothelial growth factor, or VEGF. CTGF expression has been demonstrated to be up-regulated in fibrotic tissues. Thus, we believe that targeting CTGF to block or inhibit its activity could stop or reverse tissue fibrosis. In addition, since CTGF is implicated in nearly all forms of fibrosis, we believe FG-3019 has the potential to provide clinical benefit in a wide range of clinical indications that are characterized by fibrosis.

Until recently, it was believed that fibrosis was an irreversible process. It is now generally understood that the process is dynamic and potentially amenable to reversal. Based on studies in animal models of fibrosis of the liver, kidney, muscle and cardiovascular system, it has been shown that fibrosis can be reversed. It has also been demonstrated in humans that fibrosis caused by hepatitis virus can be reversed (Chang et al. Hepatology (2010)). Additionally, we have generated data in human and animal studies that lung fibrosis can be reversed in some instances upon treatment with FG-3019. We do not believe that there is clinical evidence that therapies currently on the market directly prevent or reverse fibrosis in human disease. While certain other companies are working on topical inhibition of CTGF, we are not aware of other products in development that target CTGF inhibition for deep organ fibrosis and cancer.

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Clinical Development of FG-3019 Overview

We have performed clinical trials of FG-3019 in IPF, pancreatic cancer, liver fibrosis and diabetic kidney disease. We are currently conducting an extension study for an open-label Phase 2 trial in IPF; a randomized, double-blind placebo-controlled Phase 2 trial in IPF; an open-label Phase 2 trial in pancreatic cancer; and a randomized, double-blind, placebo-controlled Phase 2 trial in liver fibrosis. In ten Phase 1 and Phase 2 clinical studies involving FG-3019 to date, including more than 340 patients who were treated with FG-3019 (146 patients dosed for more than 6 months), FG-3019 has been well-tolerated across the range of doses studied, and there have been no dose-limiting toxicities seen thus far.

In IPF, we completed a Phase 1 single dose trial, and subsequently advanced the program to an ongoing open-label Phase 2 trial of FG-3019 in 89 patients, which has completed its one year treatment period and based on encouraging results is now in an extension phase. We are also conducting a randomized, double-blind, placebo-controlled Phase 2 trial. Both Phase 2 trials are designed to evaluate the effects of FG-3019 on pulmonary function, extent of fibrosis and health-related quality of life.

In pancreatic cancer, we performed an open-label, dose-finding Phase 2 trial in a total of 75 patients with advanced pancreatic cancer. We recently began a randomized, active-control, neoadjuvant Phase 2 trial combining FG-3019 with nab-paclitaxel plus gemcitabine in approximately 40 patients with locally advanced pancreatic cancer. We anticipate interim data from this study in the second half of 2015. We also expect to begin a randomized Phase 2 trial of FG-3019 in metastatic pancreatic cancer patients in 2016. Actual dates depend on a variety of factors and are subject to numerous risks and uncertainties, including with respect to patient enrollment, safety results, manufacturing, third party contractors, and government regulators, some of which are out of our control. See also Risk Factors beginning on page 100, and particularly those risk factors under the heading Risks Related to the Development and Commercialization of Our Product Candidates.

We are conducting a Phase 2 clinical trial with FG-3019 in liver fibrosis associated with hepatitis B, or HBV, in Hong Kong and Thailand, where the prevalence of HBV is high.

Early clinical development included studies in diabetic kidney disease. Although no adverse outcomes were observed, we decided not to pursue this indication at this time based on the difficulty of the regulatory path and the extensive clinical trials likely to be required for approval for the treatment of diabetic kidney disease.

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The table below provides a summary of our clinical trials involving FG-3019:

Completed and Ongoing FG-3019 Clinical Trials

Study, Study #	Study Design	Dose (mg/kg)	Frequency	Treatment Duration (weeks)	Subjects
Phase 1 IPF, FGCL-MC3019-002	Open-label, dose-escalation	1, 3, or 10	Single		21
Phase 2 IPF, FGCL-3019-049	Open-label, dose-escalation	15 or 30	Every 3 weeks	45 weeks	89*
Phase 2 IPF, FGCL-3019-067	Double-blind, placebo-controlled (1:1)	30 mg/kg	Every 3 weeks	45 weeks	Target 136**
Phase 2 Pancreatic Cancer, FGCL-MC3019-028	Open-label, dose-escalation	3, 10, 15, 25, 35, or 45 17.5 or 22.5	Every other week Weekly	Until disease progression 1 to 89 weeks	75
Phase 2 Pancreatic Cancer, FGCL-3019-069	Open-label, active control (1:1)	35	Cycle 1 = Days 1, 8 and 15 Subsequent Cycles = Every other week	24 weeks	Target 40**
Phase 2 HBV- Liver Fibrosis, FGCL-3019-801	Double-blind, placebo-controlled (2:1)	15 or 45	Every 3 weeks	45 weeks	113
Phase 1 Diabetic Kidney Disease, FGCL-MC3019-003	Open-label, dose-escalation	3 or 10	Days 0, 14, 28 and 42	6 weeks	24
Phase 2 Diabetic Kidney Disease, FGCL-3019-029	Double-blind, placebo-controlled (1:1:1)	5 or 10	Every 2 weeks Every 4 weeks	12 weeks 12 weeks	38
Phase 2 Diabetic Kidney Disease, FGCL-3019-032	Double-blind, placebo-controlled	3 or 10	Biweekly	26 weeks	46

* Study 049 completed its one year treatment period and, based on encouraging results, is now in an ongoing extension phase.
** Currently enrolling.

Idiopathic Pulmonary Fibrosis

Understanding IPF and the Limitations of Current Therapies

IPF is a form of progressive pulmonary fibrosis, or abnormal scarring, that destroys the structure and function of the lungs. As tissue scarring progresses in the lungs, transfer of oxygen into the bloodstream is increasingly impaired. Average life expectancy at the time of confirmatory diagnosis of IPF is estimated to be between 3 to 5

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years, with approximately two-thirds of patients dying within five years of diagnosis. Thus, the survival rates are comparable to some of the most deadly cancers. The cause of IPF is unknown but is believed to be related to unregulated cycles of injury, inflammation and fibrosis.

Patients with IPF experience debilitating symptoms, including shortness of breath and difficulty performing routine functions, such as walking and talking. Other symptoms include chronic dry, hacking cough, fatigue, weakness, discomfort in the chest, loss of appetite and weight loss. Over the last decade, refinements in diagnosis criteria and enhancements in high-resolution computed tomography, or HRCT, imaging technology have enabled more reliable diagnosis of IPF and clearer distinction from other interstitial lung diseases.

The U.S. prevalence and incidence of IPF are estimated to be 44,000 to 135,000 cases, and 21,000 new cases per year, respectively, based on Raghu et al. (Am J Respir Crit Care Med (2006)) and on data from the United Nations Population Division. We believe that with the availability of technology to enable more accurate diagnoses, the number of individuals diagnosed per year with IPF will continue to increase. In 2011, Decision Resources Group estimated that there will be approximately $4.6 billion in sales of IPF drugs in the United States and Europe in 2020.

Pirfenidone has been approved to treat IPF in Europe, Canada, Japan and the United States. According to the FDA advisory committee submission by its sponsor, pirfenidone has been shown to have a modest effect on slowing the progression of IPF as measured by forced vital capacity, or FVC, in a minority (less than 15%) of patients. Nintedanib has also been approved to treat IPF in the United States and the EU. We believe that FG-3019 has the potential to stabilize or reverse lung fibrosis and if approved, improve the prognosis for patients with IPF.

Reversal of Lung Damage in Preclinical Models with FG-3019 in Pulmonary Fibrosis

While there are no established animal models for IPF, we selected the mouse model of radiation-induced lung damage from a variety of other models because we believe that it most closely approximates the process of lung fibrosis seen in humans. We conducted a proof of concept study of FG-3019 using this model as summarized in the figures below.

In this model, a single irradiation of the thorax causes lung tissue damage that over time results in progressive fibrosis. Lung density, indicative of tissue damage, was monitored by HRCT and began to increase eight to 12 weeks after irradiation.

Sixteen weeks after irradiation, measured lung density was significantly elevated and continued to increase in the placebo-treated animals until reaching a plateau at Week 30. Therapeutic treatment with FG-3019 began at Week 16. Significant decreases in lung fibrosis were measurable at Week 18 and it continued to decrease over the eight weeks of FG-3019 treatment through Week 24.

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FG-3019 Treatment Starting 16 Weeks After Irradiation Reverses Lung Fibrosis in Mice as Measured by HRCT (Mean ± SE)

* indicates FG-3019-treated lung density is significantly different (p£ 0.05) from placebo-treated

Rapid reversal of lung damage was confirmed by examining tissue histology which showed substantial changes within two weeks of initiating treatment. Prior to FG-3019 treatment (Week 16) lung histology showed lung damage characterized by increased cellularity and tissue remodeling. After two weeks of treatment with FG-3019 (Week 18), damage had been reversed and the structure of the lung more closely resembled that of a non-irradiated or normal mouse. The figure below is representative of the typical pattern of structural changes observed in the mice in this study.

Two Weeks After FG-3019 Treatment: Structural Changes Could be Seen by Lung Histology in Mice

Week 16

Pre-Treatment

Week 18

2 Weeks after starting FG-3019 Treatment

Normal

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As shown below, reduced lung density consistently correlated with improved lung function, as measured by blood oxygenation.

Improvement of Lung Fibrosis Corresponds with Improvement in Lung Function in Mice

Gene expression changes were also examined at Week 18, two weeks after initiation of treatment with FG-3019. Irradiation induced increased expression of genes involved in ECM deposition, such as fibronectin, collagen type 1 alpha 1, lysyl oxidase, CTGF and lysyl oxidase-like 2. FG-3019 treatment was shown to reduce expression of these genes, as illustrated below.

Examples of Changes in Gene Expression by mRNA Microarray Analysis (mean ± SE) after FG-3019 Treatment in Mice

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Clinical Trials of FG-3019 for IPF

Study 002 was a Phase 1 open-label study to determine the safety and PKs of escalating single doses of FG-3019. Patients with a diagnosis of IPF by clinical features and surgical lung biopsy received a single IV dose of FG-3019 at 1, 3, or 10 mg/kg. A total of 21 patients were enrolled in the study; 6 patients received a dose of 1 mg/kg, 9 patients received 3 mg/kg, and 6 patients received 10 mg/kg. FG-3019 was well tolerated across the range of doses studied; and there were no dose-limiting toxicities. Treatment emergent adverse events that were considered to be possibly related by the principal investigator to FG-3019 were mild and self-limited, consisting of pyrexia, cough and headache.

We completed the initial one-year treatment portion of Study 049, a Phase 2 open-label, dose-escalation study to evaluate the safety, tolerability, and efficacy of FG-3019 in 89 patients with IPF. FG-3019 was administered at a dose of 15 mg/kg in Cohort 1 (53 patients) and 30 mg/kg in Cohort 2 (36 patients) by IV infusion every 3 weeks for 45 weeks. Nineteen patients from Cohort 1 participated in the current 1 year extension of dosing. Efficacy endpoints are pulmonary function assessments, extent of pulmonary fibrosis as measured by quantitative imaging and measures of health-related quality of life.

HRCT is typically used to diagnose IPF based on visual assessments of computed tomography, or CT, images of lung fibrosis. We used quantitative HRCT to measure changes in fibrosis in this Study 049. We used software to quantify whole lung fibrosis from the compilation of 1 mm HRCT sections of the entire lung. The computer algorithm, which our vendor validated, provides an overall determination of the percentage of the lung that contains individually the three characteristic forms of IPF fibrosis, including reticular IPF fibrosis which is expected to make the most dynamic contribution to overall lung fibrosis.

The extent of lung fibrosis as measured by quantitative HRCT has been shown to be accurate and reproducible (Kim et al. Eur Radiol (2011)). Recent publications based on similar quantitative HRCT methods have identified an association between worsening pulmonary fibrosis and mortality in IPF (Maldonado et al. Eur Resp J (2014); Oda et al. Respiratory Research (2014)). However, HRCT has not been used by the FDA to establish efficacy in IPF.

Eighty-nine patients in this Phase 2 open label study received at least one dose of FG-3019. We defined disease severity in terms of baseline pulmonary function, measured as the FVC percent of the predicted value for a healthy matched person of the same age, or FVC percent predicted. Severe disease was FVC percent predicted < 55%, moderate disease was FVC percent predicted between 55% and 80%, and mild disease was FVC percent predicted >80%.

In Cohort 1, we enrolled patients with a wide range of disease severity to assess safety and efficacy across the full spectrum. Baseline FVC percent predicted for Cohort 1 was 43% to 90%, with a mean of 62.8%. In contrast, other IPF clinical trials, such as those for pirfenidone and nintedanib, have enrolled patients who on average had mild to moderate disease (mean FVC percent predicted 73.1% to 85.5%). Fourteen patients in Cohort 1 withdrew, and ten of the 14 had severe disease.

In order to enroll IPF patients similar to those in other IPF trials, we amended the protocol for Cohort 2 to include only patients with mild to moderate disease (FVC ³ 55% predicted). Baseline FVC percent predicted for Cohort 2 was 53% to 112%, with a mean of 72.7%. Based on this definition of disease severity, 37 patients in Cohort 1 and 32 patients in Cohort 2 had mild to moderate disease.

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Disease Severity in Enrolled and Evaluated Patients Treated with FG-3019 in FGCL-3019-049

		Cohort 1				Cohort 2			
	FVC % Predicted	Severe < 55%	Moderate 55% to 80%	Mild > 80%	Total	Severe < 55%	Moderate 55% to 80%	Mild > 80%	Total
			N				N		
Total	**Enrolled**	16	34	3	53	4	22	10	36
	Complete	5	30	3	38	1	17	10	28
Evaluated	**Enrolled**		34	3	37		22	10	32
	Complete		30	3	33		17	10	27

The table below provides a summary of the observed quantitative change in fibrosis for patients in Cohorts 1 and 2 as measured by HRCT. Twenty-four percent of these patients had improved fibrosis at Week 48. We believe that this is the first trial to demonstrate reversal of fibrosis in IPF. Stable fibrosis has been considered the only achievable favorable outcome in IPF. The table below sets forth the number of patients who showed stable or improved fibrosis at Weeks 24 and 48 compared to the amount of fibrosis at the start of the trial.

Changes in Fibrosis in Patients with Mild to Moderate IPF Treated with FG-3019 in FGCL-3019-049

	Stable or Improved Compared to Baseline		Improved Compared to Baseline		Improved Compared to Week 24
	Week 24	Week 48	Week 24	Week 48	Week 48
Cohort 1	21/45(47%)	14/38(37%)	12/45(27%)	12/38(32%)	8/38(21%)
Cohort 2	12/29(41%)	9/28(32%)	5/29(17%)	4/28(14%)	8/26(31%)
Combined	33/74(45%)	23/66(35%)	17/74(23%)	16/66(24%)	16/64(25%)

Fibrosis improvement or stabilization in patients with mild to moderate disease as measured by HRCT correlated with improvement or stabilization of pulmonary function measured by FVC ($p<0.0001$; $r=-0.59$ Cohorts 1 and 2 combined). The figure below shows FVC changes up to Week 48 for patients with stable or improved fibrosis versus patients with worsening fibrosis. Patients with stable or improved fibrosis showed improved pulmonary function, on average, which was significantly different or better than patients with worsening fibrosis who showed a substantial decline in FVC ($p= 0.0001$, Cohorts 1 and 2 combined). Patients with worsening fibrosis had pulmonary function that was similar to the annual decline in pulmonary function for typical IPF patients.

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Categorical Analysis of FVC Change from Baseline (BL) (mean ±SE) in FGCL-3019-049

The FVC changes observed in Study 049 are compared to the changes reported in Phase 3 clinical trials for pirfenidone and nintedanib in the table below.

Comparison of FGCL-3019-049 Mean FVC Change in One year to

Phase 3 Results for Pirfenidone and Nintedanib

		Mean Change of FVC in One Year			
	N				
	Pbo/Active	Placebo	Active	Difference	%
Pirfenidone I*	174/174	-350	-181	169	48.3%
Pirfenidone II*	173/171	-274	-220	54	19.8%
Pirfenidone III	238/223	-280	-164	116	41.5%
Nintedanib I	204/307	-205	-95	110	53.6%
Nintedanib II	217/327	-205	-95	110	53.6%
FG-3019	0/66		-140		

* Week 48, FVC (rank ANCOVA w/ imputation)
Linear slope analysis

Eighty-nine patients had at least one adverse event. The most common reported events were cough, fatigue, shortness of breath, upper respiratory tract infection, sore throat, bronchitis, nausea, dizziness and urinary tract infection. To date, including the 1-year extension of dosing, there have been 45 SAEs in 31 patients, four of which were considered possibly related by the principal investigator to study treatment. During the first year of treatment there were 32 SAEs in 24 patients. Adverse events observed to date are consistent with typical conditions observed in this patient population.

In aggregate, the data from the Phase 2 open-label, dose-escalation study indicate that a subset of FG-3019 treated IPF patients experienced improvements in lung fibrosis with commensurate improvement in pulmonary function and a potential for prolonged benefit with continued treatment. These results are consistent with the

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mouse disease model results which showed that FG-3019 treatment can reverse lung fibrosis and result in improved pulmonary function. We believe that our patient data showing correlated improvements in both fibrosis and lung function in some patients have not been seen in previously published IPF clinical studies.

Clinical Development Plan for FG-3019 in IPF

Study 067 is an ongoing Phase 2, randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of FG-3019 in approximately 136 IPF patients with mild to moderate disease (baseline FVC percentage predicted between 55% and 90%). Patients are being randomized (1:1) to 30 mg/kg of FG-3019 or placebo, every 3 weeks, for 45 weeks. As with our open-label Phase 2 trial, Study 049, the primary efficacy endpoint for Study 067 is change in FVC from baseline. Secondary endpoints are extent of pulmonary fibrosis as measured by quantitative HRCT, other pulmonary function assessments and measures of health-related quality of life. The study is currently enrolling. We anticipate reporting data from this study in the second half of 2016. However, the actual date will depend on a variety of factors and are subject to numerous risks and uncertainties, including with respect to patient enrollment, safety results, manufacturing, third party contractors and government regulators, some of which are out of our control. See also Risk Factors beginning on page 100, and particularly those risk factors under the heading Risks Related to the Development and Commercialization of Our Product Candidates.

Pancreatic Cancer

Understanding Pancreatic Cancer and the Limitations of Current Therapies

Pancreatic ductal adenocarcinoma, or pancreatic cancer, is the fourth leading cause of cancer deaths in the United States. U.S. prevalence of pancreatic cancer is estimated to be 44,000. According to the National Cancer Institute, in 2014 there are projected to be approximately 46,000 new cases of pancreatic cancer and approximately 39,000 deaths from the disease in the United States. According to the World Health Organization, or WHO, and based on data from the United Nations Population Division, there were approximately 79,000 new cases of pancreatic cancer and approximately 78,000 deaths in the EU in 2012. The National Cancer Center of Japan estimated that in 2010 (latest year available) there were 32,330 new cases of pancreatic cancer. In 2013, Decision Resources Group estimated that there will be approximately $1.3 billion in sales of pancreatic cancer drugs in 2022.

Pancreatic cancer is aggressive and typically not diagnosed until it is largely incurable. Most patients are diagnosed after the age of 45, and according to the American Cancer Society, 94% of patients die within five years from diagnosis. The majority of patients are treated with chemotherapy, but pancreatic cancer is highly resistant to chemotherapy. Approximately 15% to 20% of patients are treated with surgery; however, even for those with successful surgical resection, the median survival is approximately two years, with a five year survival rate of 15% to 20% (Neesse et al. Gut (2011)). Radiation treatment may be used for locally advanced diseases, but it is not curative.

The duration of effect of approved anti-cancer agents to treat pancreatic cancer is limited. Gemcitabine demonstrated improvement in median overall survival from approximately four to six months, and erlotinib in combination with gemcitabine demonstrated an additional ten days of survival. Nab-paclitaxel in combination with gemcitabine was recently approved by the FDA for the treatment of pancreatic cancer, having demonstrated median survival of 8.5 months. These drugs illustrate that progress in treatment for pancreatic cancer has been limited, and there remains a need for substantial improvement in patient survival and quality of life. The approved chemotherapeutic treatments for pancreatic cancer target the cancer cells themselves. Tumors are composed of cancer cells and associated non-cancer tissue, or stroma, of which ECM is a major component. In certain cancers such as pancreatic cancer, both the stroma and tumor cells produce CTGF which in turn promotes the proliferation and survival of stromal and tumor cells. CTGF also induces ECM deposition that provides advantageous conditions for tumor cell adherence and proliferation,

and promotes metastasis, or tumor cell migration, to other parts of the body.

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Pancreatic cancers are generally resistant to powerful chemotherapeutic agents, and there is now growing interest in the use of an anti-fibrotic agent to diminish the supportive role of stroma in tumor cell growth and metastasis. The anti-tumor effects observed with FG-3019 indicate that it has the potential to inhibit tumor expansion through effects on tumor cell proliferation and apoptosis as well as reduce metastasis.

Preclinical Models of FG-3019 for Pancreatic Cancer

We tested FG-3019 in mouse models of pancreatic cancer, where it has demonstrated reduction of tumor mass and metastasis in several models, including the genetically engineered KPC mouse model. This is a preferred model for studying pancreatic cancer because all KPC mice spontaneously develop pancreatic cancer that closely approximates many features of the human disease, including similar genetic mutations, expression of CTGF, extensive stroma, metastases and ascites, or abdominal fluid, formation. KPC mouse tumors, like human pancreatic cancer tumors, are highly resistant to anti-cancer therapies. We performed two short-term studies of tumor responses to treatment and a long-term study of survival which were all conducted with staggered enrollment as mice developed tumors of sufficient size.

After initiation of treatment, mice randomized to FG-3019 alone survived for 11 days, which is comparable to the historical experience with gemcitabine alone of 7.5 days. The combination of FG-3019 plus gemcitabine increased survival to 29 days.

In additional studies, malignant hemorrhagic ascites were significantly reduced and liver metastases were reduced (although the reduction was not statistically significant) with the combination of FG-3019 plus gemcitabine. Both FG-3019 and FG-3019 plus gemcitabine increased tumor cell apoptosis significantly compared to gemcitabine alone. Our data suggest that FG-3019 may increase tumor cell apoptosis and improve survival in mice by inhibiting expression of XIAP, or X-linked inhibitor of apoptosis. XIAP is one of a family of proteins whose function is to inhibit apoptosis. Elevated expression of XIAP promotes cell survival and is one mechanism by which tumor cells can become resistant to chemotherapeutic agents. FG-3019 decreased XIAP levels significantly whereas gemcitabine did not decrease XIAP levels. The combination of FG-3019 and gemcitabine was even more effective as shown in the figure below.

FG-3019 Plus Gemcitabine Treatment Increased Survival (11-13 Mice per Group) in the KPC Mouse Model

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FG-3019 Plus Gemcitabine Treatment Reduced Metastasis and Ascites in the KPC Mouse Model

(mean ±SE) (*Indicates Statistically Significant Difference from Gemcitabine + IgG)

FG-3019 Plus Gemcitabine Treatment Reduced Expression of Tumor Pro-Survival Gene XIAP and

Increased the Number of Apoptotic Cells in the KPC Mouse Model

Median inter-quartile ranges and maximum

and minimum observations

Clinical Trials of FG-3019 for Pancreatic Cancer

We completed an open-label Phase 2 (FGCL-MC3019-028) dose finding trial of FG-3019 combined with gemcitabine plus erlotinib in patients with previously untreated locally advanced (stage 3) or metastatic (stage 4) pancreatic cancer. The trial tested FG-3019 doses of 3 mg/kg, 10 mg/kg, 15 mg/kg, 25 mg/kg, 35 mg/kg and 45 mg/kg administered every two weeks, and FG-3019 doses of 17.5 mg/kg and 22.5 mg/kg administered weekly after a double loading dose. On Day 15, treatment began with gemcitabine 1000 mg/m^2 weekly for three weeks in a four week cycle and erlotinib 100 mg daily. Treatment continued until progression of the cancer or the

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patient withdrew for other reasons. Patients were then followed until death. Tumor status was evaluated by CT imaging every eight weeks until disease progression to assess changes in tumor mass.

Seventy-five patients were enrolled in this study with 66 (88%) having stage 4 metastatic cancer. The study demonstrated a dose-related increase in survival, as described in the figure below. At the lowest doses, no patients survived for even one year while at the highest doses up to 31% of patients survived one year.

Effect of FG-3019 Dose on One Year Survival in Pancreatic Cancer

* QW = weekly; Q2W = twice weekly

A post-hoc analysis found that there was a significant relationship between survival and trough levels of plasma FG-3019 measured immediately before the second dose (Cmin), as illustrated below. Cmin greater than or equal to 150 μg/mL was associated with significantly improved progression-free survival (p=0.01) and overall survival (p=0.03) versus those patients with Cmin less than 150 μg/mL. For patients with Cmin ≥ 150 μg/mL median survival was 9.4 months compared to median survival of 4.8 months for patients with Cmin < 150 μg/mL. Similarly, 37% of patients with Cmin ≥ 150 μg/mL survived for longer than one year compared to 11% for patients with Cmin < 150 μg/mL. These data suggest that sufficient blockade of CTGF requires FG-3019 threshold blood levels of approximately 150 μg/mL in order to improve survival in patients with advanced pancreatic cancer.

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Increased Pancreatic Cancer Survival Associated with Increased Plasma Levels of FG-3019

The Kaplan-Meier plot provides a representation of survival of all patients in the clinical trial. Each vertical drop in the curve represents a recorded event (death) of one or more patients. When a patient s event cannot be determined either because he or she has withdrawn from the study or because the analysis is completed before the event has occurred, that patient is censored and denoted by a symbol ( ) on the curve at the time of the last reliable assessment of that patient.

In the study, the majority of adverse events were mild to moderate, and were consistent with those observed for erlotinib plus gemcitabine treatment without FG-3019. There were 99 treatment emergent SAEs; six of which were assessed as possibly related by the principal investigator, and 93 as not related to study treatment. We did not identify any evolving dose-dependent pattern, and higher doses of FG-3019 were not associated with higher numbers of SAEs or greater severity of the SAEs observed.

In both the KPC mouse study and in this clinical trial, FG-3019 treatment had a substantial effect on survival with no apparent increase to the toxicity of the chemotherapeutic regimen.

Clinical Development Plan for FG-3019 in Pancreatic Cancer

For pancreatic cancer, we have recently begun enrolling an open-label, randomized (1:1) Phase 2 trial (FGCL-3019-069) of FG-3019 combined with gemcitabine plus nab-paclitaxel chemotherapy versus the chemotherapy regimen alone in patients with marginally inoperable pancreatic cancer that has not been previously treated. Approximately 40 patients are expected to be treated for up to 6 months and the number may be increased based on preliminary results. The overall goal of the trial is to determine whether the FG-3019 combination can convert inoperable pancreatic cancer to operable cancer. Tumor removal is the only chance for cure of pancreatic cancer, but only 15% to 20% of patients are eligible for surgery. The use of an anti-fibrotic agent in combination with chemotherapy may shrink the tumor size enough to enable surgical removal free from major blood vessels. The patients will then be followed for disease progression and overall survival. We anticipate reporting data from the study in the second half of 2015. We also plan to perform numerous studies of the effects of treatment on gene and protein expression using pre-treatment and post-treatment tumor biopsies.

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We also plan to perform a randomized (1:1) Phase 2 trial of FG-3019 combined with gemcitabine and nab-paclitaxel compared to the chemotherapy regimen alone to assess disease progression and survival in patients with previously untreated metastatic pancreatic cancer. The overall goal is to confirm our open-label Phase 2 data that suggest combinations of FG-3019 and chemotherapy may increase survival. We plan to open this study for enrollment in 2016.

Liver Fibrosis

Understanding Liver Fibrosis and the Limitations of Current Therapies

Fibrosis in the liver is caused primarily by hepatitis virus infection, obesity associated disorders such as non-alcoholic steatohepatitis, or NASH, and excessive consumption of alcohol. Repetitive injury to the liver from these causes leads to worsening fibrosis culminating in liver cirrhosis, organ failure and increased risk of hepatocellular carcinoma. There are no approved pharmaceutical treatments for liver fibrosis in the United States. Treating the underlying cause of disease may stabilize or reverse fibrosis, but only liver transplantation can treat fibrosis that has advanced to cirrhosis.

Despite advances in HBV and HCV antiviral therapy, reversal of fibrosis is slow, and largely observed in patients with mild to moderate fibrosis. Nonetheless, a significant proportion of hepatitis patients have pre-cirrhotic or cirrhotic liver fibrosis and treatments that address the fibrotic process itself would provide benefit for patients with approaching liver failure. Aside from weight loss, there are no available treatments for NASH. The American Liver Foundation estimates a prevalence of 0.9 to 2.5 million cases in the United States for advanced NASH. As in other forms of fibrosis, elevated tissue and plasma levels of CTGF have correlated with disease severity.

According to the World Health Organization, about 240 million people worldwide are chronically infected with HBV and approximately 130 to 150 million people are chronically infected with HCV. NASH and non-alcoholic fatty liver disease are associated with obesity and are becoming increasingly important causes of cirrhosis. NASH has been estimated to affect 5% to 7% of the general population (Starley et al. Hepatology (2010)).

Clinical Development of FG-3019 for Liver Fibrosis

A randomized, placebo-controlled Phase 2 clinical trial is currently being conducted with FG-3019 in 113 patients with HBV-associated liver fibrosis in Hong Kong and Thailand, where the prevalence of HBV is high. The primary endpoint of the trial is change in fibrosis as assessed in liver biopsies. Efficacy data comparing low and high doses of FG-3019 compared to placebo are expected in 2015. We recently terminated a small pilot clinical study in HCV in Hong Kong.

Our future clinical development strategy for liver fibrosis is under active consideration. The need and opportunity for an anti-fibrotic therapy to prevent cirrhosis associated with hepatitis and NASH patients are sizable. However, there is no regulatory consensus on study end-points because clinical manifestations of liver disease do not become apparent until fibrosis is advanced. As with HRCT for pulmonary fibrosis, the imaging technologies are improving for assessment of liver fibrosis, and we are evaluating their applicability to clinical trials for liver fibrosis. There are active efforts by the FDA and liver medical societies to focus on clinical trial design for liver fibrosis and address this challenge. Liver biopsies, the gold standard for measuring liver fibrosis, have significant risks and sample only a small portion of the liver. In a manner similar to our approach to IPF where we assess lung fibrosis by quantitative HRCT, we are currently exploring other non-invasive measurements of overall liver fibrosis and function.

FG-3019 for Duchenne Muscular Dystrophy

In the United States, 1 in 3,500 boys have Duchenne muscular dystrophy, or DMD, and there are currently no approved disease-modifying treatments. Most children, despite taking steroids to mitigate progressive muscle

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loss, are wheelchair bound by age 12, and median survival is age 25. DMD is caused by absence of the dystrophin protein resulting in abnormal muscle structure and function and buildup of fibrosis in muscle, leading to diminished mobility, pulmonary function and cardiac function. Constant myofiber breakdown results in persistent activation of myofibroblasts and altered production of ECM resulting in extensive fibrosis in skeletal muscles of DMD patients. Desguerre et al. (2009) showed that muscle fibrosis was the only myo-pathologic parameter that significantly correlated with poor motor outcome as assessed by quadriceps muscle strength, manual muscle testing of upper and lower limbs, and age at ambulation loss.

Higher CTGF levels correlate with more skeletal muscle fibrosis, and increased CTGF mRNA levels have been found in human DMD muscle and in the mdx mouse model, an accepted model of DMD (Pessina (2014)). It has also been shown in mdx mice that increased CTGF expression occurs concurrently with the progression of cardiac fibrosis, or cardiomyopathy (Au (2011)), and precedes the onset of overt cardiac dysfunction. Vial et al (2008) published results indicating that CTGF induced several ECM constituents and had an inhibitory effect on muscle cell differentiation by decreasing nuclear translocation of myogenin and myosin. CTGF treatment of myoblasts induced their de-differentiation, or failure to become mature muscle cells. These data suggest that in muscle tissue, CTGF directly impacts not just fibrosis but muscle cell phenotype. Morales (2011) showed that CTGF over-expression in tibialis anterior muscle of normal mice induced extensive skeletal muscle damage. CTGF over-expression induced fibrosis and caused a decrease of the specific isometric contractile force of the muscle. When CTGF over-expression stopped, the pathology was reversed. As compared with the mdx mouse model of DMD, both mdx mice with hemizygous CTGF gene deletion (causing a reduction of CTGF levels), and mdx mice treated with FG-3019 performed better in an exercise endurance test, had better muscle strength in isolated muscles and reduced skeletal muscle impairment, apoptotic damage and fibrosis. The figures below show decreased fibrosis (as measured by collagen) and increased muscle strength (as measured by relative tetanus %) in the FG-3019 treated mdx mice as compared to the mdx control mice.

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The figure below shows the results in a 5-minute treadmill exercise tolerance test performed by Morales, Hum Mol Genet-Suppl Data (2013). The FG-3019-treated mdx mice stopped fewer times to rest than the untreated mdx mice (mdx-Control), and were more similar to normal mice.

Cardiomyopathy and resultant heart failure are important determinants of morbidity and mortality in DMD. Au (2011) showed that at 29 weeks of age, normal mice showed no signs of myocardial fibrosis while mdx mice developed cardiac fibrosis and increased collagen expression that continued to week 43. The onset of fibrosis was associated with increased CTGF expression.

In a 2009/2010 study, which we used in support of our patent titled Methods for Treatment of Muscular Dystrophy issued in 2014, Brandan et al. found that there was a tendency of FG-3019 to increase contraction of the diaphragm muscle in a limited number of FG-3019-treated mdx mice on an electromyographic test, as compared with untreated mdx mice. These results suggest the potential for improvement of respiratory function using this therapeutic approach.

We currently plan to conduct a clinical trial with FG-3019 to assess its ability to impact muscle pathology and improve muscle function in DMD patients. In October 2014 we met with the TREAT-NMD Advisory Committee for Therapeutics to discuss clinical trial design, target patients and appropriate endpoint measures. The advisory committee provided to FibroGen a summary report of the meeting with a synopsis posted on the TREAT-NMD website. In March 2015, we had a follow-on advisory committee meeting, which included some of the members of the TREAT-NMD committee, to refine the clinical trial design. We intend to initiate a clinical trial in the second half of 2015.

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FG-3019 for Radiation Countermeasures

The National Institute of Allergy and Infectious Diseases, or NIAID, has sponsored the consortium, Medical Countermeasures Against Radiological Threats, or MCART, to develop medical countermeasures to treat the key pathological conditions and delayed effects resulting from acute radiation exposure. MCART is mandated to develop animal models that adhere to all criteria of FDA s *Guidance for Industry Product Development Under the Animal Rule* (May 2014). Under this draft FDA guidance, the FDA may grant conditional marketing approval based on adequate and well-controlled animal efficacy studies when human challenge studies would not be ethical and field trials after accidental or intentional human exposure have not been feasible, provided the results of those animal studies establish that the drug is reasonably likely to produce clinical benefit and certain other conditions are met.

FibroGen has initiated discussions with MCART at the University of Maryland regarding evaluation of FG-3019 in their established model of whole thorax lung irradiation (WTLI) in non-human primates. If efficacy can be demonstrated in non-human primates comparable to that achieved in the radiation inducted fibrosis in mice, it could enable limited FDA approval of FG-3019 as a medical countermeasure. Such an approval could potentially lead to procurement of FG-3019 for national health security.

Other Potential Indications for FG-3019

We believe that FG-3019 has potential to be a treatment for cancers and a broad array of fibrotic disorders, including:

Cancers melanoma, breast cancer, and squamous cell lung carcinoma for which there is an estimated U.S. prevalence of over 80,000 patients.

Lung scleroderma lung disease

Liver NASH, graft rejection

Kidney diabetic nephropathy, focal segmental glomerular sclerosis

Cardiovascular system congestive heart failure, pulmonary arterial hypertension

Investigational New Drug and Clinical Trial Applications

FG-3019 is being studied in the United States for the treatment of IPF under an IND that we submitted to the FDA in August 2003. FG-3019 is also being studied in the United States for the treatment of locally advanced or metastatic pancreatic cancer under an IND that we submitted to the FDA in September 2004. We have not submitted an IND for liver fibrosis as the Phase 2 clinical studies are being conducted in Hong Kong and Thailand. We submitted the CTA for FG-3019 in liver fibrosis in Thailand in September 2012 and two clinical trial certificates (CTA equivalent) for FG-3019 in liver fibrosis in Hong Kong in May of 2010 and March of 2013.

Commercialization Strategy for FG-3019

Our goal, if FG-3019 is successful, is to be a leader in the development and commercialization of novel approaches for inhibiting deep organ fibrosis and treating some forms of cancer. To date, we have retained exclusive worldwide rights for FG-3019. We plan to retain commercial rights to FG-3019 in North America and will also continue to evaluate the opportunities to establish co-development partnerships for FG-3019 as well as commercialization collaborations for territories outside of North America.

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COLLABORATIONS

Our Collaboration Partnerships for Roxadustat

Astellas

We have two agreements with Astellas for the development and commercialization of roxadustat, one for Japan, and one for Europe, the Commonwealth of Independent States, the Middle East and South Africa. Under these agreements we provided Astellas the right to develop and commercialize roxadustat for anemia in these territories.

We share responsibility with Astellas for clinical development activities required for United States and EU regulatory approval of roxadustat, and share equally those development costs under the agreed development plan for such activities. Astellas will be responsible for clinical development activities and all associated costs required for regulatory approval in all other countries in the Astellas territories. Astellas will own and have responsibility for regulatory filings in its territories. We are responsible, either directly or through our contract manufacturers, for the manufacture and supply of all quantities of roxadustat to be used in development and commercialization under the agreements.

The Astellas agreements will continue in effect until terminated. Either party may terminate the agreements for certain material breaches by the other party. In addition, Astellas will have the right to terminate the agreements for certain specified technical product failures, upon generic sales reaching a particular threshold, upon certain regulatory actions, or upon our entering into a settlement admitting the invalidity or unenforceability of our licensed patents. Astellas may also terminate the agreements for convenience upon advance written notice to us. In the event of any termination of the agreements, Astellas will transfer and assign to us the regulatory filings for roxadustat and will assign or license us the relevant trademarks used with the products in the Astellas territories. Under certain terminations, Astellas is also obligated to pay us a termination fee.

Consideration under these agreements includes a total of $360.1 million in upfront and non-contingent payments, and milestone payments totaling $557.5 million, of which $542.5 million are development and regulatory milestones, and $15.0 million are commercial-based milestones. Total consideration, excluding development cost reimbursement and product sales-related payments, could reach $917.6 million. The aggregate amount of such consideration received through December 31, 2014 totals $462.6 million.

Additionally, under these agreements, Astellas pays 100% of the commercialization costs in their territories. Astellas will pay us a transfer price for our manufacture and delivery of roxadustat based on a calculation based on net sales of roxadustat in the low 20% range.

In addition, Astellas has separately invested $80.5 million in the equity of FibroGen, Inc. to date.

AstraZeneca

We also have two agreements with AstraZeneca for the development and commercialization of roxadustat for anemia, one for China, or the China agreement, and one for the United States and all other countries not previously licensed to Astellas (the RoW), or the U.S. / RoW agreement. Under these agreements we provided AstraZeneca the right to develop and commercialize roxadustat for anemia in these territories.

We will share responsibility with AstraZeneca for clinical development activities required for United States regulatory approval of roxadustat. AstraZeneca will be responsible for all of our development costs incurred under the agreed

development plan for roxadustat in the United States and EU, to the extent those costs are not covered by Astellas, after an initial 50% development cost sharing period in which our funding obligations are limited to a total of $116.5 million. Thereafter, AstraZeneca will be solely responsible for additional development costs. In China, our subsidiary FibroGen China will conduct the development work for CKD anemia and will hold all of the regulatory licenses issued by China regulatory authorities and be primarily responsible for regulatory, clinical and manufacturing. China development costs are shared 50/50. AstraZeneca is

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also responsible for 100% of development expenses in all other licensed territories outside of China. We are responsible, through our contract manufacturers, for the manufacture and supply of all quantities of roxadustat to be used in development and commercialization under the agreements.

Under the AstraZeneca agreements, we receive upfront and subsequent non-contingent payments totaling $402.2 million, a portion of which we have received and the remainder of which we expect to receive in various amounts through 2016, including a $62 million time based development milestone which became non-contingent as of July 30, 2014. Potential milestone payments under the agreements total $1.2 billion, of which $571.0 million are development and regulatory milestones, and $652.5 million are commercial-based milestones. Total consideration under the agreements, excluding development cost reimbursement, transfer price payments, royalties and profit share, could reach $1.6 billion. The aggregate amount of such consideration received through December 31, 2014 totals $220.2 million.

Payments under these agreements include over $500 million in upfront, non-contingent and other payments received or expected to be received prior to the first U.S. approval, excluding development expense reimbursement.

AstraZeneca purchased 1,111,111 shares of our common stock at the initial public offering price for an aggregate purchase price of $20 million in a private placement concurrent with our initial public offering. In connection with the purchase of our shares of common stock in the private placement, AstraZeneca has also entered into a standstill agreement which provides that, until November 2019, neither AstraZeneca nor its representatives will, directly or indirectly, among other things, acquire any additional securities or assets of ours, solicit proxies for our securities, participate in a business combination involving us, or seek to influence our management or policies, except with the prior consent of our board of directors and in certain other specified circumstances involving a change of control of our company. In addition, AstraZeneca has agreed to vote its shares in favor of nominees to our board of directors, increases in the authorized capital stock of the company and amendments to our equity plans approved by the board of directors, in each case as recommended by a majority of our board of directors. AstraZeneca has also agreed, subject to specified exceptions, not to sell shares purchased by it in the private placement for the two-year period following such purchase and to limitations on the volume of its sales of such shares thereafter. In addition, AstraZeneca entered into a 180-day lock-up agreement in favor of the underwriters of our initial public offering.

Under the U.S./RoW agreement, AstraZeneca will pay for all commercialization costs in the U.S. and RoW, AstraZeneca will be responsible for the United States commercialization of roxadustat, with FibroGen undertaking specified promotional activities in the ESRD segment in the United States. In addition, we will receive a transfer price for delivery of commercial product based on a percentage of net sales in the low- to mid-single digit range and AstraZeneca will pay us a tiered royalty on net sales of roxadustat in the low 20% range.

Under the China agreement, which is conducted through FibroGen China, the commercial collaboration is structured as a 50/50 profit share. AstraZeneca will conduct commercialization activities in China as well as serve as the master distributor for roxadustat and will fund roxadustat launch costs in China until FibroGen China has achieved profitability. At that time, AstraZeneca will recoup 50% of their historical launch costs out of initial roxadustat profits in China.

AstraZeneca may terminate the U.S./RoW agreement upon specified events, including our bankruptcy or insolvency, our uncured material breach, technical product failure, or upon 180 days prior written notice at will. If AstraZeneca terminates the U.S/RoW agreement at will, in addition to any unpaid non-contingent payments, it will be responsible to pay for a substantial portion of the post-termination development costs under the agreed development plan until regulatory approval.

AstraZeneca may terminate the China agreement upon specified events, including our bankruptcy or insolvency, our uncured material breach, technical product failure, or upon advance prior written notice at will. If AstraZeneca terminates our China agreement at will, it will be responsible to pay for transition costs as well as make a specified payment to FibroGen China.

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In the event of any termination of the agreements, but subject to modification upon termination for technical product failure, AstraZeneca will transfer and assign to us any regulatory filings and approvals for roxadustat in the affected territories that they may hold under our agreements, grant us licenses and conduct certain transition activities.

Information about collaboration partners that accounted for more than 10% of our total revenue or accounts receivable for the last three fiscal years is set forth in Note 14 to our consolidated financial statements under Item 8 of this Annual Report.

COMPETITION

The pharmaceutical and biotechnology industries are highly competitive, particularly in some of the indications we are developing drug candidates, including anemia in CKD, IPF, pancreatic cancer and liver fibrosis. We face competition from multiple other pharmaceutical and biotechnology companies, many of which have significantly greater financial, technical and human resources and experience in product development, manufacturing and marketing. These potential advantages of our competitors are particularly a risk in IPF, pancreatic cancer and liver fibrosis, where we do not currently have a development or commercialization partner.

We expect any products that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, convenience of administration and delivery, price, the level of generic competition and the availability of reimbursement from government and other third party payors.

If either of our lead product candidates is approved, they will compete with currently marketed products, and product candidates that may be approved for marketing in the future, for treatment of the following indications:

Roxadustat Anemia in CKD

If roxadustat is approved for the treatment of anemia in patients with CKD, competing drugs are expected to include ESAs such as epoetin alfa (EPOGEN® marketed by Amgen Inc. in the United States, Procrit® marketed by Johnson & Johnson, Inc. in the United States, and Eprex® also marketed by Johnson & Johnson in other markets and Espo® marketed by Kyowa Hakko Kirin, or KHK, in Japan and China), darbepoetin (Aranesp® marketed by Amgen in the United States and Europe, and by KHK in Hong Kong; NESP® marketed by KHK in Japan, Korea, Singapore, Taiwan, Thailand), as well as Mircera® (marketed by Hoffmann-La Roche, or Roche, in Europe and approved in the United States) and NeoRecormon®/Epogin® (marketed by Roche in China and Japan). ESAs have been used in the treatment of anemia in CKD for over 20 years, serving a significant majority of dialysis patients as well as those non-dialysis patients receiving anemia therapy under nephrology care. NDD-CKD patients who are not under the care of nephrologists, including those with diabetes and hypertension, do not typically receive ESAs and are often left untreated. Physicians and patients currently treated with ESAs may be reluctant to switch to roxadustat from products with which they have become familiar. We, and our collaboration partners, will also likely face competition from potential new anemia therapies currently in clinical development. For example, while roxadustat is currently the only HIF-PH inhibitor in Phase 3 development, Akebia Pharmaceuticals, Inc., Bayer Corporation and GlaxoSmithKline plc are all in Phase 2 development of HIF-PH inhibitor product candidates for anemia in CKD indications. We may face competition for patient recruitment and enrollment for clinical trials and potentially in commercial sales. In addition, there are other companies developing biologic therapies for treatment of other anemia indications. For example, Acceleron Pharma Inc., in partnership with Celgene Corporation, is in Phase 2 development of protein therapeutic candidates to treat anemia and associated complications in patients with ß-thalassemia and MDS, and has received orphan drug status from the EMA and FDA for these indications. Noxxon Pharma AG is developing an anti-hepcidin Spiegelmer® lexaptepid pegol (NOX-H94), a mirror image of a natural oligonucleotide, which is in Phase 2 development in cancer patients for the treatment of anemia associated with chronic disease, as well as in

ESA-hyporesponsive patients on dialysis.

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The introduction of biosimilars for ESAs into the U.S. market may occur by the time roxadustat enters the market and may increase the competition for roxadustat and alter the competitive and pricing landscape. A biosimilar product is a follow-on version of an existing, branded biologic product. Under current laws, an application for a biosimilar product should not be approved by the FDA until 12 years after the existing, patent-protected product was approved under a BLA. The patents for epoetin alfa (EPOGEN) expired in 2004 in the EU, and in the United States the remaining patents will expire by May 2015. Several biosimilar versions of currently marketed ESAs are available for sale in the EU and many other markets, and several biosimilar versions of epoetin alfa are currently under development or regulatory review in the United States and other territories, including Hospira s Retacrit , an EPOGEN and Procrit biosimilar which has been marketed in Europe, and for which Hospira s BLA was filed with the FDA in February 2015. In China, biosimilars of epoetin alfa are offered by Chinese pharmaceutical companies such as EPIAO marketed by 3SBio Inc. and Xue Da Sheng marketed by Hayao Biological.

Two of the largest operators of dialysis clinics in the United States, DaVita Healthcare Partners Inc., or DaVita, and Fresenius Medical Care AG & Co. KGaA, or Fresenius, collectively represent more than 60% of the dialysis market in the United States, and have entered into long-term supply agreements with Amgen that began in January 2012 for 7 years and 3 years, respectively. DaVita is committed to purchase over 90% of its anemia drug needs under an exclusive arrangement. The Fresenius arrangement with Amgen is non-exclusive, and Fresenius has recently announced that a pilot study with Mircera is underway. Successful penetration in this market would require a significant agreement with at least either Fresenius or DaVita, on favorable terms and on a timely basis. The currently marketed ESA products are also supported by large pharmaceutical companies with greater experience and expertise in commercialization in the anemia market, including securing reimbursement, government contracts and relationships with key opinion leaders. We expect that significant resources will be required from us and our collaboration partners, AstraZeneca and Astellas, to overcome the challenges of bringing a new product into an established market with concentrated buyers.

FG-3019

We are currently in Phase 2 development of FG-3019 to treat IPF, pancreatic cancer and liver fibrosis. Most of our competitors have significantly more resources and expertise in development, commercialization and manufacturing, particularly due to the fact that we have not yet established a co-development partnership for FG-3019. For example, both Roche (through its acquisition of InterMune) and Boehringer Ingelheim Pharma GmbH & Co. KG, who have received approval for product candidates for the treatment of IPF in the United States, have successfully developed and commercialized drugs in various indications and have built sales organizations that we do not currently have; both have more resources and more established relationships when competing with us for patient recruitment and enrollment for clinical trials or, if we are approved, in the market.

Idiopathic Pulmonary Fibrosis

If approved to treat IPF, FG-3019 would compete with pirfenidone, which is approved for marketing in Europe, Canada and Japan. As of October 2014, Roche (through its acquisition of InterMune) has obtained approval in the United States for pirfenidone for the treatment of IPF and Boehringer Ingelheim has obtained approval in the United States and the EU for nintedanib for the treatment of IPF. We believe that if FG-3019 can be shown to safely stabilize or reverse lung fibrosis, and thus stabilize or improve lung function, it can compete with pirfenidone and nintedanib for market share in IPF. However, it may be difficult to encourage treatment providers and patients to switch to FG-3019 from a product they are already familiar with. We will also likely face competition from potential new IPF therapies.

FG-3019 is an injectable protein, which may be more expensive and less convenient than small molecules such as nintedanib and pirfenidone. Other potential competitive product candidates in various stages of Phase 2 development for IPF include Gilead Sciences, Inc. s simtuzumab, Bristol-Myers Squibb s BMS-986020, and Biogen Idec s STX-100.

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Pancreatic Cancer

We are developing FG-3019 to be used in combination with Abraxane® (nab-paclitaxel) and gemcitabine in pancreatic cancer. Celgene s Abraxane was launched in the United States and Europe in 2013 and 2014, respectively, and was the first drug approved in this disease in nearly a decade. Merrimack Pharmaceuticals, Inc. has completed a pivotal Phase 3 clinical trial of MM-398 for the treatment of patients with metastatic pancreatic cancer who have previously failed treatment with gemcitabine. In November 2014, Merrimack announced that it had received Fast Track designation from the FDA and intended to start the NDA submission process in December 2014 with the goal of completing the NDA submission in the first quarter, or early in the second quarter, of 2015. In addition, treatments for cancer are often used in combination instead of as monotherapy; thus, we also face competition for FG-3019 from other agents seeking approval in conjunction with gemcitabine and Abraxane. Examples include: Threshold Pharmaceuticals, Inc. in partnership with Merck KGaA, is in Phase 3 clinical trials of its compound TH-302 in combination with gemcitabine and in Phase 1 clinical trials for TH-302 in combination with gemcitabine and Abraxane, for the treatment of pancreatic cancer; and Halozyme Therapeutics, Inc. is in Phase 2 clinical trials to treat pancreatic cancer with its compound PEGPH20 in combination with gemcitabine and Abraxane.

There are a number of other product candidates in clinical trials for pancreatic cancer, many of which are in combination with existing chemotherapies, as both first-line and second-line therapy for metastatic pancreatic cancer. We will not only face a large number of product candidates competing for patient recruitment and enrollment for our clinical trials, but we could also face a substantial number of competitors if FG-3019 is approved for the treatment of pancreatic cancer.

Liver Fibrosis

If approved to treat HBV and HCV associated liver fibrosis, FG-3019 would compete with advances in HBV and HCV antiviral therapy, which may significantly decrease the potential market for FG-3019 in liver fibrosis. HBV and HCV therapies include: Gilead s sofosbuvir (Sovaldi®), Abbvie s Viekira Pak , entecavir (Baraclude®), adefovir (Hepsera®), lamivudine (Epivir®), simeprevir (Olysio®), tenofovir (Viread®), telbivudine (Tyzeka®), and interferon alpha-2a and PEGylated interferon alpha-2a (Pegasys®). Nonetheless, a significant proportion of hepatitis patients have pre-cirrhotic or cirrhotic liver fibrosis and treatments that address the fibrotic process itself could provide benefit for patients with approaching liver failure. Potential antifibrotic competitors in the area of liver fibrosis include Gilead s simtuzumab and Intercept Pharmaceuticals, Inc. s obeticholic acid (OCA).

Duchenne Muscular Dystrophy

Currently, no disease modifying drugs have received full approval to treat DMD, and no disease modifying products are commercially available outside of the European Economic Area. If approved and launched commercially to treat DMD, FG-3019 may face competition for some patients from Sarepta Therapeutics, Inc, as well as BioMarin, and PTC Therapeutics, Santhera Pharmaceuticals, Pfizer, Summit plc and Tivorsan Pharmaceuticals. BioMarin recently completed its acquisition of Prosensa Holding, N.V. Prosensa, along with Sarepta have entered clinical development with therapeutics based on exon-skipping technology which seeks to help patients produce functioning forms of the dystrophin protein. The lead molecules for both Prosensa (drisapersen) and Sarpeta (eteplirsen) focus on skipping exon-51. Therapies skipping exon-51 target only 13% of the patients who have DMD. To reach other DMD patients with their technology Prosensa and Sarepta would need to generate a new clinical candidate for each type of mutation in the dystrophin gene. PTC Therapeutics product ataluren (Translarna™) received conditional approval in Europe in 2014.Translarna targets a different set of DMD patients from those being targeted by Prosensa s and Sarepta s therapeutics that skip exon-51; however, it is also limited to a subset of patients who carry a specific mutation. Conversely, FG-3019 is intended to treat DMD patients without limitation to type of mutation. Santhera

Pharmaceuticals recently reported positive Phase 3 data with its drug idebenone (Raxone®/Catena®) in a trial measuring changes in lung function for DMD patients. Idebenone is a synthetic short-chain benzoquinone and a cofactor for the enzyme NAD(P)H:quinone

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oxidoreductase (NQO1). Pfizer s product candidate, which is in Phase 2 development, is an antibody targeting myostatin which is a protein that regulates muscle growth. The goal of the program is to increase muscle growth and muscle strength in patients with DMD. Summit plc and Tivorsan Pharmaceuticals are both working on drugs involving the utrophin pathway. The goal of these programs is to increase the production the utrophin protein to compensate for the nonfunctional dystrophin protein produced by DMD patients. Utrophin is a protein similar to dystrophin. Summit is conducting a Phase 1b trial and Tivorsan is conducting preclinical work.

MANUFACTURE AND SUPPLY

We have historically and in the future plan to continue to enter into contractual arrangements with qualified third-party manufacturers to manufacture and package our products and product candidates for territories outside of China. We believe that this manufacturing strategy enables us to more efficiently direct financial resources to the research, development and commercialization of product candidates rather than diverting resources to establishing a significant internal manufacturing infrastructure, unless there is additional strategic value for establishing manufacturing capabilities, such as in China. As our product candidates proceed through development, we are discussing the timing of entry into longer term commercial supply agreements with key suppliers and manufacturers in order to meet the ongoing and planned clinical and commercial supply needs for ourselves and our partners. Our timing of entry into these agreements is based on the current development plans for roxadustat, FG-3019 and FG-5200.

Roxadustat

Roxadustat is a small-molecule drug manufactured from generally available commercial starting materials and chemical technologies and multi-purpose equipment available from many third party contract manufacturers. Our third party manufacturers of roxadustat Phase 3 study material include Shanghai SynTheAll Pharmaceutical Co., Ltd. and STA Pharmaceutical Hong Kong Limited and their respective affiliates, or collectively WuXi STA, and Catalent Pharma Solutions, or Catalent. WuXi STA is located in China and currently supplies our API, and intermediate needs for those materials used in our Phase 3 clinical trials. WuXi STA has passed inspections by several regulatory agencies, including the FDA and CFDA, and is cGMP compliant. Catalent is located in the United States and supplies our Phase 3 tablet materials and provides tablet development services. Catalent has passed several regulatory inspections, including by the FDA, and manufactures commercial products for other clients.

To date, we believe that roxadustat has been manufactured under current Good Manufacturing Practices, or cGMP, regulations and in compliance with applicable regulatory requirements for the manufacture of drug substance and drug product used in clinical trials and we and Astellas have performed audits of the existing roxadustat manufacturers. The intended commercial manufacturing route outside of China has been successfully scaled up to multiple hundred kilogram scale and produced more than a metric ton of roxadustat drug substance. We are in discussions with multiple parties, including WuXi STA and other potential suppliers regarding longer term commercial supply arrangements.

In China, we plan to use the clinical material from WuXi STA and will conduct bioequivalence tests before NDA product is manufactured at the FibroGen China manufacturing facility in China. We plan to use API and drug product from our FibroGen China manufacturing facility upon commercialization. Until our FibroGen China manufacturing facility is qualified and licensed for the China market, we have no internal manufacturing capabilities and will continue to rely on external contract manufacturers. Even when our manufacturing facility is available to manufacture in and for China, we may use contract manufacturers to supplement commercial supply for China.

Irix Letter Agreement

In July 2002, we and IRIX Pharmaceuticals, Inc., a third party manufacturer, entered into a Letter of Agreement for IRIX Pharmaceuticals Single Source Manufacturing Agreement, or the Letter of Agreement, in connection

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with a contract manufacturing arrangement for clinical supplies of HIF-PH inhibitors, including roxadustat. The Letter of Agreement contained a service agreement that included terms and schedule for the delivery of clinical materials, and also included a term sheet for a single source agreement for the GMP manufacture of HIF-PH inhibitors, including roxadustat. Specifically, pursuant to the Letter of Agreement, we and IRIX agreed to negotiate a single source manufacturing agreement that included a first right to negotiate a manufacturing contract for HIF-PH inhibitors, including roxadustat, provided that IRIX is able to match any third party bids within 5%, and the exclusive right to manufacture extends for five years after approval of an NDA. Any agreement would provide that no minimum amounts would be specified until appropriate by forecast, that we and our commercialization partner would have the rights to contract with independent third parties that exceed IRIX s internal capabilities or in the event that we or our commercialization partner determines for reasons of continuity and security that such a need exists, provided that IRIX would supply a majority of the product if it is able to meet the requirements and the schedule required by us and our partner. Subsequent to the Letter of Agreement, we and IRIX have entered into several additional service agreements. IRIX has requested in writing that we honor the Letter of Agreement with respect to the single source manufacturing agreement. To date, we have offered to IRIX opportunities to bid for the manufacture of HIF-PH inhibitors, including roxadustat.

FG-3019

To date, FG-3019 has been manufactured using specialized biopharmaceutical process techniques under an agreement with a qualified third party contract manufacturer, Boehringer Ingelheim. Our contract manufacturer is the sole source for the current clinical supply of the drug substance and drug product for FG-3019. Our contract manufacturer is only obligated to supply the amounts of FG-3019 as agreed on pursuant to work orders that are executed from time to time under our agreement as we determine need for clinical material, and we are not required to make fixed or minimum annual purchases. Our existing agreement allows us to transfer the cell line manufacturing process to another third party manufacturer at our expense, and our contractor is obligated to provide reasonable technology transfer assistance in the event of such a transfer.

FG-5200

The manufacture of FG-5200 requires three distinct steps under cGMP and involves three parties in three locations. Our proprietary recombinant human collagen is produced under contract by a third party in Finland. After quality assurance release, the material is then shipped to our vendor for conversion to a freeze-dried form suitable for production of the FG-5200 medical device. We are currently designing a fabrication plant within the FibroGen China manufacturing facility where the freeze dried collagen will be shipped for the production of FG-5200, first for preclinical and clinical testing using a small scale, pilot process and then potentially as an automated process for commercial use.

GOVERNMENT REGULATION

The clinical testing, manufacturing, labeling, storage, distribution, record keeping, advertising, promotion, import, export and marketing, among other things, of our product candidates are subject to extensive regulation by governmental authorities in the United States and other countries. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations, including in Europe and China, requires the expenditure of substantial time and financial resources. Failure to comply with the applicable requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the applicable regulatory authority to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension

of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by FDA and the Department of Justice, or other governmental entities.

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U.S. Product Approval Process

In the United States, the FDA regulates drugs and biological products, or biologics, under the Public Health Service Act, as well as the FDCA which is the primary law for regulation of drug products. Both drugs and biologics are subject to the regulations and guidance implementing these laws. Pharmaceutical products are also subject to regulation by other governmental agencies, such as the Federal Trade Commission, the Office of Inspector General of the U.S. Department of Health and Human Services, the Consumer Product Safety Commission and the Environmental Protection Agency. The clinical testing, manufacturing, labeling, storage, distribution, record keeping, advertising, promotion, import, export and marketing, among other things, of our product candidates are subject to extensive regulation by governmental authorities in the United States and other countries. The steps required before a drug or biologic may be approved for marketing in the United States generally include:

- Preclinical laboratory tests and animal tests conducted under Good Laboratory Practices.
- The submission to the FDA of an Investigational New Drug application, or IND application for human clinical testing, which must become effective before each human clinical trial commence.
- Adequate and well-controlled human clinical trials to establish the safety and efficacy of the product and conducted in accordance with Good Clinical Practices.
- The submission to the FDA of an NDA, in the case of a small molecule drug product, or a Biologic License Application, or BLA, in the case of a biologic product.
- FDA acceptance, review and approval of the NDA or BLA, as applicable.
- Satisfactory completion of an FDA inspection of the manufacturing facilities at which the product is made to assess compliance with cGMPs.

The testing and approval process requires substantial time, effort and financial resources, and the receipt and timing of any approval is uncertain. The FDA may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to a potentially unacceptable health risk.

Preclinical studies include laboratory evaluations of the product candidate, as well as animal studies to assess the potential safety and efficacy of the product candidate. Preclinical studies must be conducted in compliance with FDA regulations regarding GLPs. The results of the preclinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of the IND, which includes the results of preclinical testing and a protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the first phase or phases of the clinical trial lends themselves to an efficacy determination. The IND will become effective automatically 30 days after receipt by the FDA, unless the FDA raises concerns or questions about the conduct of the trials as outlined in the IND prior to that time. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed. The IND must become effective before clinical trials may be commenced.

Clinical trials involve the administration of the product candidates to healthy volunteers, or subjects, or patients with the disease to be treated under the supervision of a qualified principal investigator. Clinical trials must be conducted under the supervision of one or more qualified principal investigators in accordance with GCPs and in accordance with protocols detailing the objectives of the applicable phase of the trial, dosing procedures, research subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Progress reports detailing the status of clinical trials must be submitted to the FDA annually. Sponsors must also timely report to the FDA serious and unexpected adverse events, any clinically important increase in the rate of a serious suspected adverse event over that listed in the protocol or investigator s brochure, or any findings from other studies or tests that suggest a significant risk in humans exposed to the product candidate. Further, the protocol for each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, ethical factors, and the safety of human subjects and the possible liability of the institution.

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Clinical trials are typically conducted in three sequential phases prior to approval, but the phases may overlap and different trials may be initiated with the same drug candidate within the same phase of development in similar or different patient populations. These phases generally include the following:

Phase 1. Phase 1 clinical trials represent the initial introduction of a product candidate into human subjects, frequently healthy volunteers. In Phase 1, the product candidate is usually tested for pharmacodynamic and pharmacokinetic properties such as safety, including adverse effects, dosage tolerance, absorption, distribution, metabolism and excretion.

Phase 2. Phase 2 clinical trials usually involve studies in a limited patient population to (1) evaluate the efficacy of the product candidate for specific indications, (2) determine dosage tolerance and optimal dosage and (3) identify possible adverse effects and safety risks.

Phase 3. If a product candidate is found to be potentially effective and to have an acceptable safety profile in Phase 2 studies, the clinical trial program will be expanded to Phase 3 clinical trials to further evaluate clinical efficacy, optimal dosage and safety within an expanded patient population at geographically dispersed clinical study sites.

Phase 4. Phase 4 clinical trials are conducted after approval to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of drugs approved under accelerated approval regulations, or when otherwise requested by the FDA in the form of post-market requirements or commitments. Failure to promptly conduct any required Phase 4 clinical trials could result in withdrawal of approval.

The results of preclinical studies and clinical trials, together with detailed information on the manufacture, composition and quality of the product candidate, are submitted to the FDA in the form of an NDA (for a drug) or BLA (for a biologic), requesting approval to market the product. The application must be accompanied by a significant user fee payment. The FDA has substantial discretion in the approval process and may refuse to accept any application or decide that the data is insufficient for approval and require additional preclinical, clinical or other studies.

Review of Application

Once the NDA or BLA submission has been accepted for filing, which occurs, if at all, 60 days after submission, the FDA informs the applicant of the specific date by which the FDA intends to complete its review. This is typically 12 months from the date of submission. The review process is often extended by FDA requests for additional information or clarification. The FDA reviews NDAs and BLAs to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product s identity, strength, quality and purity. Before approving an NDA or BLA, the FDA may inspect the facilities at which the product is manufactured and will not approve the product unless the manufacturing facility complies with cGMPs and will also inspect clinical trial sites for integrity of data supporting safety and efficacy. During the approval process, the FDA also will determine whether a risk evaluation and mitigation strategy, or REMS, is necessary to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the application must submit a proposed REMS; the FDA will not approve the application without an approved REMS, if required. A REMS can substantially increase the costs of obtaining approval. The FDA may also convene an advisory committee of external experts to provide input on certain review issues relating to risk, benefit and interpretation of clinical trial data. The FDA may delay approval of an NDA if applicable regulatory criteria are not satisfied and/or the FDA requires additional testing or information. The FDA may require post-marketing testing and surveillance to monitor safety or efficacy of a product. FDA will issue either an approval of the NDA or BLA or a Complete Response Letter detailing the deficiencies and information required in order for

reconsideration of the application.

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Pediatric Exclusivity and Pediatric Use

Under the Best Pharmaceuticals for Children Act, or BPCA, certain drugs or biologics may obtain an additional six months of exclusivity in an indication, if the sponsor submits information requested in writing by the FDA, or a Written Request, relating to the use of the active moiety of the drug or biologic in children. The FDA may not issue a Written Request for studies on unapproved or approved indications or where it determines that information relating to the use of a drug or biologic in a pediatric population, or part of the pediatric population, may not produce health benefits in that population.

We have not received a Written Request for such pediatric studies with respect to our product candidates, although we may ask the FDA to issue a Written Request for studies in the future. To receive the six-month pediatric market exclusivity, we would have to receive a Written Request from the FDA, conduct the requested studies in accordance with a written agreement with the FDA or, if there is no written agreement, in accordance with commonly accepted scientific principles, and submit reports of the studies. A Written Request may include studies for indications that are not currently in the labeling if the FDA determines that such information will benefit the public health. The FDA will accept the reports upon its determination that the studies were conducted in accordance with and are responsive to the original Written Request, agreement, or commonly accepted scientific principles, as appropriate, and that the reports comply with the FDA s filing requirements.

In addition, the Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric studies for most drugs and biologicals, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs, BLAs and supplements thereto must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must include the evaluation of the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA, on its own initiative or at the request of the sponsor, may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted by FDA if they believe that additional safety or effectiveness data in the adult population needs to be collected before the pediatric studies begin. After April 2013, the FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Post-Approval Requirements

Even after approval, drugs and biologics manufactured or distributed pursuant to FDA approvals are subject to continuous regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA or BLA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product s safety and effectiveness after commercialization.

In addition, entities involved in the manufacture and distribution of approved drugs and biologics are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are

strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

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Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may also result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- Restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls.
- Fines, warning letters or holds on post-approval clinical trials.
- Refusal of the FDA to approve pending NDAs or BLAs or supplements to approved NDAs or BLAs, or suspension or revocation of product license approvals.
- Product seizure or detention, or refusal to permit the import or export of products.
- Injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Prescription Drug Marketing Act

The distribution of pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level and sets minimum standards for the registration and regulation of drug distributors at the state level. Under the PDMA and state law, states require the registration of manufacturers and distributors who provide pharmaceuticals in that state, including in certain states manufacturers and distributors who ship pharmaceuticals into the state even if such manufacturers or distributors have no place of business within the state. The PDMA and state laws impose requirements and limitations upon drug sampling to ensure accountability in the distribution of samples. The PDMA sets forth civil and criminal penalties for violations of these and other provisions.

Federal and State Fraud and Abuse and Data Privacy and Security and Transparency Laws and Regulations

In addition to FDA restrictions on marketing of pharmaceutical products, federal and state healthcare laws restrict certain business practices in the biopharmaceutical industry. These laws include, but are not limited to, anti-kickback, false claims, data privacy and security, and transparency statutes and regulations.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any good, facility, item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payment, ownership interests and providing anything at less than its fair market value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common

activities from prosecution, the exemptions and safe harbors are drawn narrowly, and our practices may not in all cases meet all of the criteria for a statutory exception or safe harbor protection. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Several courts have interpreted the statute s intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated. The intent standard under the Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, PPACA, to a stricter intent standard such that a person or entity no longer needs to have actual knowledge of this statute or the specific intent to violate it in order to have committed a violation. In addition, PPACA codified case law 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 civil False Claims Act (discussed below). Further, civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The federal false claims laws prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment or approval to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes any request or demand for money or property presented to the US government. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies marketing of the product for unapproved, and thus non-reimbursable, uses. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payers and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of, or payment for, healthcare benefits, items or services.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA s privacy and security standards directly applicable to business associates independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney s fees and costs associated with pursuing federal civil actions. In addition, state laws govern 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.

Additionally, the federal Physician Payments Sunshine Act within the PPACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available

under Medicare, Medicaid or the Children s Health Insurance Program (with certain exceptions) to report information related to certain payments or other transfers of value made or distributed to physicians and

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teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members.

Also, many states have similar healthcare statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer. Some states require the posting of information relating to clinical studies. In addition, California requires pharmaceutical companies to implement a comprehensive compliance program that includes a limit on expenditures for, or payments to, individual medical or health professionals. If our operations are found to be in violation of any of the health regulatory laws described above or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil and/or administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion of products from reimbursement under government programs, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products will be sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Pharmaceutical Coverage, Pricing and Reimbursement

In both domestic and foreign markets, our sales of any approved products will depend in part on the availability of coverage and adequate reimbursement from third-party payers. Third-party payers include government health administrative authorities, managed care providers, private health insurers and other organizations. Patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payers to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Sales of our products will therefore depend substantially, both domestically and abroad, on the extent to which the costs of our products will be paid by third-party payers. These third-party payers are increasingly focused on containing healthcare costs by challenging the price and examining the cost-effectiveness of medical products and services. In addition, significant uncertainty exists as to the coverage and reimbursement status of newly approved healthcare product candidates. The market for our products and product candidates for which we may receive regulatory approval will depend significantly on access to third-party payers drug formularies, or lists of medications for which third-party payers provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payers may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available.

Because each third-party payer individually approves coverage and reimbursement levels, obtaining coverage and adequate reimbursement is a time-consuming, costly and sometimes unpredictable process. We may be required to provide scientific and clinical support for the use of any product to each third-party payer separately with no assurance that approval would be obtained, and we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. This process could delay the market acceptance of any product and could have a negative effect on our future revenues and operating results. We cannot be certain that our products and our product candidates will be considered cost-effective. Because coverage and reimbursement determinations are made on a payer-by-payer basis, obtaining acceptable coverage and reimbursement from one payer does not guarantee that we will obtain similar acceptable coverage or reimbursement from another payer. If we are unable to obtain coverage of, and adequate reimbursement and payment levels for, our product candidates from third-party payers,

physicians may limit how much or under what circumstances they will prescribe or administer them and patients may decline to purchase them. This in turn could affect our ability to successfully commercialize our products and impact our profitability, results of operations, financial condition and future success.

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In addition, in many foreign countries, particularly the countries of the EU and China, the pricing of prescription drugs is subject to government control. In some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of a company placing the medicinal product on the market. We may face competition for our product candidates from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with our own products, which could negatively impact our profitability.

Healthcare Reform

In the United States and foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations as we begin to directly commercialize our products. In particular, there have been and continue to be a number of initiatives at the US federal and state level that seek to reduce healthcare costs. If a drug product is reimbursed by Medicare or Medicaid, pricing and rebate programs must comply with, as applicable, the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990, as amended, and the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA. The MMA imposed new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, any negotiated prices for our future products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain from non-governmental payers. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from Medicare Part D may result in a similar reduction in payments from non-governmental payers.

Moreover, the recently enacted federal Drug Supply Chain Security Act, imposes new obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements of this new federal legislation, manufacturers will be required to provide certain information regarding the drug product to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding the drug product. Further, under this new legislation, manufacturers will have drug product investigation, quarantine, disposition, and notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

Furthermore, political, economic and regulatory influences are subjecting the healthcare industry in the United States to fundamental change. Initiatives to reduce the federal budget and debt and to reform healthcare coverage are

increasing cost-containment efforts. We anticipate that Congress, state legislatures and the private sector will continue to review and assess alternative healthcare benefits, controls on healthcare spending through limitations on the growth of private health insurance premiums and Medicare and Medicaid spending, the creation of large

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insurance purchasing groups, price controls on pharmaceuticals and other fundamental changes to the healthcare delivery system. Any proposed or actual changes could limit or eliminate our spending on development projects and affect our ultimate profitability. In March 2010, PPACA was signed into law. PPACA has the potential to substantially change the way healthcare is financed by both governmental and private insurers. Among other cost containment measures, PPACA established: an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents; revised the methodology by which rebates owed by manufacturers to the state and federal government for covered outpatient drugs under the Medicaid Drug Rebate Program are calculated; increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; and extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations. In the future, there may continue to be additional proposals relating to the reform of the U.S. healthcare system, some of which could further limit the prices we are able to charge for our products, or the amounts of reimbursement available for our products. If future legislation were to impose direct governmental price controls and access restrictions, it could have a significant adverse impact on our business. Managed care organizations, as well as Medicaid and other government agencies, continue to seek price discounts. Some states have implemented, and other states are considering, price controls or patient access constraints under the Medicaid program, and some states are considering price-control regimes that would apply to broader segments of their populations that are not Medicaid-eligible. Due to the volatility in the current economic and market dynamics, we are unable to predict the impact of any unforeseen or unknown legislative, regulatory, payer or policy actions, which may include cost containment and healthcare reform measures. Such policy actions could have a material adverse impact on our profitability.

Regulation in China

The pharmaceutical industry in China is highly regulated. The primary regulatory authority is the CFDA, including its provincial and local branches. As a developer, manufacturer and supplier of drugs, we are subject to regulation and oversight by the CFDA and its provincial and local branches. The Drug Administration Law of China provides the basic legal framework for the administration of the production and sale of pharmaceuticals in China and covers the manufacturing, distributing, packaging, pricing and advertising of pharmaceutical products. Its implementing regulations set forth detailed rules with respect to the administration of pharmaceuticals in China. In addition, we are, and we will be, subject to other Chinese laws and regulations that are applicable to business operators, manufacturers and distributors in general.

Pharmaceutical Clinical Development

A new drug must be registered and approved by the CFDA before it can be manufactured and marketed for sale. To obtain CFDA approval, the applicant must conduct clinical trials, which must be approved by the CFDA and are subject to the CFDA s supervision and inspection. There are four phases of clinical trials. Application for registration of new drugs requires completion of Phase 1, 2 and 3 of clinical trials, similar to the United States. In addition, the CFDA may require the conduct of Phase 4 studies as a condition to approval.

Phase 4 studies are post-marketing studies to assess the therapeutic effectiveness of and adverse reactions to the new drug, including an evaluation of the benefits and risks, when used among the general population or specific groups, with findings used to inform adjustments to dosage, among other things.

NDA and Approval to Market

China requires approval of the NDA as well as the manufacturing facility before a drug can be marketed in China. Approval and oversight are performed at a national and provincial levels of the CFDA, involve multiple agencies and

consist of various stages of approval.

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Under the applicable drug registration regulations, drug registration applications are divided into three different types, namely Domestic New Drug Application, Domestic Generic Drug Application, and Imported Drug Application. Drugs fall into one of three categories, namely chemical medicine, biological product or traditional Chinese or natural medicine.

Class 1 refers to a new drug which has never been marketed in any country. Domestic Class 1.1 refers to a chemical drug within Class 1. FibroGen China as a domestic entity will be submitting a domestic New Drug Application under the Domestic Class 1.1 designation which is the anticipated route by which we expect roxadustat to be considered.

In order to obtain market authorization, FibroGen China must submit to the CFDA an NDA package that contains information similar to what is necessary for a U.S. NDA, including preclinical data, clinical data, technical data on active pharmaceutical ingredient and drug product and related stability data. The stability data must be generated from a three-batch registration campaign that is conducted at our Beijing facility, from which samples will be tested by the CFDA.

If the NDA package is acceptable, FibroGen China will be granted a New Drug License confirming the drug as suitable for marketing. In addition, FibroGen China will be granted a Manufacturing License which lists the Drug Approval Code as well as the name and address of the Manufacturing License holder. Manufacturing further requires a Pharmaceutical Production Permit, or PPP, as well as GMP certification. We recently received a PPP, certifying that our manufacturing facility and manufacturing process in that facility are suitable for the manufacture of a drug for clinical or commercial purposes. A PPP requires demonstration that the facility has: (i) legally qualified pharmaceutical and engineering professionals and necessary technical workers; (ii) the premises, facilities and hygienic environment required for drug manufacturing; (iii) institutions, personnel, instruments and equipment necessary to conduct quality control and testing for drugs to be produced; and (iv) rules and regulations to ensure the quality of drugs. The PPP is required prior to conducting the registration campaign for stability and other data for the NDA.

After NDA approval, FibroGen China will be required to conduct a three-batch validation campaign, one of which will be observed onsite by the CFDA. At the successful completion of the validation campaign and associated inspection, FibroGen China will be granted a GMP certification for the commercial production of roxadustat at our Beijing manufacturing facility. Only after the issuance of the GMP license can roxadustat be manufactured and sold commercially to the China market.

Drug Price Controls

The administration of price control of pharmaceutical products is vested in the national and provincial price administration authorities. Depending on the categories of pharmaceutical products in question, the prices of pharmaceutical products listed in the Medical Insurance Catalogs, drugs with patents and other drugs whose production or trading may constitute monopolies are subject to the control of the National Development and Reform Commission of China, or the NDRC, and the relevant provincial or local price administration authorities. With respect to pharmaceutical products manufactured in China, the national price administration authority from time to time publishes price control lists setting out the names of pharmaceutical products and their respective price ceilings. The provincial price administration authorities also publish price control lists in respect of the pharmaceutical products which are manufactured within their respective areas. The main purpose of the price control policy is to set an upper limit to the prices of pharmaceutical products to prevent excessive increases in the prices of such products. Price controls on medicines are determined based on profit margins that the relevant authority deems acceptable, the type and quality of the medicine, its production costs, the prices of substitutes and the manufacturer s compliance with applicable GMP standards. Drug companies may apply for an increase in the retail price of their drug to the relevant

national or provincial authority if their product has superior effectiveness or other advantages.

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Tendering Process for Hospital Purchases of Medicines

Provincial and municipal government agencies such as provincial or municipal health departments also operate a mandatory tender process for purchases by hospitals of a medicine included in provincial medicine catalogs. These government agencies organize tenders in their province or city and typically invite manufacturers of provincial catalog medicines that are on the hospitals formularies and are in demand by these hospitals to participate in the tender process. A government-approved committee consisting of physicians, experts and officials is delegated by these government agencies the power to review bids and select one or more medicines for the treatment of a particular medical condition. The selection is based on a number of factors, including bid price, quality and a manufacturer s reputation and service. The bidding price of a wining medicine will become the price required for purchases of that medicine by all hospitals in that province or city. This price, however, is effective only until the next tender, where the manufacturer of the winning medicine must submit a new bid. Increasingly, large hospitals are forming purchasing networks in order to increase their purchasing power. In addition, hospitals of certain provinces have begun to implement collective tender processes through online bidding, which is expected to increase the transparency and competitiveness of the tendering system and allow greater access to new entrants.

Device Regulation

In China, medical devices are classified into three different categories, Class I, Class II and Class III, depending on the degree of risk associated with each medical device and the extent of control needed to ensure safety and effectiveness. Classification of a medical device is important because the class to which a medical device is assigned determines, among other things, whether a manufacturer needs to obtain a production permit and whether clinical trials are required. Classification of a medical device also determines the types of registration required and the level of regulatory authority involved in effecting the product registration. FibroGen China has submitted a device classification application to the CFDA to designate FG-5200 corneal implants as a Domestic Class III medical device. Class III devices also require product registration and are regulated by the CFDA under the strictest regulatory control.

Before a Class III medical device can be manufactured for commercial distribution, a manufacturer must effect medical device registration by proving the safety and effectiveness of the medical device to the satisfaction of respective levels of the food and drug administration and clinical trials are required for registration of Class III medical devices. In order to conduct a clinical trial on a Class III medical device, the CFDA requires manufacturers to apply for and obtain in advance a favorable inspection result for the device from an inspection center jointly recognized by the CFDA and the State Administration of Quality Supervision, Inspection and Quarantine. The application for clinical trials involving a Class III medical device with high risk must be approved by the CFDA before the manufacturer may begin clinical trials. A registration application for a Class III medical device must provide required pre-clinical and clinical trial data and information about the medical device and its components regarding, among other things, device design, manufacturing and labeling. The CFDA must provide the application data to the technical evaluation institute for an evaluation opinion within three working days after its acceptance of the application package and decide, within twenty business days after its receipt of the evaluation opinion, whether the application for registration is approved. However, the time for conducting any detection, expert review and hearing process, if necessary, will not be counted in the abovementioned time limit. If the CFDA requires supplemental information, the approval process may take much longer. The registration is valid for five years and application is required for renewal upon expiration of the existing registration certificate. Once a device is approved, a manufacturer must possess a production permit from the provincial level food and drug administration before manufacturing Class III medical devices.

Foreign Regulation Outside of China

We are planning on seeking approval for roxadustat, and potentially for our other product candidates, in Europe, Japan and China as well as other countries. In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding

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quality, safety and efficacy and governing, among other things, clinical trials, manufacturing, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the United States apply similarly in the context of other countries we are seeking approval in, including Europe and China, the approval process varies between countries and jurisdictions and can involve different amounts of product testing and additional administrative review periods. For example, in Europe, a sponsor must submit a clinical trial application, or CTA, much like an IND prior to the commencement of human clinical trials. A CTA must be submitted to each national health authority and an independent ethics committee.

For other countries outside of the EU, such as China and the countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary from country to country. The time required to obtain approval in other countries and jurisdictions might differ from or be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory approval process in other countries.

Regulatory Exclusivity for Approved Products

U.S. Patent Term Restoration

Depending upon the timing, duration, and specifics of the FDA approval of our product candidates, some of our United States patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to 5 years as compensation for patent term lost during product development and the FDA regulatory review process. The patent term restoration period is generally one-half the time between the effective date of an initial IND and the submission date of an NDA or BLA, plus the time between the submission date of the NDA or BLA and the approval of that product candidate application. Patent term restoration cannot, however, extend the remaining term of a patent beyond a total of 14 years from the product s approval date. In addition, only one patent applicable to an approved product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves applications for any patent term extension or restoration. In the future, we expect to apply for restoration of patent term for patents relating to each of our product candidates in order to add patent life beyond the current expiration date of such patents, depending on the length of the clinical trials and other factors involved in the filing of the relevant NDA or BLA.

Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain applications of companies seeking to reference another company s NDA or BLA. The Hatch-Waxman Act provides a 5-year period of exclusivity to any approved NDA for a product containing a new chemical entity (NCE) never previously approved by FDA either alone or in combination with another active moiety. No application or abbreviated new drug application (ANDA) directed to the same NCE may be submitted during the 5-year exclusivity period, except that such applications may be submitted after 4 years if they contain a certification of patent invalidity or non-infringement of the patents listed with the FDA by the innovator NDA.

Biologic Price Competition and Innovation Act

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, established an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The abbreviated regulatory approval pathway

establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as interchangeable based on similarity to an existing branded product. Under the

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BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator BLA holder. The BPCIA is complex and is only beginning to be interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and interpretation are subject to uncertainty.

Orphan Drug Act

FG-3019 has received orphan drug designation in IPF 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, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States there is no reasonable expectation that the cost of developing and making a drug product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting an NDA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. The designation of such drug also entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug or biological product as defined by the FDA or if our drug candidate is determined to be contained within the competitor s product for the same indication or disease. If a drug product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity in any indication.

Orphan designation status in the EU has similar but not identical benefits in that jurisdiction.

Products receiving orphan designation in the EU can receive ten years of market exclusivity, during which time no similar medicinal product for the same indication may be placed on the market. The ten-year market exclusivity 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 initial applicant consents to a second orphan medicinal product application; or the initial applicant cannot supply enough orphan medicinal product. An orphan product can also obtain an additional two years of market exclusivity in the EU for pediatric studies. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

Foreign Country Data Exclusivity

The EU also provides opportunities for additional market exclusivity. For example, in the EU, upon receiving marketing authorization, an NCE generally receives eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the EU from referencing the innovator s data to assess a generic application. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator s data may be referenced, but no generic product can be marketed until the expiration of the market exclusivity.

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In China, there is also an opportunity for data exclusivity for a period of six years for data included in an NDA applicable to a new chemical entity. According to the Provisions for Drug Registration, the Chinese government protects undisclosed data from drug studies and prevents the approval of an application made by another company that uses the undisclosed data for the approved drug. In addition, if an approved drug manufactured in China qualifies as an innovative drug, such as Domestic Class 1.1, and the CFDA determines that it is appropriate to protect public health with respect to the safety and efficacy of the approved drug, the CFDA may elect to monitor such drug for up to five years. During this post-marketing observation period, the CFDA will not grant approval to another company to produce, change dosage form of or import the drug while the innovative drug is under observation. The approved manufacturer is required to provide an annual report to the regulatory department of the province, autonomous region or municipality directly under the central government where it is located. Each of the data exclusivity period and the observation period runs from the date of approval for production of the new chemical entity or innovative drug, as the case may be.

INTELLECTUAL PROPERTY

Our success depends in part upon our ability to obtain and maintain patent and other intellectual property protection for our product candidates including compositions-of-matter, dosages, and formulations, manufacturing methods, and novel applications, uses and technological innovations related to our product candidates and core technologies. We also rely on trade secrets, know-how and continuing technological innovation to further develop and maintain our competitive position.

Our policy is to seek to protect our proprietary position by, among other methods, filing United States and foreign patent applications related to our proprietary technologies, inventions and any improvements that we consider important to the development and implementation of our business and strategy. Our ability to maintain and solidify our proprietary position for our products and technologies will depend, in part, on our success in obtaining and enforcing valid patent claims. Additionally, we may benefit from a variety of regulatory frameworks in the United States, Europe, China and other territories that provide periods of non-patent-based exclusivity for qualifying drug products. *See Government Regulation Regulatory Exclusivity for Approved Products .*

We cannot ensure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications that may be filed by us in the future, nor can we ensure that any of our existing or subsequently granted patents will be useful in protecting our drug candidates, technological innovations, and processes. Additionally, any existing or subsequently granted patents may be challenged, invalidated, circumvented or infringed. We cannot guarantee that our intellectual property rights or proprietary position will be sufficient to permit us to take advantage of current market trends or otherwise to provide or protect competitive advantages. Furthermore, our competitors may be able to independently develop and commercialize similar products, or may be able to duplicate our technologies, business model, or strategy, without infringing our patents or otherwise using our intellectual property.

Our patent portfolio, on a worldwide basis, encompasses over 200 granted patents and 150 pending patent applications, including over 90 granted patents and 100 pending patent applications relating to roxadustat (FG-4592) and FG-3019. Our currently granted patents with respect to composition-of-matter for roxadustat and for FG-3019 are expected to expire in 2024 or 2025, and a U.S. patent relating to crystalline forms of roxadustat is expected to expire in 2033. Additional patents and patent applications relating to manufacturing processes, formulations, and various therapeutic uses, including treatment of specific indications and improvement of clinical parameters provide additional protection for product candidates. Currently granted patents are expected to expire between 2022 and 2025, and pending patent applications, if granted, could extend patent protection to between 2033 and 2034.

The protection afforded by any particular patent depends upon many factors, including the type of patent, scope of coverage encompassed by the granted claims, availability of extensions of patent term, availability of legal

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remedies in the particular territory in which the patent is granted, and validity and enforceability of the patent. Changes in either patent laws or in the interpretation of patent laws in the United States and other countries could diminish our ability to protect our inventions and to enforce our intellectual property rights. Accordingly, we cannot predict with certainty the enforceability of any granted patent claims or of any claims that may be granted from our patent applications.

The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Our ability to maintain and solidify our proprietary position for our products and core technologies will depend on our success in obtaining effective claims and enforcing those claims once granted. We have been in the past and are currently involved in various administrative proceedings with respect to our patents and patent applications and may, as a result of our extensive portfolio, be involved in such proceedings in the future. Additionally, in the future, we may claim that a third party infringes our intellectual property or a third party may claim that we infringe its intellectual property. In any of the administrative proceedings or in litigation, we may incur significant expenses, damages, attorneys fees, costs of proceedings and experts fees, and management and employees may be required to spend significant time in connection with these actions.

Because of the extensive time required for clinical development and regulatory review of a product candidate we may develop, it is possible that any patent related to our product candidates may expire before any of our product candidates can be commercialized, or may remain in force for only a short period of time following commercialization, thereby reducing the advantage afforded by any such patent.

The patent positions for our most advanced programs are summarized below.

Roxadustat (FG-4592) Patent Portfolio

Our roxadustat patent portfolio includes four granted U.S. patents and one pending U.S. patent application offering protection for roxadustat including composition-of-matter, pharmaceutical compositions, and methods for treating anemia using roxadustat or its analogs. Exclusive of any patent term extension, the granted U.S. patents relating to the composition-of-matter of roxadustat are due to expire in 2024 or 2025. A corresponding regional patent application has been granted in Europe and validated in multiple European Patent Convention member states. Additional corresponding patents and patent applications provide broad international protection in multiple territories worldwide. Exclusive of any patent term extension, these granted foreign patents and pending patent applications, if granted, would extend patent protection to 2024. A crystalline forms patent issued by the U.S. Patent and Trademark Office is due to expire in 2033, as would patents granted from the corresponding foreign patent applications currently pending worldwide.

Under the Hatch-Waxman Act, we believe that, if roxadustat is approved, we will be eligible for the full five year patent term extension for a granted U.S. patent relating to roxadustat, which extension would expire in 2029 or 2030, depending on the patent extended. *See Government Regulation Regulatory Exclusivity for Approved Products U.S. Patent Term Restoration.*

We also hold various U.S. and foreign granted patents and pending patent applications directed to manufacturing processes for and formulations of roxadustat, crystalline forms and polymorphs of roxadustat, and methods for use of roxadustat to treat anemia or associated conditions, or to improve clinical parameters relating to anemia. Exclusive of any patent term extension, these granted patents are due to expire in 2024 to 2033, and pending patent applications, if granted, could extend patent protection to 2032 to 2034.

Roxadustat China Patent Portfolio

Our Chinese patent portfolio relating to roxadustat includes four granted Chinese patents covering roxadustat composition-of-matter and pharmaceutical compositions and uses thereof, as well as medicaments containing roxadustat for treating conditions including anemia of chronic disease, iron deficiency, and ischemic disorders.

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These granted patents are due to expire in 2022 through 2024. Our roxadustat patent portfolio in China also includes 15 pending Chinese patent applications relating to composition-of-matter, pharmaceutical compositions containing roxadustat, manufacturing processes for roxadustat, polymorphs and crystalline forms of roxadustat, and various other aspects relating to the treatment of anemia or improvement of anemia-related parameters using roxadustat, which pending applications, if granted, could be expected to expire between 2022 and 2033.

We believe that roxadustat, as a new chemical entity, would be eligible for six years of data exclusivity in China. Furthermore, upon approval as a new drug, roxadustat may receive up to five years of market exclusivity under a CFDA-imposed new drug monitoring period. *See Government Regulation Regulatory Exclusivity for Approved Products Data Exclusivity*

HIF Anemia-related Technologies Patent Portfolio

We also have an extensive worldwide patent portfolio providing broad protection for proprietary technologies relating to the treatment of anemia. This portfolio currently contains over 45 granted patents and 65 pending patent applications providing exclusivity for use of compounds falling within various and overlapping classes of HIF-PH inhibitors to achieve various therapeutic effects.

This extensive portfolio reflects a series of discoveries we made from the initial days of our HIF program through the present time. Our research efforts have resulted in progressive innovation, and the corresponding patents and patent applications reflect the success of our HIF program. Such discoveries include the ability of HIF-PH inhibitors:

To induce endogenous erythropoietin in anemic CKD patients.

To increase efficacy of EPO signaling.

To enhance EPO responsiveness of the bone marrow, for example, by increasing EPO receptor expression.

To overcome the suppressive and inhibitory effects of inflammatory cytokines, such as members of the interleukin 1, IL-1, and interleukin 6, IL-6, cytokine families, on EPO production and responsiveness.

To increase effective metabolism of iron.

To increase iron absorption and bioavailability, as measured using clinical parameters such as percent transferrin saturation, or TSAT%.

To overcome iron deficiency through effects on iron regulatory factors such as ferroportin and hepcidin.

To provide coordinated erythropoiesis resulting in increased reticulocyte hemoglobin content, or CHr, and increased mean corpuscular volume, or MCV.

To improve kidney function.

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The table below sets forth representative granted U.S. patents relating to these and other inventions, including the projected expiration dates of these patents.

PATENT NO.	TITLE	PROJECTED EXPIRATION
6,855,510	Pharmaceuticals and Methods for Treating Hypoxia and Screening Methods Therefor	July 2022
8,466,172	Stabilization of Hypoxia Inducible Factor (HIF) Alpha	December 2022
8,629,131	Enhanced Erythropoiesis and Iron Metabolism	June 2024
8,604,012	Enhanced Erythropoiesis and Iron Metabolism	June 2024
8,609,646	Enhanced Erythropoiesis and Iron Metabolism	June 2024
8,604,013	Enhanced Erythropoiesis and Iron Metabolism	June 2024
8,614,204	Enhanced Erythropoiesis and Iron Metabolism	June 2026
7,713,986	Compounds and Methods for Treatment of Chemotherapy-Induced Anemia	June 2026
8,318,703	Methods for Improving Kidney Function	February 2027

In addition to the U.S. patents listed above, our HIF anemia-related technologies portfolio includes corresponding foreign patents granted and patent applications pending in various territories worldwide.

In March 2013, we obtained the grant of European Patent No. 1463823 (the 823 patent), which claims, among other things, the use of a heterocyclic carboxamide compound selected from the group consisting of pyridine carboxamides, quinoline carboxamides, isoquinoline carboxamides, cinnoline carboxamides and beta-carboline carboxamides that inhibits HIF-PH enzyme activity in the manufacture of a medicament for increasing EPO in the prevention, pretreatment, or treatment of anemia. The granted claims of the 823 patent encompass the use of roxadustat for the treatment of anemia. On December 5, 2013, Akebia Therapeutics, Inc. filed an opposition to the 823 patent with the European Patent Office. An opposition is a mechanism providing for a third-party challenge to a granted European patent. While we believe the 823 patent will be upheld in its entirety, the ultimate outcome of the opposition remains uncertain, and ultimate resolution of the proceeding may take two to four years or longer. However, narrowing or even revocation of the 823 patent would not affect our exclusivity for roxadustat or our freedom-to-operate with respect to use of roxadustat for the treatment of anemia. Akebia and other third parties may initiate additional or similar proceedings with the European Patent Office or other similar foreign jurisdictions.

FG-3019 Patent Portfolio

Our FG-3019 patent portfolio includes two granted U.S. patents and one allowed U.S. patent application providing composition-of-matter protection for FG-3019 and related antibodies, and methods of using FG-3019 or related antibodies in the treatment of fibroproliferative disorders, including IPF, liver fibrosis, and pancreatic cancer, which cases are owned by us or are exclusively licensed by us from Medarex, Inc. (now Bristol-Myers Squibb Co.). Exclusive of any patent term extension, the U.S. patents relating to composition-of-matter of FG-3019 are due to expire in 2024 or 2025. A corresponding regional patent application has been granted in Europe and validated in multiple European Patent Convention member states. Additional corresponding patents and patent applications provide broad international protection in multiple territories worldwide. Exclusive of any patent term extension, these foreign patents, and any patents that may grant from the pending foreign patent applications, are due to expire in 2024.

Under the Hatch-Waxman Act, we believe that, if FG-3019 is approved, we will be eligible for a full five year patent term extension for one U.S. patent relating to FG-3019. In addition, we believe that FG-3019, if approved under a BLA, should qualify for a 12-year period of exclusivity currently permitted by the BPCIA. See *Government*

Regulation Regulatory Exclusivity for Approved Products .

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We also hold additional granted U.S. and foreign patents and pending patent applications directed to the use of FG-3019 to treat IPF, liver fibrosis, pancreatic cancer and other disorders. Exclusive of any patent term extension, these granted patents are due to expire in 2022 to 2025, and pending patent applications, if granted, could extend patent protection to between 2031 and 2033.

Trade Secrets and Know-How

In addition to patents, we rely upon proprietary 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 and other terms in agreements with our commercial partners, collaboration partners, consultants and employees. Such agreements are designed to protect our proprietary information, and may also grant us ownership of technologies that are developed through a relationship with a third party, such as through invention assignment provisions. Agreements may expire and we could lose the benefit of confidentiality, or our agreements may be breached and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

To the extent that our commercial partners, collaboration partners, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

In-Licenses

Dana-Farber Cancer Institute

Effective March 2006, we entered into a license agreement with the Dana-Farber Cancer Institute, or DFCI, under which we obtained an exclusive license to certain patent applications, patents and biological materials for all uses. The patent rights relate to inhibition of prolyl hydroxylation of the alpha subunit of hypoxia-inducible factor (HIF-alpha), and include granted U.S. and foreign patents due to expire in 2022, exclusive of possible patent term extension. The licensed patents relate to use of HIF-PH inhibitors such as roxadustat.

Under the DFCI agreement, we are obligated to pay DFCI for past and ongoing patent prosecution expenses for the licensed patents. We are also obligated to pay DFCI annual maintenance fees, development milestone payments of up to $425,000, sales milestone payments of up to $3 million, and a sub-single digit royalty on net sales by us or our affiliates or sublicensees of products that are covered by the licensed patents or incorporate the licensed biological materials. In addition, each sublicense we grant is subject to a one-time fixed amount payment to DFCI.

Unless earlier terminated, the agreement will continue in effect, on a country-by-country basis, until the expiration of all licensed patents in a country or, if there is no patent covering a licensed product incorporating the licensed biological materials, until 20 years after the effective date of the agreement. DFCI may terminate the agreement for our uncured material breach, if we cease to carry on our business and development activities with respect to all licensed products, if we fail to comply with our insurance obligations, or if we are convicted of a felony related to the manufacture, use, sale or importation of licensed products. We may terminate the agreement at any time on prior written notice to DFCI.

University of Miami

In May 1997, we entered into a license agreement with the University of Miami, or the University, amended in July 1999, under which we obtained an exclusive, worldwide license to certain patent applications and patents for all uses.

The current patent rights include U.S. and foreign patents that relate to biologically active fragments of connective tissue growth factor (CTGF), and corresponding nucleic acids, proteins, and antibodies, and are due to expire in 2019, exclusive of any patent term extension that may be available. The licensed patents relate to FG-3019 and related products.

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Under the University agreement, we are obligated to pay for all ongoing patent prosecution expenses for the licensed patents. We are also obligated to pay an upfront licensing fee of $21,500, all of which has been paid, and development milestone payments of up to $450,000, of which $50,000 has been paid, as well as an additional milestone payment, in the low hundreds of thousands of dollars, for each new indication for which we obtain approval for a licensed product, and a single digit royalty, subject to certain reductions, on net sales of licensed products by us or our affiliates or sublicensees.

Unless earlier terminated, the agreement will continue in effect, on a country-by-country basis, until the expiration of all licensed patents in a country. The University may terminate the agreement for our uncured material breach or bankruptcy. We may terminate the agreement for the University s uncured material breach or at any time on prior written notice to the University.

Bristol-Myers Squibb Company (Medarex, Inc.)

Effective July 9, 1998 and as amended on June 30, 2001 and January 28, 2002, we entered into a research and commercialization agreement with Medarex, Inc. and its wholly-owned subsidiary GenPharm International, Inc. (now, collectively, part of Bristol-Myers Squibb Company, or Medarex) to develop fully human monoclonal antibodies for potential anti-fibrotic therapies. Under the agreement, Medarex was responsible for using its proprietary immunizable transgenic mice or HuMAb-Mouse technology during a specified research period, or the Research Period, to produce fully human antibodies against our proprietary antigen targets, including CTGF, for our exclusive use.

The agreement granted us an option to obtain an exclusive worldwide, royalty-bearing, commercial license to develop antibodies derived from Medarex s HuMAb-Mouse technology, for use in the development and commercialization of diagnostic and therapeutic products. In December 2002, we exercised that option with respect to twelve antibodies inclusive of the antibody from which FG-3019 is derived. We granted back to Medarex an exclusive, worldwide, royalty-free, perpetual, irrevocable license, with the right to sublicense, to certain inventions created during the parties research collaboration, with such license limited to use by Medarex outside the scope of our licensed antibodies.

As a result of the exercise of our option to obtain the commercial license, Medarex is precluded from (i) knowingly using any technology involving immunizable transgenic mice containing unrearranged human immunoglobulin genes with any of our antigen targets that were the subject of the agreement, (ii) granting to a third party a commercial license that covers such antigen targets or those antibodies derived by Medarex during the Research Period, and (iii) using any antibodies derived by Medarex during the Research Period, except as permitted under the agreement for our benefit or to prosecute patent applications in accordance with the agreement.

Medarex retained ownership of the patent rights relating to certain mice, mice materials, antibodies and hybridoma cell lines used by Medarex in connection with its activities under the agreement, and Medarex also owns certain claims in patents covering inventions that arise during the Research Period, which claims are directed to (i) compositions of matter (e.g., an antibody) except formulations of antibodies for therapeutic or diagnostic use, or (ii) methods of production. We own the patent rights to any inventions that arise during the Research Period that relate to antigens, as well as claims in patents covering inventions directed to (a) methods of use of an antibody, or (b) formulations of antibodies for therapeutic or diagnostic use. Upon exercise of our option to obtain the commercial license, we obtained the sole right but not obligation to control prosecution of patents relating solely to the licensed antibodies or products. Medarex has back-up patent prosecution rights in the event we decline to further prosecute or maintain such patents.

In addition to research support payments by us to Medarex during the Research Period, and an upfront commercial license fee in the form of 181,819 shares of FibroGen Series D Convertible Preferred Stock paid upon exercise of our

option, we committed development-related milestone payments of up to $11 million per

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therapeutic product containing a licensed antibody, and we have paid a $1 million development-related milestone, in the form of 133,333 shares of FibroGen Series G Convertible Preferred Stock, for FG-3019 to date. At our election, the remaining milestone payments may be paid in common stock of FibroGen, Inc., or cash.

With respect to our sales and sales by our affiliates, the agreement also requires us to pay Medarex low single-digit royalties for licensed therapeutic products and low double-digit royalties, plus certain capped sales-based bonus royalties, for licensed diagnostic products. With respect to sales of licensed products by a sublicensee, we may elect to pay the same foregoing royalties or a high double-digit percentage of all payments received by us from such sublicensee. We are also required to reimburse Medarex any pass-through royalties, if any, payable under Medarex s upstream license agreements with Medical Research Council and DNX. Royalties payable by us under the agreement are on a licensed product-by-licensed product and country-by-country basis and subject to reductions in specified circumstances, and royalties are payable for a period until either expiration of patents covering the applicable licensed product or a specified number of years following the first commercial sale of such product in the applicable country.

Unless earlier terminated, the agreement will continue in effect for as long as there are royalty payment obligations by us or our sublicensees. Either party may terminate the agreement for certain material breaches by the other party, or for bankruptcy, insolvency or similar circumstances. In addition, we may also terminate the agreement for convenience upon written notice.

Third Party Filings

Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing products. Because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in granted patents that use of our product candidates or proprietary technologies may infringe.

If a third party claims that we infringe its intellectual property rights, we may face a number of issues, including but not limited to, litigation expenses, substantial damages, attorney fees, injunction, royalty payments, cross-licensing of our patents, redesign of our products, or processes and related fees and costs.

We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our products, product candidates, and/or proprietary technologies infringe their intellectual property rights. If one of these patents were to be found to cover our products, product candidates, proprietary technologies, or their uses, we could be required to pay damages and could be restricted from commercializing our products, product candidates or using our proprietary technologies unless we obtain a license to the patent. A license may not be available to us on acceptable terms, if at all. In addition, during litigation, the patent holder might obtain a preliminary injunction or other equitable right, which could prohibit us from making, using or selling our products, technologies, or methods.

EMPLOYEES

As of February 28, 2015, we had 348 full-time employees, 102 of whom held Ph.D. or M.D. degrees, 272 of whom were engaged in research and development and 76 of whom were engaged in business development, finance, information systems, facilities, human resources or administrative support. None of our U.S. employees are represented by a labor union. The employees of FibroGen China are represented by a labor union under the China Labor Union Law. None of our employees have entered into a collective agreement with us. We consider our employee relations to be good.

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FACILITIES

Our corporate and research and development operations are located in San Francisco, California, where we lease approximately 234,000 square feet of office and laboratory space with approximately 35,000 square feet subleased. The lease for our San Francisco headquarters expires in 2023. We also lease approximately 67,000 square feet of office and manufacturing space in Beijing, China. Our lease in China expires in 2021. We believe our facilities are adequate for our current needs and that suitable additional or substitute space would be available if needed.

LEGAL PROCEEDINGS

We are not currently a party to any material legal proceedings.

FINANCIAL INFORMATION

Information regarding our revenues, net loss and total assets is contained in our consolidated financial statements under Item 8 of this Annual Report, which information is incorporated by reference here. For the specifics of our segment and geographic revenue, please see Note 14 to our consolidated financial statements.

Research and development expenses for fiscal years ended December 31, 2014, 2013 and 2012 were $150.8 million, $85.7 million and $74.2 million, respectively. We expect our research and development expenses to continue to increase in the future as we advance our product candidates through clinical trials and expand our product candidate portfolio.

Our revenue to date has been generated primarily from our collaboration agreements with Astellas and AstraZeneca AB for the development and commercialization of roxadustat. For fiscal years ended December 31, 2014, 2013 and 2012, this revenue related to our collaboration agreements accounted for 99.9%, 99.9% and 98.8%, respectively, of our total revenue.

AVAILABLE INFORMATION

Our internet website address is www.fibrogen.com. In addition to the information about us and our subsidiaries contained in this Annual Report, information about us can be found on our website. Our website and information included in or linked to our website are not part of this Annual Report.

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended (the Exchange Act), are available free of charge through our website as soon as reasonably practicable after they are electronically filed with or furnished to the Securities and Exchange Commission (SEC). The public may read and copy the materials we file with the SEC at the SEC s Public Reference Room at 100 F Street, NE, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. Additionally the SEC maintains an internet site that contains reports, proxy and information statements and other information. The address of the SEC s website is www.sec.gov.

CORPORATE INFORMATION

We were incorporated in 1993 in Delaware. Our headquarters are located at 409 Illinois Street, San Francisco, California 94158 and our telephone number is (415) 978-1200. Our website address is www.FibroGen.com. The information contained on, or that can be accessed through, our website is not part of, and is not incorporated into, this

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Our subsidiaries consist of the following: 1) FibroGen Europe Oy (FibroGen Europe), a majority owned entity incorporated in Finland in 1996; 2) Skin Sciences, Inc., a majority owned entity incorporated in the State of Delaware in 1995; 3) FibroGen International (Cayman) Limited, a wholly owned entity incorporated in the Cayman Islands in 2011; 4) FibroGen China Anemia Holdings Ltd., a majority owned entity incorporated in the Cayman Islands in 2012; 5) FibroGen International (Hong Kong) Limited, a majority owned entity incorporated in Hong Kong in 2011; and 6) FibroGen (China) Medical Technology Development Co., Ltd. (FibroGen China), a majority owned entity incorporated in China in 2011.

FibroGen, the FibroGen logo and other trademarks or service marks of FibroGen, Inc. appearing in this Annual Report are the property of FibroGen, Inc. This Annual Report contains additional trade names, trademarks and service marks of others, which are the property of their respective owners. We do not intend our use of display of other companies trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies.

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ITEM 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below in addition to the other information included or incorporated by reference in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes and Management s Discussion and Analysis of Financial Condition and Results of Operations, before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Although we have discussed all known material risks, the risks described below are not the only ones that we may face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.

Risks Related to Our Financial Condition and History of Operating Losses

We have incurred significant losses since our inception and anticipate that we will continue to incur losses for the foreseeable future and may never achieve or sustain profitability. We may require additional financings in order to fund our operations.

We are a clinical-stage biopharmaceutical company with two lead product candidates in clinical development, roxadustat, or FG-4592 in anemia in CKD, and FG-3019 in idiopathic pulmonary fibrosis, or IPF, pancreatic cancer and liver fibrosis. Pharmaceutical product development is a highly risky undertaking. To date, we have focused our efforts and most of our resources on hypoxia-inducible factor, or HIF, and fibrosis biology research, as well as developing our lead product candidates. We are not profitable and, other than in 2006 and 2007 due to income received from our Astellas collaboration, have incurred losses in each year since our inception. We have not generated any significant revenue based on product sales to date. We continue to incur significant research and development and other expenses related to our ongoing operations. Our net loss for the years ended December 31, 2012, 2013 and 2014 was approximately $32.6 million, $14.9 million and $59.5 million, respectively. As of December 31, 2014, we had an accumulated deficit of $322.3 million. As of December 31, 2014, we had capital resources consisting of cash, cash equivalents and short-term investments of $179.8 million plus $144.1 million of long-term investments classified as available for sale securities despite contractual development and cost coverage commitments from our collaboration partners, AstraZeneca AB, or AstraZeneca, and Astellas Pharma Inc., or Astellas, and the potential to receive milestone and other payments from these partners, we anticipate we will continue to incur losses for the foreseeable future, and we anticipate these losses will increase as we continue our development of, and seek regulatory approval for our product candidates. If we do not successfully develop and obtain regulatory approval for our existing or any future product candidates and effectively manufacture, market and sell any product candidates that are approved, we may never generate product sales, and even if we do generate product sales, we may never achieve or sustain profitability on a quarterly or annual basis. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders equity and working capital. Our failure to become and remain profitable would depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations.

We believe that we will continue to expend substantial resources for the foreseeable future as we continue late-stage clinical development of roxadustat, grow our operations in China, expand our clinical development efforts on FG-3019, seek regulatory approval and prepare for the commercialization of our product candidates, and pursue additional indications. These expenditures will include costs associated with research and development, conducting preclinical trials and clinical trials, obtaining regulatory approvals in various jurisdictions, and manufacturing and supplying products and product candidates for ourselves and our partners. In particular, in our planned Phase 3 clinical trial program for roxadustat, which we believe will be the largest Phase 3 program ever conducted for an anemia

product candidate, we are expecting to enroll approximately 7,000 to 8,000 patients worldwide. We are conducting this Phase 3 program in conjunction with Astellas and AstraZeneca, and we are substantially dependent on Astellas and AstraZeneca for the funding of this large program. The outcome of any clinical trial and/or regulatory approval process is highly uncertain and we are unable to fully estimate the actual

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costs necessary to successfully complete the development and regulatory approval process for our compounds in development and any future product candidates. We believe that the net proceeds from our initial public offering, our existing cash, cash equivalents and short-term investments and expected third party collaboration revenues will allow us to fund our operating plans through at least the next 12 months. Our operating plans or third party collaborations may change as a result of many factors, which are discussed in more detail below, and other factors that may not currently be known to us, and we therefore may need to seek additional funds sooner than planned, through offerings of public or private securities, debt financings or other sources, such as royalty monetization or other structured financings. Such financings may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may adversely affect our business. We may also seek additional capital due to favorable market conditions or strategic considerations even if we currently believe that we have sufficient funds for our current or future operating plans.

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

- the rate of progress in the development of our product candidates;
- the costs of development efforts for our product candidates, such as FG-3019, that are not subject to reimbursement from our collaboration partners;
- the costs necessary to obtain regulatory approvals, if any, for our product candidates in the United States, China and other jurisdictions, and the costs of post-marketing studies that could be required by regulatory authorities in jurisdictions where approval is obtained;
- the continuation of our existing collaborations and entry into new collaborations;
- the time and unreimbursed costs necessary to commercialize products in territories in which our product candidates are approved for sale;
- the revenues from any future sales of our products as well as revenue earned from profit share, royalties and milestones;
- the level of reimbursement or third party payor pricing available to our products;
- the costs of establishing and maintaining manufacturing operations and obtaining third party commercial supplies of our products, if any, manufactured in accordance with regulatory requirements;
- the costs we incur in maintaining domestic and foreign operations, including operations in China;

regulatory compliance costs; and

the costs we incur in the filing, prosecution, maintenance and defense of our extensive patent portfolio and other intellectual property rights.

Additional funds may not be available when we require them, or on terms that are acceptable to us. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate our research and development efforts or other operations or activities that may be necessary to commercialize our product candidates.

All of our recent revenue has been earned from collaboration partners for our product candidates under development.

During the past three years, substantially all of our revenues were from our collaboration partners, including $108.8 million earned under our current collaborations with Astellas and $196.0 million earned under our current collaborations with AstraZeneca, constituting 99%, 100% and 100% of our revenues for 2012, 2013 and 2014, respectively.

We will require substantial additional capital to achieve our development and commercialization goals, which for our lead product candidate, roxadustat, is currently contemplated to be provided under our existing third party collaborations with Astellas and AstraZeneca.

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If either or both of these collaborations were to be terminated, we could require significant additional capital in order to proceed with development and commercialization of our product candidates, or we may require additional partnering in order to help fund such development and commercialization. If adequate funds or partners are not available to us on a timely basis or on favorable terms, we may be required to delay, limit, reduce or terminate our research and development efforts or other operations.

If we are unable to continue to progress our development efforts and achieve milestones under our collaboration agreements, our revenues may decrease and our activities may fail to lead to commercial products.

Substantially all of our revenues to date have been, and a significant portion of our future revenues are expected to be, derived from our existing collaboration agreements. Revenues from research and development collaborations depend upon continuation of the collaborations, reimbursement of development costs, the achievement of milestones and royalties and profits from our product sales, if any, derived from future products developed from our research. If we are unable to successfully advance the development of our product candidates or achieve milestones, revenues under our collaboration agreements will be substantially less than expected.

Risks Related to the Development and Commercialization of Our Product Candidates

We are substantially dependent on the success of our lead product candidate, roxadustat, and our second compound in development, FG-3019.

To date, we have invested a substantial portion of our efforts and financial resources in the research and development of roxadustat, which is currently our lead product candidate. Roxadustat is our only product candidate that has advanced into a potentially pivotal trial, and it may be years before the studies required for its approval are completed, if ever. Our other product candidates are less advanced in development and may never enter into pivotal studies. We have completed 26 Phase 1 and 2 clinical studies with roxadustat in North America, Europe and Asia, in which over 1,400 subjects have participated and for which we reported favorable primary and secondary safety and efficacy endpoint results. Based on our discussions with the United States Food and Drug Administration, or FDA, we believe that we have an acceptable plan for the conduct of our Phase 3 clinical trial program. We have also had discussions with China regulatory authorities regarding the conduct of Phase 3 clinical trials in China, which are part of our global Phase 3 clinical trial program for safety data. We have also discussed our Phase 3 clinical development program with three national health authorities in the EU and obtained scientific advice from the European Medicines Agency. Our near-term prospects, including maintaining our existing collaborations with Astellas and AstraZeneca, will depend heavily on successful Phase 3 development and commercialization of roxadustat.

Our other lead product candidate, FG-3019, is currently in clinical development for IPF, pancreatic cancer and liver fibrosis. FG-3019 requires substantial further development and investment. We do not have a collaboration partner for support of this compound, and, while we have promising open-label safety data and potential signals of efficacy, we would need to complete larger and more extensive controlled clinical trials to validate the results to date in order to continue further development of this product candidate. In addition, although there are many potentially promising indications beyond IPF, pancreatic cancer and liver fibrosis, we are still exploring indications for which further development of, and investment for, FG-3019 may be appropriate. Accordingly, the costs and time to complete development and related risks are currently unknown. Moreover, FG-3019 is a monoclonal antibody, which may require experience and expertise that we may not currently possess as well as financial resources that are potentially greater than those required for our small molecule lead compound, roxadustat.

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The clinical and commercial success of roxadustat and FG-3019 will depend on a number of factors, many of which are beyond our control, and we may be unable to complete the development or commercialization of roxadustat or FG-3019.

The clinical and commercial success of roxadustat and FG-3019 will depend on a number of factors, including the following:

- the timely initiation, continuation and completion of our Phase 3 clinical trials for roxadustat, which will depend substantially upon requirements for such trials imposed by the FDA and other regulatory agencies and bodies and the continued commitment and coordinated and timely performance by our third party collaboration partners, AstraZeneca and Astellas;

- the timely initiation and completion of our Phase 2 clinical trials for FG-3019, including in IPF and pancreatic cancer;

- our ability to demonstrate the safety and efficacy of our product candidates to the satisfaction of the relevant regulatory authorities;

- whether we are required by the FDA or other regulatory authorities to conduct additional clinical trials, and the scope and nature of such clinical trials, prior to approval to market our products;

- the timely receipt of necessary marketing approvals from the FDA and foreign regulatory authorities, including pricing and reimbursement determinations;

- the ability to successfully commercialize our product candidates, if approved, for marketing and sale by the FDA or foreign regulatory authorities, whether alone or in collaboration with others;

- our ability and the ability of our third party manufacturing partners to manufacture quantities of our product candidates at quality levels necessary to meet regulatory requirements and at a scale sufficient to meet anticipated demand at a cost that allows us to achieve profitability;

- our success in educating health care providers and patients about the benefits, risks, administration and use of our product candidates, if approved;

- acceptance of our product candidates, if approved, as safe and effective by patients and the healthcare community;

the success of efforts to enter into relationships with large dialysis organizations involving the administration of roxadustat to dialysis patients;

the achievement and maintenance of compliance with all regulatory requirements applicable to our product candidates;

the maintenance of an acceptable safety profile of our products following any approval;

the availability, perceived advantages, relative cost, relative safety, and relative efficacy of alternative and competitive treatments;

our ability to obtain and sustain an adequate level of pricing or reimbursement for our products by third party payors;

our ability to enforce successfully our intellectual property rights for our product candidates and against the products of potential competitors; and

our ability to avoid or succeed in third party patent interference or patent infringement claims.

Many of these factors are beyond our control. Accordingly, we cannot assure you that we will ever be able to achieve profitability through the sale of, or royalties from, our product candidates. If we or our collaboration partners are not successful in obtaining approval for and commercializing our product candidates, or are delayed in completing those efforts, our business and operations would be adversely affected.

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We may be unable to obtain regulatory approval for our product candidates, or such approval may be delayed or limited, due to a number of factors, many of which are beyond our control.

The clinical trials and the manufacturing of our product candidates are and will continue to be, and the marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to develop and, if approved, market any product candidates. Before obtaining regulatory approval for the commercial sale of any product candidate, we must demonstrate through extensive preclinical trials and clinical trials that the product candidate is safe and effective for use in each indication for which approval is sought. The regulatory review and approval process is expensive and requires substantial resources and time, and in general very few product candidates that enter development receive regulatory approval. Accordingly, we may be unable to successfully develop or commercialize roxadustat or FG-3019 or any of our other product candidates.

We have not obtained regulatory approval for any of our product candidates and it is possible that roxadustat and FG-3019 will never receive regulatory approval in any country. Regulatory authorities may delay, limit or deny approval of roxadustat or FG-3019 for many reasons, including, among others:

- our failure to adequately demonstrate to the satisfaction of regulatory authorities that roxadustat is safe and effective in treating anemia in chronic kidney disease, or CKD, or that FG-3019 is safe and effective in treating IPF, pancreatic cancer or liver fibrosis;

- our failure to demonstrate that a product candidate s clinical and other benefits outweigh its safety risks;

- the determination by regulatory authorities that additional clinical trials are necessary to demonstrate the safety and efficacy of roxadustat or FG-3019, or that ongoing clinical trials need to be modified in design, size, conduct or implementation;

- our product candidates may exhibit an unacceptable safety signal as they advance through clinical trials, in particular controlled Phase 3 trials;

- the contract research organizations, or CROs, that conduct clinical trials on our behalf may take actions outside of our control that materially adversely impact our clinical trials;

- we or third party contractors manufacturing our product candidates may not maintain current good manufacturing practices, or cGMP, successfully pass inspection or meet other applicable manufacturing regulatory requirements;

- regulatory authorities may not agree with our interpretation of the data from our preclinical trials and clinical trials;

collaboration partners may not perform or complete their clinical programs in a timely manner, or at all; or

principal investigators may determine that one or more serious adverse events, or SAEs, is related or possibly related to roxadustat, and any such determination may adversely affect our ability to obtain regulatory approval, whether or not the determination is correct.

Any of these factors, many of which are beyond our control, could jeopardize our or our collaboration partners abilities to obtain regulatory approval for and successfully market roxadustat. Because our business and operations in the near-term are almost entirely dependent upon roxadustat, any significant delays or impediments to regulatory approval could have a material adverse effect on our business and prospects.

Furthermore, in both the United States and China, we also expect to be required to perform additional clinical trials in order to obtain approval or as a condition to maintaining approval due to post-marketing requirements. If the FDA requires a risk evaluation and mitigation strategy, or REMS, for any of our product candidates if approved, the substantial cost and expense of complying with a REMS or other post-marketing requirements may limit our ability to successfully commercialize our product candidates.

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Our Phase 2 clinical trial results to date for roxadustat may not be indicative of the results that may be obtained in larger, controlled Phase 3 clinical trials required for approval.

Clinical development is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Success in preclinical and early clinical trials may not be predictive of similar results in larger, controlled clinical trials, and successful results from early or small clinical trials may not be replicated or show as favorable an outcome, even if successful. For example, in the past we developed an earlier generation product candidate aimed at treating anemia in CKD that resulted in a clinical hold for a safety signal seen in that product in Phase 2 clinical trials. The clinical hold applied to that product candidate and roxadustat and was lifted for both product candidates after submission of the requested data to the FDA. While we have not seen similar safety concerns involving roxadustat to date, our Phase 2 clinical trials have involved a relatively small number of patients exposed to roxadustat for a relatively short period of time compared to the Phase 3 clinical trials that we will be conducting, and only a fraction of the patients in the Phase 2 clinical trials were randomized to placebo. Accordingly, the Phase 2 clinical trials that we have conducted may not have uncovered safety issues, even if they exist. In addition, some of the safety concerns associated with the treatment of patients with anemia in CKD using erythropoiesis stimulating agents, or ESAs, did not emerge for many years until placebo-controlled studies had been conducted in large numbers of patients. The biochemical pathways that we believe are affected by roxadustat are implicated in a variety of biological processes and disease conditions, and it is possible that the use of roxadustat to treat larger numbers of patients will demonstrate unanticipated adverse effects, including possible drug interactions, which may negatively impact the safety profile, use and market acceptance of roxadustat. We studied the potential interaction between roxadustat and three statins (atorvastatin, rosuvastatin and simvastatin), which are used to lower levels of lipids in the blood. An adverse effect associated with increased statin plasma concentration is myopathy, which typically presents in a form of myalgia. The studies indicated the potential for increased exposure to those statins when roxadustat is taken simultaneously with those statins and suggested the need for statin dose reductions for patients receiving higher statin doses. We are planning additional clinical pharmacology studies to evaluate if the effect of any such interaction can be minimized or eliminated by a modification of the dosing schedule that would separate the administration of roxadustat and the statin. It is possible that the potential for interaction between roxadustat and statins could lead to label provisions for statins or roxadustat relating, for example, to dose scheduling or recommended statin dose limitations. In CKD patients statin therapy is often initiated earlier than treatment for anemia, and risks of myopathy have been shown to decrease with increased time on drug. While we believe the prior statin treatment history of such patients at established doses may reduce the risk of adverse effects from any interaction with roxadustat and facilitate any appropriate dose adjustments, we cannot be sure that this will be the case.

The FDA has informed us that our Phase 3 trials must include, as a safety endpoint, a major adverse cardiac events, or MACE, endpoint, which is a composite endpoint designed to identify major safety concerns, in particular relating to cardiovascular events such as cardiovascular death, myocardial infarction and stroke. In addition, we expect that our Phase 3 clinical trials supporting approval in Europe will be required to include MACE+ as a safety endpoint which, in addition to the MACE endpoints, also incorporates measurements of hospitalization rates due to heart failure or unstable angina. As a result, our ongoing and planned Phase 3 clinical trials may identify unanticipated safety concerns in the patient population under study. The FDA has also informed us that the MACE endpoint will need to be evaluated separately for our Phase 3 trials in non-dialysis dependent-CKD patients and our Phase 3 trials in dialysis dependent-CKD patients. The MACE endpoint will be evaluated in pooled analysis across Phase 3 studies of similar study populations and requires demonstration of non-inferiority relative to comparator, which means that the MACE event rate in roxadustat-treated patients must have less than a specified probability of exceeding the rate in the comparator trial by a specified hazard ratio. The number of patients necessary in order to permit a statistical analysis with adequate ability to detect the relative risk of MACE or MACE+ events in different arms of the trial, referred to as statistical power, depends on a number of factors, including the rate at which MACE or MACE+ events occur per

patient-year in the trial, treatment duration of the patients, the required hazard ratio, and the required statistical power and confidence intervals.

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In addition, we cannot be sure that the potential advantages that we believe roxadustat may have for treatment of patients with anemia in CKD as compared to the use of ESAs will be substantiated by our Phase 3 clinical trials or that we will be able to include a discussion of such advantages in our labeling should we obtain approval. We believe that roxadustat may have certain benefits as compared to ESAs based on the data from our Phase 2 clinical trials conducted to date, including safety benefits, the absence of a hypertensive effect, the potential to lower cholesterol levels and the potential to correct anemia without the use of IV iron. However, our belief that roxadustat may offer those benefits is based on a limited amount of data from our Phase 2 clinical trials and our understanding of the likely mechanisms of action for roxadustat. Some of these benefits, such as those associated with the apparent effects on blood pressure and cholesterol, are not fully understood and, even if roxadustat receives marketing approval, we do not expect that it will be approved for the treatment of high blood pressure or high cholesterol based on the data from our Phase 3 trials, and we may not be able to refer to any such benefits in the labeling. While the data from our Phase 2 trials suggests roxadustat may reduce LDL, or low-density lipoprotein, and reduce the ratio of LDL to HDL, or high-density lipoprotein, the data show it may also reduce HDL, which may be a risk to patients. In addition, causes of the safety concerns associated with the use of ESAs to achieve specified target Hb levels have not been fully elucidated. While we believe that the issues giving rise to these concerns with ESAs are likely due to factors other than the Hb levels achieved, we cannot be certain that roxadustat will not be associated with similar, or more severe, safety concerns.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early stage development, and we may face similar setbacks. In addition, the CKD patient population has many afflictions that may cause severe illness or death, which may be attributed to roxadustat in a manner that negatively impacts the safety profile of our product candidate. If the results of our ongoing or future clinical trials for roxadustat are inconclusive with respect to efficacy, if we do not meet our clinical endpoints with statistical significance, or if there are unanticipated safety concerns or adverse events that emerge during clinical trials, we may be prevented from or delayed in obtaining marketing approval for roxadustat, and even if we obtain marketing approval, any sales of roxadustat may suffer.

Our Phase 2 results to date for FG-3019 may not be indicative of the results that may be obtained in larger, controlled Phase 2 clinical trials or Phase 3 clinical trials required for approval.

We have conducted only a limited number of Phase 2 clinical trials with FG-3019. We have conducted an open-label Phase 2 dose escalation study of FG-3019 for IPF in 89 patients and a Phase 2 dose finding trial of FG-3019 combined with gemcitabine plus erlotinib in 75 patients with pancreatic cancer. We cannot be sure that the results of these trials will be substantiated in double-blinded trials with larger numbers of patients, that larger trials will demonstrate the efficacy of FG-3019 for these or other indications or that safety issues will not be uncovered in further trials. In the Phase 2 clinical trial for IPF, we used quantitative high resolution computed tomography, or HRCT, to measure the extent of lung fibrosis. While we believe that quantitative HRCT is an accurate measure of lung fibrosis, it is a novel technology that has not yet been accepted by the FDA as a primary endpoint in pivotal clinical trials. In addition, while we believe that the animal studies that we have conducted to date demonstrate that FG-3019 has the potential to arrest or reverse fibrosis and reduce tumor mass, we cannot be sure that these results will be indicative of the effects of FG-3019 in human trials. In addition, the IPF and pancreatic cancer patient populations are extremely ill and routinely experience SAEs, including death, which may be attributed to FG-3019 in a manner that negatively impacts the safety profile of our product candidate. If the additional Phase 2 clinical trials that we are planning for FG-3019 in IPF and pancreatic cancer do not show favorable efficacy results or result in safety concerns, or if we do not meet our clinical endpoints with statistical significance, or demonstrate an acceptable risk-benefit profile, we may be prevented from or delayed in obtaining marketing approval for FG-3019 in one or both of these indications.

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We do not know whether our ongoing or planned Phase 3 clinical trials in roxadustat or Phase 2 clinical trials in FG-3019 will need to be redesigned based on interim results, be able to achieve sufficient enrollment or be completed on schedule, if at all.

Clinical trials can be delayed or terminated for a variety of reasons, including delay or failure to:

address any physician or patient safety concerns that arise during the course of the trial;

obtain required regulatory or institutional review board, or IRB, approval or guidance;

reach timely agreement on acceptable terms with prospective CROs and clinical trial sites;

recruit, enroll and retain patients through the completion of the trial;

maintain clinical sites in compliance with clinical trial protocols;

initiate or add a sufficient number of clinical trial sites; and

manufacture sufficient quantities of product candidate for use in clinical trials.

In addition, we could encounter delays if a clinical trial is suspended or terminated by us, by the relevant IRBs at the sites at which such trials are being conducted, or by the FDA or other regulatory authorities. A suspension or termination of clinical trials may result from any number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, changes in laws or regulations, or a principal investigator s determination that a serious adverse event could be related to our product candidates. Any delays in completing our clinical trials will increase the costs of the trial, delay the product candidate development and approval process and jeopardize our ability to commence marketing and generate revenues. Any of these occurrences may materially and adversely harm our business and operations and prospects.

Our product candidates may cause or have attributed to them undesirable side effects or have other properties that delay or prevent their regulatory approval or limit their commercial potential.

Undesirable side effects caused by our product candidates or that may be identified as related to our product candidates by physician investigators conducting our clinical trials or even competing products in development that utilize a similar mechanism of action or act through a similar biological disease pathway could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the delay or denial of regulatory approval by the FDA or other regulatory authorities and potential product liability claims. Adverse events and SAEs that emerge during treatment with our product candidates or other compounds acting through similar biological pathways may be deemed to be related to our product candidate and may result in:

our Phase 3 clinical trial development plan becoming longer and more extensive;

regulatory authorities increasing the data and information required to approve our product candidates and imposing other requirements; and

our collaboration partners terminating our existing agreements.

The occurrence of any or all of these events may cause the development of our product candidates to be delayed or terminated, which could materially and adversely affect our business and prospects. See Business Our Development Program for Roxadustat and Business FG-3019 for the Treatment of Fibrosis and Cancer for a discussion of the adverse events and serious adverse events that have emerged in clinical trials of roxadustat and FG-3019.

Clinical trials of our product candidates may not uncover all possible adverse effects that patients may experience.

Clinical trials are conducted in representative samples of the potential patient population which may have significant variability. Clinical trials are by design based on a limited number of subjects and of limited duration for exposure to the product used to determine whether, on a potentially statistically significant basis, the planned

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safety and efficacy of any product candidate can be achieved. As with the results of any statistical sampling, we cannot be sure that all side effects of our product candidates may be uncovered, and it may be the case that only with a significantly larger number of patients exposed to the product candidate for a longer duration, may a more complete safety profile be identified. Further, even larger clinical trials may not identify rare serious adverse effects or the duration of such studies may not be sufficient to identify when those events may occur. There have been other products, including ESAs, that have been approved by the regulatory authorities but for which safety concerns have been uncovered following approval. Such safety concerns have led to labelling changes or withdrawal of ESA products from the market, and any of our product candidates may be subject to similar risks. For example, roxadustat for use in anemia in CKD is being developed to address a very diverse patient population expected to have many serious health conditions at the time of administration of roxadustat, including diabetes, high blood pressure and declining kidney function.

Although to date we have not seen evidence of significant safety concerns with our product candidates currently in clinical trials, patients treated with our products, if approved, may experience adverse reactions and it is possible that the FDA or other regulatory authorities may ask for additional safety data as a condition of, or in connection with, our efforts to obtain approval of our product candidates. If safety problems occur or are identified after our product candidates reach the market, we may, or regulatory authorities may require us to amend the labeling of our products, recall our products or even withdraw approval for our products.

We may fail to enroll a sufficient number of patients in our clinical trials in a timely manner, which could delay or prevent clinical trials of our product candidates.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on the rate at which we can recruit and enroll patients in testing our product candidates. Patients may be unwilling to participate in clinical trials of our product candidates for a variety of reasons, some of which may be beyond our control:

- severity of the disease under investigation;
- availability of alternative treatments;
- size and nature of the patient population;
- eligibility criteria for and design of the study in question;
- perceived risks and benefits of the product candidate under study;
- ongoing clinical trials of competitive agents;

physicians and patients perceptions as to the potential advantages of our product candidates being studied in relation to available therapies or other products under development;

our, our CRO s, and our trial sites efforts to facilitate timely enrollment in clinical trials;

patient referral practices of physicians; and

ability to monitor patients and collect patient data adequately during and after treatment.

Patients may be unwilling to participate in our clinical trials for roxadustat due to adverse events observed in other drug treatments of anemia in CKD, and patients currently controlling their disease with existing ESAs may be reluctant to participate in a clinical trial with an investigational drug. We may not be able to successfully initiate or continue clinical trials if we cannot rapidly enroll a sufficient number of eligible patients to participate in the clinical trials required by regulatory agencies. If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate on-going or planned clinical trials, any of which could have a material and adverse effect on our business and prospects.

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If we or third party manufacturers on which we rely cannot manufacture our product candidates and/or products at sufficient yields, we may experience delays in development, regulatory approval and commercialization.

Completion of our clinical trials and commercialization of our product candidates require access to, or development of, facilities to manufacture our product candidates at sufficient yields and at commercial scale. We have limited experience manufacturing, or managing third parties in manufacturing any of our product candidates in the volumes that are expected to be necessary to support large-scale clinical trials and sales. Our efforts to establish these capabilities may not meet our requirements as to scale-up, yield, cost, potency or quality in compliance with cGMP. Our clinical trials must be conducted with product produced under applicable cGMP regulations. Failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Even an experienced third party manufacturer may encounter difficulties in production, which difficulties may include:

- costs and challenges associated with scale-up and attaining sufficient manufacturing yields, in particular for biologic products such as FG-3019, which is a monoclonal antibody;
- supply chain issues, including the timely availability and shelf life requirements of raw materials and supplies;
- quality control and assurance;
- shortages of qualified personnel and capital required to manufacture large quantities of product;
- compliance with regulatory requirements that vary in each country where a product might be sold;
- capacity limitations and scheduling availability in contracted facilities; and
- natural disasters that affect facilities and possibly limit production.

For example, we have a limited amount of FG-3019 in storage and there are long lead times required to manufacture and scale-up the manufacture of additional supply. If we are unable to manufacture sufficient quantities of FG-3019 on a timely basis, it may limit our ability to replenish inventory or delay our development of FG-3019 in some or all indications. Any delay or interruption in the supply of our product candidates or products could have a material adverse effect on our business and operations.

Even if we are able to obtain regulatory approval of our product candidates, the label we obtain may limit the indicated uses for which our product candidates may be marketed.

With respect to roxadustat, we expect that regulatory approvals, if obtained at all, will limit the approved indicated uses for which roxadustat may be marketed, as ESAs have been subject to significant safety limitations on usage as directed by the Black Box warnings included in their labels. See Business Roxadustat For the Treatment of Anemia in

Chronic Kidney Disease Limitations of the Current Standard of Care for Anemia in CKD . In addition, in the past, an approved ESA was voluntarily withdrawn due to serious safety issues discovered after approval. The safety concerns relating to ESAs may result in labeling for roxadustat containing similar warnings even if our Phase 3 clinical trials do not suggest that roxadustat has similar safety issues. Even if the label for roxadustat does not contain all of the warnings contained in the Black Box warning for ESAs, the label for roxadustat may contain other warnings that limit the market opportunity for roxadustat. These warnings could include warnings against exceeding specified Hb targets and other warnings that derive from the lack of clarity regarding the basis for the safety issues associated with ESAs, even if our Phase 3 clinical trials do not themselves raise safety concerns.

As an organization, we have never completed a Phase 3 clinical trial or submitted a New Drug Application, or NDA, before, and may be unable to do so efficiently or at all for roxadustat or any product candidate we are developing.

We are currently conducting Phase 2 clinical trials for FG-3019 and we may need to conduct additional Phase 2 clinical trials before initiating our Phase 3 clinical trials for FG-3019. We intend to conduct Phase 3 clinical trials

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of roxadustat, and if our Phase 2 clinical trials are successful for FG-3019, we intend to conduct Phase 3 clinical trials for FG-3019. The conduct of Phase 3 clinical trials and the submission of a successful NDA is a complicated process. As an organization, we have not completed a Phase 3 clinical trial before, have limited experience in preparing, submitting and prosecuting regulatory filings, and have not submitted an NDA before. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to NDA submission and approval of roxadustat or for any other product candidate we are developing, even if our earlier stage clinical trials are successful. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials would prevent us from or delay us in commercializing roxadustat or any other product candidate we are developing.

If we are unable to establish sales, marketing and distribution capabilities or enter into or maintain agreements with third parties to market and sell our product candidates, we may not be successful in commercializing our product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sales, marketing or distribution of pharmaceutical products in any country. To achieve commercial success for any product for which we obtain marketing approval, we will need to establish sales and marketing capabilities or make and maintain our existing arrangements with third parties to perform these services at a level sufficient to support our commercialization efforts.

To the extent that we would undertake sales and marketing of any of our products directly, there are risks involved with establishing our own sales, marketing and distribution capabilities. Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- our inability to effectively manage geographically dispersed sales and marketing teams;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

With respect to roxadustat, we are dependent on the commercialization capabilities of our collaboration partners, AstraZeneca and Astellas. If either such partner were to terminate its agreement with us, we would have to commercialize on our own or with another third party. We will have limited or little control over the commercialization efforts of such third parties, and either of them may fail to devote the necessary resources and attention to sell and market our products, if any, effectively. If they are not successful in commercializing our product candidates, our business and financial condition would suffer.

We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully, than we do.

The development and commercialization of new pharmaceutical products is highly competitive. Our future success depends on our ability to achieve and maintain a competitive advantage with respect to the development and commercialization of our product candidates. Our objective is to discover, develop and commercialize new products with superior efficacy, convenience, tolerability and safety. We expect that in many cases, the products that we commercialize will compete with existing, market-leading products of companies that have large, established commercial organizations.

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If roxadustat is approved and launched commercially, competing drugs are expected to include ESAs such as EPOGEN® and Aranesp®, commercialized by Amgen Inc., Procrit® and Eprex®, commercialized by Johnson & Johnson Inc., and Mircera®, which has received marketing approval in the United States, has been commercialized by Hoffmann-La Roche, or Roche, outside of the United States, and which Roche is able to commercialize in the United States beginning in mid-2014 if it chooses to do so. ESAs have been used in the treatment of anemia in CKD for over 20 years, serving a significant majority of DD-CKD patients on Medicare. It may be difficult to encourage treatment providers and patients to switch from products with which they have become familiar to roxadustat. In addition, the introduction of safer or more effective complement therapies to ESAs, such as safer iron supplementation therapies, may enhance the competitiveness of ESA therapy.

We may also face competition from potential new anemia therapies currently in clinical development. For example, there are several other HIF product candidates in various stages of active development for anemia indications that may be in competition with roxadustat for patient recruitment and enrollment for clinical trials and may be in direct competition with roxadustat if and when it is approved and launched commercially. These candidates are being developed by such companies as Akebia Pharmaceuticals, Inc., or Akebia, Bayer Corporation, GlaxoSmithKline plc and Japan Tobacco Inc. Some of these product candidates may enter the market prior to roxadustat. There may be new therapies for renal-related diseases that could limit the market or level of reimbursement available for roxadustat if and when it is commercialized. In addition, there are other companies developing biologic therapies for treatment of other anemia indications that we may also seek to pursue in the future.

The introduction of biosimilars for ESAs into the market in the United States may occur by the time roxadustat enters the market and may increase the competition for roxadustat and alter the competitive and pricing landscape. A biosimilar product is a follow-on version of an existing, branded biologic product. Under current laws, an application for a biosimilar product should not be approved by the FDA until 12 years after the existing, patent-protected product was approved under a Biologics License Application, or BLA. The patents for the existing, branded product must expire in a given market before biosimilars may enter that market with limited or no risk of being sued for patent infringement. The patents for epoetin alfa, a version of EPOGEN, expired in 2004 in the European Union, and the remaining patents have expired or will expire by May 2015 in the United States. Several biosimilar versions of currently marketed ESAs are available for sale in the EU and other biosimilars are currently under development or regulatory review in the United States and other territories, including Hospira s Retacrit , an EPOGEN and Procrit biosimilar which has been marketed in Europe, and for which Hospira s BLA was filed with the FDA in February 2015.

Furthermore, in the case of roxadustat, many of our existing and potential competitors have distribution relationships with leading dialysis providers and customers as well as brand recognition and reimbursement. Two of the largest operators of dialysis clinics in the United States, DaVita Healthcare Partners Inc., or DaVita, and Fresenius SE & Co. KGaA, or Fresenius, represent more than 60% of the dialysis market in the United States and have entered into long-term sales agreements with Amgen that began in January 2012, which in the case of Fresenius, includes an exclusive relationship. As a result, successful penetration of this market would require AstraZeneca to reach a significant agreement with Fresenius or DaVita, the two largest dialysis clinics in the United States, on favorable terms and on a timely basis.

If FG-3019 is approved and launched commercially to treat IPF, competing drugs are expected to include Roche s pirfenidone, which is approved for marketing in Europe, Canada, Japan and the United States, and Boehringer Ingelheim s nintedanib which has been approved in the United States and the EU. Nintedanib is also in development for non-small cell lung cancer and ovarian cancer. Other potential competitive product candidates in various stages of Phase 2 development for IPF include Gilead Sciences, Inc. s simtuzumab, Bristol-Myers Squibb s BMS-986020, and Biogen Idec s STX-100.

If FG-3019 is approved and launched commercially to treat pancreatic cancer, we expect it to be used in combination instead of as monotherapy; and, likely competition for FG-3019 would be from other agents also seeking approval in combination with gemcitibine and nab-paclitaxel from companies such as Threshold

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Pharmaceuticals, Inc., and Halozyme Therapeutics, Inc. Gemcitabine and/or nab-paclitaxel are the current standard of care in the first-line treatment of metastatic pancreatic cancer. Celgene Corporation s Abraxane® (nab-paclitaxel) was launched in the U.S. and Europe in 2013 and 2014, respectively, and was the first drug approved in this disease in nearly a decade. Other chemotherapies include capecitabine (Xeloda®), oxaliplatin (Eloxatin®), fluorouracil or leucovorin. There are a number of product candidates in clinical trials for pancreatic cancer, many of which are in combination with existing chemotherapies, as both first-line and second-line therapy for metastatic pancreatic cancer. In a recent Phase 3 clinical trial in first-line metastatic pancreatic cancer comparing gemcitabine with the regimen known as FOLFIRINOX, which is a combination of oxaliplatin, irinotecan, fluorouracil and leucovorin. Merrimack Pharmaceuticals, Inc. has completed a pivotal Phase 3 clinical trial of MM-398 for the treatment of patients with metastatic pancreatic cancer who have previously failed treatment with gemcitabine. In November 2014, Merrimack announced that it had received Fast Track designation from the FDA and intended to start the NDA submission process in December 2014 with the goal of completing the NDA submission in the first quarter, or early in the second quarter, of 2015.

If FG-3019 is approved and launched commercially to treat Duchenne muscular dystrophy, or DMD, FG-3019 may face competition for some patients from Sarepta Therapeutics, Inc, as well as BioMarin, and PTC Therapeutics, Santhera Pharmaceuticals, Pfizer, Summit plc and Tivorsan Pharmaceuticals. BioMarin recently completed its acquisition of Prosensa Holding, N.V. Prosensa, along with Sarepta, have entered clinical development with therapeutics based on exon-skipping technology which seeks to help patients produce functioning forms of the dystrophin protein. PTC Therapeutics product ataluren (Translarna™) received conditional approval in Europe in 2014. Translarna targets a different set of DMD patients from those being targeted by Prosensa s and Sarepta s existing exon-skipping therapeutics (which skip exon-51); however it is also limited to a subset of patients who carry a specific mutation. Conversely, FG-3019 is intended to treat DMD patients without limitation to type of mutation. Santhera Pharmaceuticals recently reported positive Phase 3 data with its drug idebenone (Raxone®/Catena®) in a trial measuring changes in lung function for DMD patients. Idebenone is a synthetic short-chain benzoquinone and a cofactor for the enzyme NAD(P)H:quinone oxidoreductase (NQO1). Pfizer s product candidate, which is in Phase 2 development is an antibody targeting myostatin which is a protein that regulates muscle growth. The goal of the program is to increase muscle growth and muscle strength in patients with DMD. Summit plc and Tivorsan Pharmaceuticals are both working on drugs involving the utrophin pathway. Utrophin is a protein similar to dystrophin. Summit is conducting a Phase 1b trial and Tivorsan is conducting preclinical work.

The success of any or all of these potential competitive products may negatively impact the development and potential for success of FG-3019. In addition, any competitive products that are on the market or in development may compete with FG-3019 for patient recruitment and enrollment for clinical trials or may force us to change our clinical trial comparators, whether placebo or active, in order to compare FG-3019 against another drug, which may be the new standard of care.

Moreover, many of our competitors have significantly greater resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients, manufacturing pharmaceutical products, and commercialization. In the potential anemia market for roxadustat, for example, large and established companies such as Amgen and Roche, among others, compete aggressively to maintain their market shares. In particular, these companies have greater experience and expertise in securing reimbursement, government contracts and relationships with key opinion leaders; conducting testing and clinical trials; obtaining and maintaining regulatory approvals and distribution relationships to market products; and marketing approved products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in later stages of development, and have collaboration agreements in our target markets with leading dialysis companies and research institutions. These competitors have in the past successfully prevented new and competing products from entering into the anemia market, and we expect that their

resources will represent challenges for us and our collaboration partners, AstraZeneca and Astellas. If we and our collaboration partners are not able to compete effectively against existing and potential competitors, our business and financial condition may be materially and adversely affected.

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Our future commercial success depends upon attaining significant market acceptance of our product candidates, if approved, among physicians, patients, third party payors and others in the health care community.

Even if we obtain marketing approval for roxadustat, FG-3019 or any other product candidates that we may develop or acquire in the future, these product candidates may not gain market acceptance among physicians, third party payors, patients and others in the health care community. Market acceptance of any approved product depends on a number of other factors, including:

- the clinical indications for which the product is approved and the labeling required by regulatory authorities for use with the product, including any warnings that may be required in the labeling;
- acceptance by physicians and patients of the product as a safe and effective treatment and the willingness of the target patient population to try new therapies and of physicians to prescribe new therapies;
- the cost, safety, efficacy and convenience of treatment in relation to alternative treatments;
- the restrictions on the use of our products together with other medications, if any;
- the availability of adequate coverage and reimbursement or pricing by third party payors and government authorities;
- the ability of treatment providers, such as dialysis clinics, to enter into relationships with us without violating their existing agreement; and
- the effectiveness of our sales and marketing efforts.

For example, in the case of roxadustat, two of the largest operators of dialysis clinics in the United States, DaVita and Fresenius, represent more than 60% of the dialysis market in the United States and have entered into long-term sales agreements with Amgen that began in January 2012, which in the case of Fresenius, includes an exclusive relationship.

Limited reimbursement or insurance coverage of our approved products, if any, by third party payors may render our products less attractive to patients and healthcare providers.

Market acceptance and sales of any approved products will depend significantly on reimbursement or coverage of our products by third party payors and may be affected by existing and future healthcare reform measures or the prices of related products for which reimbursement third party applies. Coverage and reimbursement by a third party payor may depend upon a number of factors, including the third party payor s determination that use of a product is:

a covered benefit under its health plan;

safe, effective and medically necessary;

appropriate for the specific patient;

cost-effective; and

neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product from a government or other third party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to the payor, which we may not be able to provide. Furthermore, the reimbursement policies of third party payors may significantly change in a manner that renders our clinical data insufficient for adequate reimbursement or otherwise limits the successful marketing of our products. Even if we obtain coverage for our product candidates, third party payors may not establish adequate reimbursement amounts, which may reduce the demand for, or the price of, our products. If reimbursement is not available or is available only to limited levels, we may not be able to commercialize certain of our products.

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In countries outside of the United States, price controls may limit the price at which products such as roxadustat, if approved, are sold. For example, reference pricing is used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or our partner may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available products in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unacceptable levels, we or our partner may elect not to commercialize our products in such countries, and our business and financial condition could be adversely affected.

Risks Related to Our Reliance on Third Parties

If our collaborations with Astellas or AstraZeneca were terminated, or if Astellas or AstraZeneca were to prioritize other initiatives over their collaborations with us, whether as a result of a change of control or otherwise, our ability to successfully develop and commercialize our lead product candidate, roxadustat, would suffer.

We have entered into collaboration agreements with respect to the development and commercialization of our lead product candidate, roxadustat, with Astellas and AstraZeneca. These agreements provide for reimbursement of our development costs by our collaboration partners and also provide for commercialization of roxadustat throughout the major territories of the world.

Our agreements with Astellas and AstraZeneca provide each of them with the right to terminate their respective agreements with us, upon the occurrence of negative clinical results, delays in the development and commercialization of our product candidates or adverse regulatory requirements or guidance. The termination of any of our collaboration agreements would require us to fund and perform the further development and commercialization of roxadustat in the affected territory, or pursue another collaboration, which we may be unable to do, either of which could have an adverse effect on our business and operations. In addition, each of those agreements provides our respective partners the right to terminate any of those agreements upon written notice for convenience. Moreover, if Astellas or AstraZeneca, or any successor entity, were to determine that their collaborations with us are no longer a strategic priority, or if either of them or a successor were to reduce their level of commitment to their collaborations with us, our ability to develop and commercialize roxadustat could suffer. In addition, some of our collaborations are exclusive and preclude us from entering into additional collaboration agreements with other parties in the area or field of exclusivity.

If we fail to establish and maintain strategic collaborations related to our product candidates, we will bear all of the risk and costs related to the development and commercialization of any such product candidate, and we may need to seek additional financing, hire additional employees and otherwise develop expertise at significant cost. This in turn may negatively affect the development of our other product candidates as we direct resources to our most advanced product candidates.

Conflicts with our collaboration partners could jeopardize our collaboration agreements and our ability to commercialize product candidates.

Our collaboration partners have certain rights to control decisions regarding the development and commercialization of our product candidates with respect to which they are providing funding. If we have a disagreement over strategy and activities, our plans for obtaining approval may be revised and negatively affect the anticipated timing and potential for success of our product candidates. Even if a product under a collaboration agreement is approved, we will remain substantially dependent on the commercialization strategy and efforts of our collaboration partners, and neither

of our collaboration partners has experience in commercialization of a novel drug such as roxadustat in the dialysis market.

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With respect to our collaboration agreements for roxadustat, there are additional complexities in that we and our collaboration partners, Astellas and AstraZeneca, must reach consensus on our Phase 3 development program. Multi-party decision-making is complex and involves significant time and effort, and there can be no assurance that the parties will cooperate or reach consensus, or that one or both of our partners will not ask to proceed independently in some or all of their respective territories or functional areas of responsibility in which the applicable collaboration partner would otherwise be obligated to cooperate with us. Any disputes or lack of cooperation with us by either Astellas or AstraZeneca may negatively impact the timing or success of our planned Phase 3 clinical studies.

We intend to conduct proprietary research programs in specific disease areas that are not covered by our collaboration agreements. Our pursuit of such opportunities could, however, result in conflicts with our collaboration partners in the event that any of our collaboration partners takes the position that our internal activities overlap with those areas that are exclusive to our collaboration agreements, and we should be precluded from such internal activities. Moreover, disagreements with our collaboration partners could develop over rights to our intellectual property. In addition, our collaboration agreements may have provisions that give rise to disputes regarding the rights and obligations of the parties. Any conflict with our collaboration partners could lead to the termination of our collaboration agreements, delay collaborative activities, reduce our ability to renew agreements or obtain future collaboration agreements or result in litigation or arbitration and would negatively impact our relationship with existing collaboration partners.

Certain of our collaboration partners could also become our competitors in the future. If our collaboration partners develop competing products, fail to obtain necessary regulatory approvals, terminate their agreements with us prematurely or fail to devote sufficient resources to the development and commercialization of our product candidates, the development and commercialization of our product candidates and products could be delayed.

We rely on third parties for the conduct of most of our preclinical and clinical trials for our product candidates, and if our third party contractors do not properly and successfully perform their obligations under our agreements with them, we may not be able to obtain or may be delayed in receiving regulatory approvals for our product candidates.

We rely heavily on university, hospital, dialysis centers and other institutions and third parties, including the principal investigators and their staff, to carry out our clinical trials in accordance with our clinical protocols and designs. We also rely on a number of third party contract research organizations, or CROs, to assist in undertaking, managing, monitoring and executing our ongoing clinical trials, including those for roxadustat. We expect to continue to rely on CROs, clinical data management organizations, medical institutions and clinical investigators to conduct our development efforts in the future, including our Phase 3 development program for roxadustat. We compete with many other companies for the resources of these third parties, and large pharmaceutical companies often have significantly more extensive agreements and relationships with such third party providers, and such third party providers may prioritize the requirements of such large pharmaceutical companies over ours. The third parties on whom we rely may terminate their engagements with us at any time, which may cause delay in the development and commercialization of our product candidates. If any such third party terminates its engagement with us or fails to perform as agreed, we may be required to enter into alternative arrangements, which would result in significant cost and delay to our product development program. Moreover, our agreements with such third parties generally do not provide assurances regarding employee turnover and availability, which may cause interruptions in the research on our product candidates by such third parties.

Moreover, while our reliance on these third parties for certain development and management activities will reduce our control over these activities, it will not relieve us of our responsibilities. For example, the FDA and foreign regulatory authorities require compliance with regulations and standards, including good clinical practices, or GCP, requirements, for designing, conducting, monitoring, recording, analyzing and reporting the results of clinical trials to

ensure that the data and results from trials are credible and accurate and that the rights,

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integrity and confidentiality of trial participants are protected. Although we rely on third parties to conduct our clinical trials, we are responsible for ensuring that each of these clinical trials is conducted in accordance with its general investigational plan and protocol under legal and regulatory requirements. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or other regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements.

If CROs and other third parties do not successfully carry out their duties under their agreements with us, if the quality or accuracy of the data they obtain is be compromised due to their failure to adhere to trial protocols or to regulatory requirements, or if they otherwise fail to comply with regulations and trial protocols or meet expected standards or deadlines, the trials of our product candidates may not meet regulatory requirements. If trials do not meet regulatory requirements or if these third parties need to be replaced, the development of our product candidates may be delayed, suspended or terminated, or the results may not be acceptable. If any of these events occur, we may not be able to obtain regulatory approval of our product candidates on a timely basis, at a reasonable cost, or at all.

We currently rely, and expect to continue to rely, on third parties to conduct many aspects of our clinical studies and product manufacturing, and these third parties may not perform satisfactorily.

We do not have any operating manufacturing facilities at this time, and our current manufacturing facility plans in China are not expected to satisfy the requirements necessary to support roxadustat development and commercialization outside of China. Other than in and for China specifically, we do not expect to independently manufacture our products. We currently rely, and expect to continue to rely, on third parties to scale-up, manufacture and supply roxadustat and our other product candidates outside of China. Risks arising from our reliance on third party manufacturers include:

- reduced control and additional burdens of oversight as a result of using third party manufacturers for all aspects of manufacturing activities, including regulatory compliance and quality control and assurance;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that may negatively impact our planned development and commercialization activities;
- the possible misappropriation of our proprietary technology, including our trade secrets and know-how; and
- disruptions to the operations of our third party manufacturers or suppliers unrelated to our product, including the bankruptcy of the manufacturer or supplier or a catastrophic event affecting our manufacturers or suppliers.

Any of these events could lead to development delays or failure to obtain regulatory approval, or affect our ability to successfully commercialize our product candidates. Some of these events could be the basis for action by the FDA or another regulatory authority, including injunction, recall, seizure or total or partial suspension of production.

The facilities used by our contract manufacturers to manufacture our product candidates must pass inspections by the FDA and other regulatory authorities. Although, except for China, we do not control the manufacturing operations of, and expect to remain completely dependent on, our contract manufacturers for manufacture of drug substance and finished drug product, we are ultimately responsible for ensuring that our product candidates are manufactured in compliance with cGMP requirements. If our contract manufacturers cannot successfully manufacture material that conforms to our or our collaboration partners specifications, or the regulatory requirements of the FDA or other regulatory authorities, we may not be able to secure and/or maintain regulatory

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approval for our product candidates and our development or commercialization plans may be delayed. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. In addition, although our longer-term agreements are expected to provide for requirements to meet our quantity and quality requirements to manufacture our products candidates for clinical studies and commercial sale, we will have minimal direct control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel and we expect to rely on our audit rights to ensure that those qualifications are maintained to meet our requirements. If our contract manufacturers facilities do not pass inspection by regulatory authorities, or if regulatory authorities do not approve these facilities for the manufacture of our products, or withdraw any such approval in the future, we would need to identify and qualify alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our products, if approved. Moreover, any failure of our third party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us or adverse regulatory consequences, including clinical holds, warnings or untitled letters, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which would be expected to significantly and adversely affect supplies of our products to us and our collaboration partners.

Any of our third party manufacturers may terminate their engagement with us at any time and we have not yet entered into any commercial supply agreements for the manufacture of active pharmaceutical ingredient or drug product. With respect to roxadustat, AstraZeneca and Astellas have certain rights to assume manufacturing of roxadustat and the existence of those rights may limit our ability to enter into favorable long-term supply agreements, if at all, with other third party manufacturers. In addition, our product candidates and any products that we may develop may compete with other product candidates and products for access and prioritization to manufacture. Certain third party manufacturers may be contractually prohibited from manufacturing our product due to non-compete agreements with our competitors or a commitment to grant another party priority relative to our products. There are a limited number of third party manufacturers that operate under cGMP and that might be capable of manufacturing to meet our requirements. Due to the limited number of third party manufacturers with the contractual freedom, expertise, required regulatory approvals and facilities to manufacture our products on a commercial scale, identifying and qualifying a replacement third party manufacturer would be expensive and time-consuming and may cause delay or interruptions in the production of our product candidates or products, which in turn may delay, prevent or impair our development and commercialization efforts.

We have a letter agreement with IRIX Pharmaceuticals, Inc., or IRIX, a third party manufacturer that we have used in the past, pursuant to which we agreed to negotiate a single source manufacturing agreement that included a right of first negotiation for the cGMP manufacture of HIF-PH inhibitors, including roxadustat, provided that IRIX is able to match any third party bids within 5%. The exclusive right to manufacture extends for five years after approval of an NDA for those compounds, and any agreement would provide that no minimum amounts would be specified until appropriate by forecast, that we and a commercialization partner would have the rights to contract with independent third parties that exceed IRIX s internal manufacturing capabilities or in the event that we or our commercialization partner determines for reasons of continuity of supply and security that such a need exists, provided that IRIX would supply no less than 65% of the product if it is able to provide this level of supply. Subsequent to the letter agreement, we and IRIX have entered into several additional service agreements. IRIX has requested in writing that we honor the letter agreement with respect to the single source manufacturing agreement, and if we were to enter into any such exclusive manufacturing agreement, there can be no assurance that IRIX will not assert a claim for right to manufacture roxadustat or that IRIX could manufacture roxadustat successfully and in accordance with applicable regulations for a commercial product and the specifications of our collaboration partners. On March 4, 2015, Patheon, a business unit of DPx Holdings B.V. announced that it had entered into a definitive agreement to acquire IRIX within sixty days of the announcement.

If any third party manufacturer terminates its engagement with us or fails to perform as agreed, we may be required to find replacement manufacturers, which would result in significant cost and delay to our development programs. Although we believe that there are several potential alternative manufacturers who could manufacture

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our product candidates, we may incur significant delays and added costs in identifying, qualifying and contracting with any such third party or potential second source manufacturer. In any event, with any third party manufacturer we expect to enter into technical transfer agreements and share our know-how with the third party manufacturer, which can be time-consuming and may result in delays. These delays could result in a suspension or delay of our Phase 3 clinical trials or, if roxadustat is approved and marketed, a failure to satisfy patient demand.

Certain of the components of our product candidates are acquired from single-source suppliers and have been purchased without long-term supply agreements. The loss of any of these suppliers, or their failure to supply us with supplies of sufficient quantity and quality to complete our drug substance or finished drug product of acceptable quality and an acceptable price, would materially and adversely affect our business.

We do not have an alternative supplier of certain components of our product candidates. To date, we have used purchase orders for the supply of materials that we use in our product candidates. We may be unable to enter into long-term commercial supply arrangements with our vendors, or do so on commercially reasonable terms, which could have a material adverse impact upon our business. In addition, we currently rely on our contract manufacturers to purchase from third-party suppliers some of the materials necessary to produce our product candidates. We do not have direct control over the acquisition of those materials by our contract manufacturers. Moreover, we currently do not have any agreements for the commercial production of those materials.

The logistics of our supply chain, which includes shipment of materials and intermediates from countries such as China and India adds additional time and risk to the manufacture of our product candidates. While we have in the past maintained sufficient inventory of materials, active pharmaceutical ingredient, or API, and drug product to meet our and our collaboration partners needs for roxadustat to date, the lead time and regulatory approvals required to source from and into countries outside of the United States increases the risk of delay and potential shortages of supply.

Risks Related to Our Intellectual Property

If our efforts to protect our proprietary technologies are not adequate, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection and contractual arrangements to protect the intellectual property related to our technologies. We will only be able to protect our products and proprietary information and technology by preventing unauthorized use by third parties to the extent that our patents, trade secrets, and contractual position allow us to do so. Any disclosure to or misappropriation by third parties of our trade secrets or confidential information could compromise our competitive position. Moreover, we are involved in, have in the past been involved in, and may in the future be involved in legal or administrative proceedings involving our intellectual property and initiated by third parties, which proceedings can result in significant costs and commitment of management time and attention. As our product candidates continue in development, third parties may attempt to challenge the validity and enforceability of our patents and proprietary information and technologies.

We also are involved in, have in the past been involved in, and may in the future be involved in initiating legal or administrative proceedings involving the product candidates and intellectual property of our competitors. These proceedings can result in significant costs and commitment of management time and attention, and there can be no assurance that our efforts would be successful in preventing or limiting the ability of our competitors to market competing products.

Composition-of-matter patents relating to the active pharmaceutical ingredient are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection not

limited to any one method of use. Method-of-use patents protect the use of a product for the specified method(s), and do 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. We rely on a combination of these and other types of patents to protect our product candidates, and there can be no assurance that our intellectual property will create and sustain the competitive position of our product candidates.

Biotechnology and pharmaceutical product patents involve highly complex legal and scientific questions and can be uncertain. Any patent applications that we own or license may fail to result in issued patents. Even if patents do successfully issue from our applications, third parties may challenge their validity or enforceability, which may result in such patents being narrowed, invalidated, or held unenforceable. Even if our patents and patent applications are not challenged by third parties, those patents and patent applications may not prevent others from designing around our claims and may not otherwise adequately protect our product candidates. If the breadth or strength of protection provided by the patents and patent applications we hold with respect to our product candidates is threatened, competitors with significantly greater resources could threaten our ability to commercialize our product candidates. Discoveries are generally published in the scientific literature well after their actual development, and patent applications in the United States and other countries are typically not published until 18 months after filing, and in some cases are never published. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned and licensed patents or patent applications, or that we or our licensors were the first to file for patent protection covering such inventions. Subject to meeting other requirements for patentability, for United States patent applications filed prior to March 16, 2013, the first to invent the claimed invention is entitled to receive patent protection for that invention while, outside the United States, the first to file a patent application encompassing the invention is entitled to patent protection for the invention. The United States moved to a first to file system under the Leahy-Smith America Invents Act, or AIA, effective March 16, 2013. The effects of this change and other elements of the AIA are currently unclear, as the United States Patent and Trademark Office, or USPTO, is still implementing associated regulations, and the applicability of the AIA and associated regulations to our patents and patent applications have not been fully determined. This new system also includes new procedures for challenging issued patents and pending patent applications, which creates additional uncertainty. We may become involved in opposition or interference proceedings challenging our patents and patent applications or the patents and patent applications of others, and the outcome of any such proceedings are highly uncertain. An unfavorable outcome in any such proceedings could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology and compete directly with us, or result in our inability to manufacture, develop or commercialize our product candidates without infringing the patent rights of others.

In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect proprietary know-how, information, or technology that is not covered by our patents. Although our agreements require all of our employees to assign their inventions to us, and we require all of our employees, consultants, advisors and any third parties who have access to our trade secrets, proprietary know-how and other confidential information and technology to enter into appropriate confidentiality agreements, we cannot be certain that our trade secrets, proprietary know-how and other confidential information and technology will not be subject to unauthorized disclosure or that our competitors will not otherwise gain access to or independently develop substantially equivalent trade secrets, proprietary know-how and other information and technology. Furthermore, the laws of some foreign countries, in particular, China, where we have operations, do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property globally. If we are unable to prevent unauthorized disclosure of our intellectual property related to our product candidates and technology to third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business and operations.

Intellectual property disputes with third parties and competitors may be costly and time consuming, and may negatively affect our competitive position.

Our commercial success may depend on our avoiding infringement of the patents and other proprietary rights of third parties as well as on enforcing our patents and other proprietary rights against third parties. Pharmaceutical and biotechnology intellectual property disputes are characterized by complex, lengthy and expensive litigation

over patents and other intellectual property rights. We may initiate or become a party to, or be threatened with, future litigation or other proceedings regarding intellectual property rights with respect to our product candidates and competing products.

As our product candidates progress toward commercialization, we or our collaboration partners may be subject to patent infringement claims from third parties. We attempt to ensure that our product candidates do not infringe third party patents and other proprietary rights. However, the patent landscape in competitive product areas is highly complex, and there may be patents of third parties of which we are unaware that may result in claims of infringement. Accordingly, there can be no assurance that our product candidates do not infringe proprietary rights of third parties, and parties making claims against us may seek and obtain injunctive or other equitable relief, which could potentially block further efforts to develop and commercialize our product candidates including roxadustat or FG-3019. Any litigation involving defense against claims of infringement, regardless of the merit of such claims, would involve substantial litigation expense and would be a substantial diversion of management time.

We intend, if necessary, to vigorously enforce our intellectual property in order to protect the proprietary position of our product candidates, including roxadustat and FG-3019. Active efforts to enforce our patents may include litigation, administrative proceedings, or both, depending on the potential benefits that might be available from those actions and the costs associated with undertaking those efforts against third parties. We carefully review and monitor publicly available information regarding products that may be competitive with our product candidates and assert our intellectual property rights where appropriate. We previously prevailed in an administrative challenge initiated by a major biopharmaceutical company regarding our intellectual property rights, maintaining our intellectual property in all relevant scope, and will continue to protect and enforce our intellectual property rights. Moreover, third parties may continue to initiate new proceedings in the U.S. and foreign jurisdictions to challenge our patents from time to time.

We may consider administrative proceedings and other means for challenging third party patents and patent applications. Third parties may also challenge our patents and patent applications, through interference, reexamination, *inter partes* review, and post-grant review proceedings before the USPTO or through other comparable proceedings, such as oppositions or invalidation proceedings, before foreign patent offices. An unfavorable outcome in any such challenge could require us to cease using the related technology and to attempt to license rights to it from the prevailing third party, which may not be available on commercially reasonable terms, if at all, in which case our business could be harmed. Even if we are successful, participation in administrative proceedings before the USPTO or a foreign patent office may result in substantial costs and time on the part of our management and other employees. For example, on December 5, 2013, Akebia filed an opposition to our European Patent No. 1463823, or the 823 patent, with the European Patent Office, and Akebia and other third parties may initiate or pursue similar proceedings with the European Patent Office or other corresponding foreign jurisdictions. The granted claims of the 823 patent encompass the use of roxadustat for the treatment of anemia. While we believe the 823 patent will be upheld in its entirety, the ultimate outcome of the opposition remains uncertain, and ultimate resolution of the proceeding may take a number of years and result in substantial costs to us.

Furthermore, there is a risk that any public announcements concerning the status or outcomes of intellectual property litigation or administrative proceedings may adversely affect the price of our stock. If securities analysts or our investors interpret such status or outcomes as negative or otherwise creating uncertainty, our common stock price may be adversely affected.

Our reliance on third parties and agreements with collaboration partners requires us to share our trade secrets, which increases the possibility that a competitor may discover them or that our trade secrets will be misappropriated or disclosed.

Our reliance on third party contractors to develop and manufacture our product candidates is based upon agreements that limit the rights of the third parties to use or disclose our confidential information, including our

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trade secrets and know-how. Despite the contractual provisions, the need to share trade secrets and other confidential information increases the risk that such trade secrets and information are disclosed or used, even if unintentionally, in violation of these agreements. In the highly competitive markets in which our product candidates are expected to compete, protecting our trade secrets, including our strategies for addressing competing products, is imperative, and any unauthorized use or disclosure could impair our competitive position and may have a material adverse effect on our business and operations.

In addition, our collaboration partners are larger, more complex organizations than ours, and the risk of inadvertent disclosure of our proprietary information may be increased despite their internal procedures and contractual obligations in place with our collaboration partners. Despite our efforts to protect our trade secrets and other confidential information, a competitor s discovery of such trade secrets and information could impair our competitive position and have an adverse impact on our business.

We have an extensive worldwide patent portfolio. The cost of maintaining our patent protection is high and maintaining our patent protection requires continuous review and compliance in order to maintain worldwide patent protection. We may not be able to effectively maintain our intellectual property position throughout the major markets of the world.

The USPTO and foreign patent authorities require maintenance fees and payments as well as continued compliance with a number of procedural and documentary requirements. Noncompliance may result in abandonment or lapse of the subject patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance may result in reduced royalty payments for lack of patent coverage in a particular jurisdiction from our collaboration partners or may result in competition, either of which could have a material adverse effect on our business.

We have made, and will continue to make, certain strategic decisions in balancing costs and the potential protection afforded by the patent laws of certain countries. As a result, we may not be able to prevent third parties from practicing our inventions in all countries throughout the world, or from selling or importing products made using our inventions in and into the United States or other countries. Third parties may use our technologies in territories in which we have not obtained patent protection to develop their own products and, further, may infringe our patents in territories which provide inadequate enforcement mechanisms, even if we have patent protection. Such third party products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

The laws of some foreign countries do not protect proprietary rights to the same extent as do the laws of the United States, and we may encounter significant problems in securing and defending our intellectual property rights outside the United States.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain countries. The legal systems of certain countries, particularly certain developing countries such as China, do not always favor the enforcement of patents, trade secrets, and other intellectual property rights, particularly those relating to pharmaceutical and biotechnology products, which could make it difficult for us to stop infringement of our patents, misappropriation of our trade secrets, or marketing of competing products in violation of our proprietary rights. In China, our intended establishment of significant operations will depend in substantial part on our ability to effectively enforce our intellectual property rights in that country. Proceedings to enforce our intellectual property rights in foreign countries could result in substantial costs and divert our efforts and attention from other aspects of our business, and could put our patents in these territories at risk of being invalidated or interpreted narrowly, or our patent applications at risk of not granting, and could provoke third parties to assert claims against us. We may not

prevail in all legal or other proceedings that we may initiate and, if we were to prevail, the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

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Intellectual property rights do not address all potential threats to any competitive advantage we may have.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and intellectual property rights may not adequately protect our business or permit us to maintain our competitive advantage. The following examples are illustrative:

- Others may be able to make compounds that are the same as or similar to our current or future product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed.
- We or any of our licensors or strategic partners might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed.
- We or any of our licensors or strategic partners might not have been the first to file patent applications covering certain of our inventions.
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- The prosecution of our pending patent applications may not result in granted patents.
- Granted patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors.
- Patent protection on our product candidates may expire before we are able to develop and commercialize the product, or before we are able to recover our investment in the product.
- Our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for such activities, as well as in countries in which we do not have patent rights, and may then use the information learned from such activities to develop competitive products for sale in markets where we intend to market our product candidates.

The existence of counterfeit pharmaceutical products in pharmaceutical markets may damage our brand and reputation and have a material adverse effect on our business, operations and prospects.

Counterfeit products, including counterfeit pharmaceutical products, are a significant problem, particularly in China. Counterfeit pharmaceuticals are products sold under the same or very similar brand names and/or having a similar appearance to genuine products, but which are sold without proper licenses or approvals. Such products divert sales from genuine products, often are of lower cost, often are of lower quality (having different ingredients or formulations, for example), and have the potential to damage the reputation for quality and effectiveness of the genuine product. If counterfeit pharmaceuticals illegally sold under our brand name result in adverse side effects to

consumers, we may be associated with any negative publicity resulting from such incidents. In addition, consumers may buy counterfeit pharmaceuticals that are in direct competition with our pharmaceuticals, which could have an adverse impact on our revenues, business and results of operations. With respect to China, although the government has recently been increasingly active in policing counterfeit pharmaceuticals, there is not yet an effective counterfeit pharmaceutical regulation control and enforcement system in China. As a result, we may not be able to prevent third parties from selling or purporting to sell our products in China. The proliferation of counterfeit pharmaceuticals has grown in recent years and may continue to grow in the future. The existence of and any increase in the sales and production of counterfeit pharmaceuticals, or the technological capabilities of counterfeiters, could negatively impact our revenues, brand reputation, business and results of operations.

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Risks Related to Government Regulation

The regulatory approval process is highly uncertain and we may not obtain regulatory approval for the commercialization of our product candidates.

The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable, but typically takes many years following the commencement of preclinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate s clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate, and it is possible that neither roxadustat nor FG-3019, nor any future product candidates we may discover, in-license or acquire and seek to develop in the future, will ever obtain regulatory approval.

Our product candidates could fail to receive regulatory approval from the FDA or other regulatory authorities for many reasons, including:

- disagreement over the design or implementation of our clinical trials;
- failure to demonstrate that a product candidate is safe and effective for its proposed indication;
- failure of clinical trials to meet the level of statistical significance required for approval;
- failure to demonstrate that a product candidate s clinical and other benefits outweigh its safety risks;
- disagreement over our interpretation of data from preclinical studies or clinical trials;
- disagreement over whether to accept efficacy results from clinical trial sites outside the United States where the standard of care is potentially different from that in the United States;
- the insufficiency of data collected from clinical trials of our present or future product candidates to support the submission and filing of an NDA or other submission or to obtain regulatory approval;
- disapproval of the manufacturing processes or facilities of either our manufacturing plant or third party manufacturers with whom we contract for clinical and commercial supplies; or
- changes in the approval policies or regulations that render our preclinical and clinical data insufficient for approval.

The FDA or other regulatory authorities may require more information, including additional preclinical or clinical data to support approval, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program altogether. Even if we do obtain regulatory approval, our product candidates may be approved for fewer or more limited indications than we request, approval may be contingent on the performance of costly post-marketing clinical trials, or approval may require labeling that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. In addition, if our product candidates produce undesirable side effects or safety issues, the FDA may require the establishment of REMS or other regulatory authorities may require the establishment of a similar strategy, that may, restrict distribution of our approved products, if any, and impose burdensome implementation requirements on us. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Even if we believe our current or planned clinical trials are successful, regulatory authorities may not agree that our completed clinical trials provide adequate data on safety or efficacy. Approval by one regulatory authority does not ensure approval by any other regulatory authority. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. We may not be able to file for regulatory approvals and even if we file we may not receive the necessary approvals to commercialize our product candidates in any market.

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If our product candidates obtain marketing approval, we will be subject to more extensive healthcare laws, regulation and enforcement and our failure to comply with those laws could have a material adverse effect on our results of operations and financial condition.

If we obtain approval for any of our product candidates, the regulatory requirements applicable to our operations, in particular our sales and marketing efforts, will increase significantly with respect to our operations and the potential for civil and criminal enforcement by the federal government and the states and foreign governments will increase with respect to the conduct of our business. The laws that may affect our operations in the United States 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, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;

federal civil and criminal false claims laws and civil monetary penalty 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;

the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;

HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security, and transmission of individually identifiable health information;

the federal physician sunshine requirements under PPACA, which requires manufacturers of drugs, devices, biologics, and medical supplies to report annually to the Centers for Medicare and Medicaid Services, or CMS, information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members;

foreign and state law equivalents of each of the above federal laws, such as the U.S. Foreign Corrupt Practices Act, or FCPA, anti-kickback and false claims laws that 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 pharmaceutical 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, thus complicating compliance

efforts.

The scope of these laws and our lack of experience in establishing the compliance programs necessary to comply with this complex and evolving regulatory environment increases the risks that we may violate the applicable laws and regulations. If our operations are found to be in violation of any of such laws or any other governmental 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 materially adversely affect our ability to operate our business and our financial results.

The impact of recent United States healthcare reform and other changes in the healthcare industry and in healthcare spending is currently unknown, and may adversely affect our business model.

The commercial potential for our approved products, if any, could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry and new laws, regulations

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or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, also called the MMA, altered Medicare coverage and payments for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. The MMA also provided authority for limiting the number of drugs that will be covered in any therapeutic class and as a result, we expect that there will be additional pressure to reduce costs. For example, the CMS in implementing the MMA has enacted regulations that reduced capitated payments to dialysis providers. These cost reduction initiatives and other provisions of the MMA could decrease the scope of coverage and the price that may be received for any approved dialysis products and could seriously harm our business and financial condition. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policies and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may cause a similar reduction in payments from private payors. Similar regulations or reimbursement policies have been enacted in many international markets which could similarly impact the commercial potential for our products.

Under the Medicare Improvements for Patients and Providers Act, or MIPPA, a basic case-mix adjusted composite, or bundled, payment system commenced in January 2011 and transitioned fully by January 2014 to a single reimbursement rate for drugs and all services furnished by renal dialysis centers for Medicare beneficiaries with end-stage renal disease. Specifically, under MIPPA the bundle now covers drugs, services, lab tests and supplies under a single treatment base rate for reimbursement by CMS based on the average cost per treatment, including the cost of ESAs and IV iron doses, typically without adjustment for usage. It is unknown whether roxadustat will be included in the payment bundle. If roxadustat is included in the bundle, it may reduce the price that could be charged for roxadustat, and therefore potentially limit our profitability. On the other hand, it is possible that exclusion from the bundle may limit or delay market penetration of roxadustat.

More recently, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively PPACA, was enacted in 2010 with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers. The PPACA, among other things, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and creates a new Medicare Part D coverage gap discount program, in which manufacturers 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. In addition, other legislative changes have been proposed and adopted in the United States since the PPACA was enacted. On August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation s automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect on April 1, 2013.

It is likely that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing healthcare legislation. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or

reduce costs of healthcare may adversely affect:

- the demand for any products that may be approved for sale;
- the price and profitability of our products;

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pricing, coverage and reimbursement applicable to our products;

the ability to successfully position and market any approved product; and

the taxes applicable to our pharmaceutical product revenues.

We may not be able to conduct, or contract others to conduct, animal testing in the future, which could harm our research and development activities.

Certain laws and regulations relating to drug development require us to test our product candidates on animals before initiating clinical trials involving humans. Animal testing activities have been the subject of controversy and adverse publicity. Animal rights groups and other organizations and individuals have attempted to stop animal testing activities by pressing for legislation and regulation in these areas and by disrupting these activities through protests and other means. To the extent the activities of these groups are successful, our research and development activities may be interrupted or delayed.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could result in significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, comply with the FCPA and other anti-bribery laws, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions, delays in clinical trials, or serious harm to our reputation. We have adopted a code of conduct for our directors, officers and employees, or the Code of Business Conduct and Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could harm our business, results of operations, financial condition and cash flows, including through the imposition of significant fines or other sanctions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal

of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations applicable to our operations in the United States and foreign countries. These current or future laws and regulations may impair our research, development or manufacturing efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

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Risks Related to Our International Operations

We are establishing international operations and seeking approval to commercialize our product candidates outside of the United States, in particular in China, and a number of risks associated with international operations could materially and adversely affect our business.

We expect to be subject to a number risks related with our international operations, many of which may be beyond our control. These risks include:

different regulatory requirements for drug approvals in foreign countries;

different standards of care in various countries that could complicate the evaluation of our product candidates;

different United States and foreign drug import and export rules;

reduced protection for intellectual property rights in certain countries;

unexpected changes in tariffs, trade barriers and regulatory requirements;

different reimbursement systems and different competitive drugs indicated to treat the indications for which our product candidates are being developed;

economic weakness, including inflation, or political instability in particular foreign economies and markets;

compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;

compliance with the FCPA, and other anti-corruption and anti-bribery laws;

foreign taxes, including withholding of payroll taxes;

foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;

workforce uncertainty in countries where labor unrest is more common than in the United States;

production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;

potential liability resulting from development work conducted by foreign distributors; and

business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters.

The pharmaceutical industry in China is highly regulated and such regulations are subject to change.

The pharmaceutical industry in China is subject to comprehensive government regulation and supervision, encompassing the approval, registration, manufacturing, packaging, licensing and marketing of new drugs. See Business Government Regulation Regulation in China for a discussion of the regulatory requirements that are applicable to our current and planned business activities in China. In recent years, the regulatory framework in China regarding the pharmaceutical industry has undergone significant changes, and we expect that it will continue to undergo significant changes. Any such changes or amendments may result in increased compliance costs on our business or cause delays in or prevent the successful development or commercialization of our product candidates in China. Chinese authorities have become increasingly vigilant in enforcing laws in the pharmaceutical industry, in some cases launching industry-wide investigations, oftentimes appearing to focus on foreign companies. The costs and time necessary to respond to an investigation can be material. Any failure by us or our partners to maintain compliance with applicable laws and regulations or obtain and maintain required licenses and permits may result in the suspension or termination of our business activities in China.

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Patients use of traditional Chinese medicine in violation of study protocols in our China studies may lead the CFDA and regulators in other jurisdictions in which are seeking approval to suspend our studies, reject our study data and withhold approval for roxadustat.

A common issue encountered in conducting clinical studies in China is patients use of traditional Chinese medicine in violation of study protocols. We believe that many patients with anemia in CKD are currently being treated with traditional Chinese medicine, and it is possible that such patients may continue their use of traditional Chinese medicine after enrollment in our studies and in violation of study protocols. If the patients participating in our China clinical studies do not comply with study protocols and continue to use traditional Chinese medicine, adverse events may emerge in our studies that are due to such traditional Chinese medicine or the interaction between such traditional Chinese medicine and roxadustat. In addition, the use of traditional Chinese medicine by patients in our studies may confound our study results. The occurrence of such adverse events or the confounding our study results may lead the China Food and Drug Administration, or CFDA, and regulators in other jurisdictions in which we are seeking approval to, among other things, suspend our studies, reject our study data and withhold approval for roxadustat.

We are building our own manufacturing facility in China to produce roxadustat and clinical trial material for our corneal implant program. As an organization, we have limited experience in the construction or operation of a manufacturing plant, and, accordingly we cannot assure you we will be able to meet regulatory requirements to operate our plant and to sell our products.

We recently received a Pharmaceutical Production Permit, a general manufacturing license, for our facility in China in which we intend to manufacture roxadustat and FG-5200 in support of the clinical development and potential commercialization of these product candidates in China. However, we have not yet received a license to commercially manufacture either roxadustat or FG-5200. As an organization, we have limited experience building a manufacturing facility in the past and our facility must be constructed, licensed and operated in conformity with applicable cGMP requirements. We will be obligated to comply with continuing cGMP requirements and there can be no assurance that we will receive and maintain all of the appropriate licenses required to manufacture our product candidates for clinical and commercial use in China. In addition, we and our product suppliers must continually spend time, money and effort in production, record-keeping and quality assurance and appropriate controls in order to ensure that any products manufactured in our facility meet applicable specifications and other requirements for product safety, efficacy and quality and there can be no assurance that our efforts will succeed for licensure or continue to be successful in meeting these requirements. Moreover, our facility, even if approved for the manufacture of roxadustat, would require separate approval for the separate suite being constructed for the manufacture of FG-5200, whether it is categorized as a medical device or other product under CFDA guidelines. For FG-5200, we expect to convert our existing manufacturing process to an automated process which would require us to show that implants from our new manufacturing process are comparable to the implants from our existing manufacturing process. There can be no assurance that we will successfully receive licensure and maintain approval for the manufacture of either or both of roxadustat or FG-5200, either of which would be expected to delay or preclude our ability to develop and commercialize those product candidates in China and may materially adversely affect our business and operations and prospects in China.

Manufacturing facilities in China are subject to periodic unannounced inspections by the CFDA and other regulatory authorities. We expect to depend on these facilities for our product candidates and business operations in China. Natural disasters or other unanticipated catastrophic events, including power interruptions, water shortages, storms, fires, earthquakes, terrorist attacks, government appropriation of our facility, and wars, could significantly impair our ability to operate our manufacturing facility and certain equipment, records and other materials located in these facilities would be difficult to replace or require substantial replacement lead time that would impact our ability to successfully commercialize our product candidates in China. The occurrence of any such event could materially and

adversely affect our business, financial condition, results of operations, cash flows and prospects.

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Our decision to seek approval in China for roxadustat as a domestic new drug may not be accepted, which would result in additional delay and expense.

Our Chinese subsidiary, FibroGen (China) Medical Technology Development Co., Ltd., or FibroGen China plans to seek approval for roxadustat in China as a Domestic Class 1.1 Drug, which is not a typical route to approval in China for enterprises with headquarters outside of China. Our submission for review of a New Drug Application under domestic drug regulations rather than under the imported drug regulations may not result in approval, or the regulatory authorities may determine that we are not eligible for approval as a domestic drug, which would require us to obtain approval for roxadustat first in the United States or in Europe and then to prepare and submit a new application for approval of roxadustat in China as an imported drug. This would result in significant delay in our commercialization plans for roxadustat. While we plan to provide the China-only clinical trial data required of a domestic drug, the size of our trial in China and the additional safety data from our global roxadustat Phase 3 program may not be deemed sufficient to receive approval. Elements of our plan for approval of roxadustat and other product candidates in China are based on communications with the CFDA and not on formal written regulations, findings or determinations. Accordingly, while we believe we have understandings with the CFDA regarding the domestic drug approval process and the clinical data currently required for approval, the regulatory authorities may later determine that changes are required in the drug approval process, that additional or different clinical data must be generated, or that the domestic drug route may not be available to FibroGen China, any of which could significantly delay approval of roxadustat or any of our other product candidates, and materially and adversely affect our plans and operations in China. For example, the recent backlog of CFDA review of clinical trial applications has delayed the review and ultimately start of our Phase 3 clinical trials in China. While we cannot predict how or if this will ultimately delay our application for or any approval of roxadustat in China, it is possible that such delay could have a material adverse effect on our development and commercialization of roxadustat in China.

Even if roxadustat is approved in China, we and our collaboration partner in China, AstraZeneca, may experience difficulties in successfully generating sales of roxadustat in China.

We and AstraZeneca have a profit sharing arrangement with respect to roxadustat in China. Even if roxadustat is approved for sale in China, we and AstraZeneca may experience difficulties in our marketing, commercialization and sales efforts in China, and our business and operations could be adversely affected. In particular, sales of roxadustat in China may be limited due to the complex nature of the healthcare system, low average personal income, lack of patient cost reimbursement, pricing controls, poorly developed infrastructure and potentially rapid competition from other products.

The market for treatments of anemia in CKD in China is highly competitive.

Even if roxadustat is approved in China, it will face intense competition in the market for treatments of anemia in CKD. Roxadustat would compete with ESAs, which are offered by established multinational pharmaceutical companies such as Kirin Brewery Company Limited and Roche and Chinese pharmaceutical companies such as 3SBio Inc. and Di ao Group Chengdu Diao Jiuhong Pharmaceutical Factory. Many of these competitors have substantially greater name recognition, scientific, financial and marketing resources as well as established distribution capabilities than we do. Many of our competitors have more resources to develop or acquire, and more experience in developing or acquiring, new products and in creating market awareness for those products. Many of these competitors have significantly more experience than we have in navigating the Chinese regulatory framework regarding the development, manufacturing and marketing of drugs in China, as well as in marketing and selling anemia products in China. Additionally, we believe that most patients with anemia in CKD in China are currently being treated with traditional Chinese medicine, which is widely accepted and highly prevalent in China. Traditional Chinese medicine treatments are often oral and thus convenient and low-cost, and practitioners of traditional Chinese medicine are

numerous and accessible in China. As a result, it may be difficult to persuade patients with anemia in CKD to switch from traditional Chinese medicine to roxadustat.

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There is no assurance that roxadustat will be included in the Medical Insurance Catalogs.

Eligible participants in the national basic medical insurance program in China, which consists of mostly urban residents, are entitled to reimbursement from the social medical insurance fund for up to the entire cost of medicines that are included in the Medical Insurance Catalogs. See Business Government Regulation Regulation in China. We believe that the inclusion of a drug in the Medical Insurance Catalogs can substantially improve the sales of a drug. The Ministry of Labor and Social Security in China, or the MLSS, together with other government authorities, select medicines to be included in the Medical Insurance Catalogs based on a variety of factors, including treatment requirements, frequency of use, effectiveness and price. The MLSS also occasionally removes medicines from such catalogs. There can be no assurance that roxadustat will be included, and once included, remain in the Medical Insurance Catalogs. The exclusion or removal of roxadustat from the Medical Insurance Catalogs may materially and adversely affect sales of roxadustat.

We may not be successful in the tender processes for the purchase of medicines by state-owned and state-controlled hospitals.

Most hospitals in China participate in collective tender processes for the purchase of medicines listed in the Medical Insurance Catalogs and medicines that are consumed in large volumes and commonly prescribed for clinical uses. During a collective tender process, the hospitals will establish a committee consisting of recognized pharmaceutical experts. The committee will assess the bids submitted by the various participating pharmaceutical manufacturers, taking into consideration, among other things, the quality and price of the drug product and the service and reputation of the manufacturer. Only drug products that have been selected in the collective tender processes may be purchased by participating hospitals. If we are unable to win purchase contracts through the collective tender processes in which we decide to participate, there will be limited demand for roxadustat, and sales revenues from roxadustat will be materially and adversely affected.

We plan to seek approval for FG-5200 as a medical device, with respect to which we have no development and manufacturing experience. Even if FG-5200 can be manufactured successfully and achieve regulatory approval, we may not achieve commercial success.

We plan to seek regulatory approval for FG-5200 as a medical device, with respect to which we have no development and manufacturing experience. There can be no assurance that we will achieve medical device designation or receive approval for FG-5200. In addition, we have not yet used the material planned for our clinical trials of FG-5200 in any previous clinical trials and because we have not yet received a license to manufacture FG-5200 in our China manufacturing facility or at scale, we will have to show that FG-5200 from our China manufacturing facility meets the applicable regulatory requirements. There can be no assurance that we can meet these requirements or that FG-5200 can be approved for development, manufacture and sale in China.

Even if we are able to manufacture and develop FG-5200 as a medical device in China, the size and length of any potential clinical trials required for approval are uncertain and we are unable to predict the time and investment required to obtain regulatory approval. Moreover, even if FG-5200 can be successfully developed for approval in China, our product candidate would require extensive training and investment in assisting physicians in the use of FG-5200.

The retail prices of any product candidates that we develop may be subject to control, including periodic downward adjustment, by Chinese government authorities.

The price for pharmaceutical products is highly regulated in China, both at the national and provincial level. Price controls may reduce prices to levels significantly below those that would prevail in less regulated markets or limit the volume of products which may be sold, either of which may have a material and adverse effect on potential revenues from sales of roxadustat in China. Moreover, the process and timing for the implementation of price restrictions is unpredictable, which may cause potential revenues from the sales of roxadustat to fluctuate from period to period.

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If our planned business activities in China fall within a restricted category under China Catalog for Guidance for Foreign Investment, we will need to operate in China through a variable interest entity structure.

The China Catalog for Guidance for Foreign Investment sets forth the industries and sectors that the Chinese government encourages and restricts foreign investment and participation. The Catalog for Guidance for Foreign Investment is subject to revision from time to time by China Ministry of Commerce. While we currently do not believe the development and marketing of roxadustat falls within a restricted category under the Catalog for Guidance for Foreign Investment, if roxadustat does fall under such a restricted category, we will need to operate in China through a variable interest entity, or VIE, structure. A VIE structure involves a wholly foreign-owned enterprise that would control and receive the economic benefits of a domestic Chinese company through various contractual relationships. Such a structure would subject us to a number of risks that may have an adverse effect on our business, including that China government may determine that such contractual arrangements do not comply with applicable regulations, Chinese tax authorities may require us to pay additional taxes, shareholders of our VIEs may have potential conflicts of interest with us, and we may lose the ability to use and enjoy assets held by our VIEs that are important to the operations of our business if such entities go bankrupt or become subject to dissolution or liquidation proceedings. VIE structures in China have come under increasing scrutiny from accounting firms and the SEC staff. If we do attempt to use a VIE structure and are unsuccessful in structuring it so as to qualify as a VIE, we would not be able to consolidate the financial statements of the VIE with our financial statements, which could have a material adverse effect on our operating results and financial condition.

FibroGen China would be subject to restrictions on paying dividends or making other payments to us, which may restrict our ability to satisfy our liquidity requirements.

We plan to conduct all of our business in China through FibroGen China. We may rely on dividends and royalties paid by FibroGen China for a portion of our cash needs, including the funds necessary to service any debt we may incur and to pay our operating expenses. The payment of dividends by FibroGen China is subject to limitations. Regulations in China currently permit payment of dividends only out of accumulated profits as determined in accordance with accounting standards and regulations in China. FibroGen China is not permitted to distribute any profits until losses from prior fiscal years have been recouped and in any event must maintain certain minimum capital requirements. FibroGen China is also required to set aside at least 10.0% of its after-tax profit based on Chinese accounting standards each year to its statutory reserve fund until the cumulative amount of such reserves reach 50.0% of its registered capital. Statutory reserves are not distributable as cash dividends. In addition, if FibroGen China incurs debt on its own behalf in the future, the agreements governing such debt may restrict its ability to pay dividends or make other distributions to us. As of December 31, 2014, approximately $1.0 million of our cash and cash equivalents is held in China.

Any capital contributions from us to FibroGen China must be approved by the Ministry of Commerce in China, and failure to obtain such approval may materially and adversely affect the liquidity position of FibroGen China.

The Ministry of Commerce in China or its local counterpart must approve the amount and use of any capital contributions from us to FibroGen China, and there can be no assurance that we will be able to complete the necessary government registrations and obtain the necessary government approvals on a timely basis, or at all. If we fail to do so, we may not be able to contribute additional capital to fund our Chinese operations, and the liquidity and financial position of FibroGen China may be materially and adversely affected.

We may be subject to currency exchange rate fluctuations and currency exchange restrictions with respect to our operations in China, which could adversely affect our financial performance.

If roxadustat is approved for sale in China, most of our product sales will occur in local Chinese currency and our operating results will be subject to volatility from currency exchange rate fluctuations. To date, we have not hedged against the risks associated with fluctuations in exchange rates and, therefore, exchange rate fluctuations could have an adverse impact on our future operating results. Changes in value of the Renminbi against the U.S.

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dollar, Euro and other currencies is affected by, among other things, changes in China s political and economic conditions. Currently, the Renminbi is permitted to fluctuate within a narrow and managed band against a basket of certain foreign currencies. Any significant currency exchange rate fluctuations may have a material adverse effect on our business and financial condition.

In addition, China government imposes controls on the convertibility of the Renminbi into foreign currencies and the remittance of foreign currency out of China for certain transactions. Shortages in the availability of foreign currency may restrict the ability of FibroGen China to remit sufficient foreign currency to pay dividends or other payments to us, or otherwise satisfy their foreign currency-denominated obligations. Under existing Chinese foreign exchange regulations, payments of current account items, including profit distributions, interest payments and balance of trade, can be made in foreign currencies without prior approval from the State Administration of Foreign Exchange, or SAFE, by complying with certain procedural requirements. However, approval from SAFE or its local branch is required where Renminbi is to be converted into foreign currency and remitted out of China to pay capital expenses such as the repayment of loans denominated in foreign currencies. The China government may also at its discretion restrict access in the future to foreign currencies for current account transactions. If the foreign exchange control system prevents us from obtaining sufficient foreign currency to satisfy our operational requirements, our liquidity and financial position may be materially and adversely affected.

Because FibroGen China s funds are held in banks that do not provide insurance, the failure of any bank in which FibroGen China deposit its funds could adversely affect our business.

Banks and other financial institutions in China do not provide insurance for funds held on deposit. As a result, in the event of a bank failure, FibroGen China may not have access to funds on deposit. Depending upon the amount of money FibroGen China maintains in a bank that fails, its inability to have access to cash could materially impair its operations.

We may be subject to tax inefficiencies associated with our offshore corporate structure.

The tax regulations of the United States and other jurisdictions in which we operate are extremely complex and subject to change. New laws, new interpretations of existing laws, or limitations on our ability to structure our operations and intercompany transactions may lead to inefficient tax treatment of our revenue, profits, royalties and distributions, if any are achieved. For example, under the Internal Revenue Code, certain types of income derived by our foreign subsidiaries that are controlled foreign corporations could give rise to a current inclusion of income to FibroGen, Inc., for U.S. tax purposes.

In addition, we and our foreign subsidiaries have various intercompany transactions. We may not be able to obtain certain benefits under relevant tax treaties to avoid double taxation on certain transactions among our subsidiaries. If we are not able to avail ourselves of the tax treaties we could be subject to additional taxes, which could adversely affect our financial condition and results of operations.

The enactment of legislation implementing changes in the U.S. taxation of international business activities or the adoption of other tax reform policies could materially impact our financial position and results of operations.

The current Administration has proposed, and Congress has introduced, legislation to reform the U.S. taxation of international business activities, including, but not limited to, limiting the ability of taxpayers to claim and utilize foreign tax credits, limiting the check-the-box regime, revising the rules applicable to transfers of intangible property, and deferring certain tax deductions until non-U.S. earnings are repatriated to the United States. The current Administration has made public statements indicating that it has made the issue a priority, and key members of the

U.S. Congress have conducted hearings and proposed legislation. Accordingly, depending on the final form of legislation enacted, if any, the consequences of changes to the U.S. taxation of international business activities may be significant for our China Business and other offshore activities. If any of these proposals are enacted into legislation, they could have material adverse consequences on our effective tax rate, the amount of tax we pay and our financial position and results of operations.

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We have implemented a corporate structure taking into consideration our international operations and potentially applicable tax impact on our worldwide operations, and any changes in applicable tax laws and regulations may negatively impact our financial condition and operating results.

We have developed our corporate structure to be closely aligned with the international nature of our business. There can be no assurance that the applicable tax laws and regulations will continue in effect or that the taxing authorities in any or all of the applicable jurisdictions will not challenge one or more aspects or characterizations of our corporate structure and the treatment of transactions or agreements within our corporate structure, or determine that the manner in which we operate our business is not consistent with our corporate structure. Any unfavorable changes in laws and regulations or positions by tax authorities could harm our financial position and results of operations.

Our foreign operations, particularly those in China, are subject to significant risks involving the protection of intellectual property.

We seek to protect the products and technology that we consider important to our business by filing China and international patent applications, relying on trade secrets or pharmaceutical regulatory protection or employing a combination of these methods. We currently have 3 granted patents and 15 pending patent applications relating to roxadustat in China. See Business Intellectual Property. However, the filing of a patent application does not mean that we will be granted a patent, or that any patent eventually granted will be as broad as requested in the patent application or will be sufficient to protect our technology. There are a number of factors that could cause our patents, if granted, to become invalid or unenforceable or that could cause our patent applications not to be granted, including known or unknown prior art, deficiencies in the patent application, or lack of originality of the technology. Furthermore, the terms of our patents are limited. The patents we hold and patents that may be granted from our currently pending patent applications have, absent any patent term adjustment or extension, a twenty-year protection period starting from the date of application.

Intellectual property rights and confidentiality protections in China may not be as effective as those in the United States or other countries for many reasons, including lack of procedural rules for discovery and evidence, low damage awards, and lack of judicial independence. Implementation and enforcement of Chinese intellectual property laws have historically been deficient and ineffective and may be hampered by corruption and local protectionism. Policing unauthorized use of proprietary technology is difficult and expensive, and we may need to resort to litigation to enforce or defend patents issued to us or to determine the enforceability and validity of our proprietary rights or those of others. The experience and capabilities of Chinese courts in handling intellectual property litigation varies, and outcomes are unpredictable. An adverse determination in any such litigation could materially impair our intellectual property rights and may harm our business.

We are subject to laws and regulations governing corruption, which will require us to develop and implement costly compliance programs.

We must comply with a wide range of laws and regulations to prevent corruption, bribery, and other unethical business practices, including the FCPA and anti-bribery and anti-corruption laws in other countries, particularly China. The creation and implementation of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

Anti-bribery laws prohibit us, our employees, and some of our agents or representatives from offering or providing any personal benefit to covered government officials to influence their performance of their duties or induce them to serve interests other than the missions of the public organizations in which they serve. Certain commercial bribery rules also prohibit offering or providing any personal benefit to employees and representatives of commercial

companies to influence their performance of their duties or induce them to serve interests other than their employers. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and

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maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the Department of Justice, or DOJ. The Securities and Exchange Commission, or the SEC, is involved with enforcement of the books and records provisions of the FCPA.

Compliance with these anti-bribery laws is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the anti-bribery laws present particular challenges in the pharmaceutical industry, because, in many countries including China, hospitals are state-owned or operated by the government, and doctors and other hospital employees are considered foreign government officials; furthermore, in certain countries (China in particular), hospitals and clinics are permitted to sell pharmaceuticals to their patients and are primary or significant distributors of pharmaceuticals, Certain payments to hospitals in connection with clinical studies, procurement of pharmaceuticals and other work have been deemed to be improper payments to government officials and have led to vigorous anti-bribery law enforcement actions imposing heavy fines in multiple jurisdictions, particularly in the United States and China.

It is not always possible to identify and deter violations, 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.

In the pharmaceutical industry, corrupt practices include, among others, acceptance of kickbacks, bribes or other illegal gains or benefits by the hospitals and medical practitioners from pharmaceutical manufacturers, distributors or their third party agents in connection with the prescription of certain pharmaceuticals. If our employees, affiliates, distributors or third party marketing firms violate these laws or otherwise engage in illegal practices with respect to their sales or marketing of our products or other activities involving our products, we could be required to pay damages or heavy fines by multiple jurisdictions where we operate, which could materially and adversely affect our financial condition and results of operations. The Chinese government has also sponsored anti-corruption campaigns from time to time, which could have a chilling effect on any future marketing efforts by us to new hospital customers. There have been recent occurrences in which certain hospitals have denied access to sales representatives from pharmaceutical companies because the hospitals wanted to avoid the perception of corruption. If this attitude becomes widespread among our potential customers, our ability to promote our products to hospitals may be adversely affected.

As we expand our operations in China and other jurisdictions internationally, we will need to increase the scope of our compliance programs to address the risks relating to the potential for violations of the FCPA and other anti-bribery and anti-corruption laws. Our compliance programs will need to include policies addressing not only the FCPA, but also the provisions of a variety of anti-bribery and anti-corruption laws in multiple foreign jurisdictions, including China, encompass provisions relating to books and records that will apply to us as we become a public company and include effective training for our personnel throughout our organization. The creation and implementation of anti-corruption compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required. Violation of the FCPA and other anti-corruption laws can result in significant administrative and criminal penalties for us and our employees, including substantial fines, suspension or debarment from government contracting, prison sentences, or even the death penalty in extremely serious cases in certain countries. The SEC also may suspend or bar us from trading securities on U.S. exchanges for violations of the FCPA s accounting provisions. Even if we are not ultimately punished by government authorities, the costs of investigation and review, the distraction of company personnel, legal defense costs, and harm to our reputation could be substantial and could limit our profitability or our ability to develop or commercialize our product candidates. In addition, if any of our competitors are not subject to the FCPA, they may engage in practices that will lead to their receipt of preferential treatment from foreign hospitals and enable them to secure business from foreign hospitals in ways that are unavailable to us.

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Our operations in China subject us to various Chinese labor and social insurance laws, and our failure to comply with such laws may materially and adversely affect our business, financial condition and results of operations.

We are subject to China Labor Contract Law, which became effective in 2008 and provides stronger protections for employees and imposes more obligations on employers. The Labor Contract Law places certain restrictions on the circumstances under which employers may terminate labor contracts and require economic compensation to employees upon termination of employment, among other things. In addition, companies operating in China are generally required to contribute to labor union funds and the mandatory social insurance and housing funds. Any failure by us to comply with Chinese labor and social insurance laws may subject us to late fees, fines and penalties, or cause the suspension or termination of our ability to conduct business in China, any of which could have a material and adverse effect on business, results of operations and prospects.

Uncertainties with respect to the China legal system could have a material adverse effect on us.

The legal system of China is a civil law system primarily based on written statutes. Unlike in a common law system, prior court decisions may be cited for reference but are not binding. Because the China legal system continues to rapidly evolve, the interpretations of many laws, regulations and rules are not always uniform and enforcement of these laws, regulations and rules involve uncertainties, which may limit legal protections available to us. Moreover, decision makers in China judicial system have significant discretion in interpreting and implementing statutory and contractual terms, which may render it difficult for FibroGen China to enforce the contracts it has entered into with our business partners, customers and suppliers. Different government departments may have different interpretations of certain laws and regulations, and licenses and permits issued or granted by one government authority may be revoked by a higher government authority at a later time. Navigating the uncertainty and change in China legal system will require the devotion of significant resources and time, and there can be no assurance that our contractual and other rights will ultimately be enforced.

Changes in China s economic, political or social conditions or government policies could have a material adverse effect on our business and operations.

The Chinese economy and Chinese society continue to undergo significant change. Adverse changes in the political and economic policies of the Chinese government could have a material adverse effect on the overall economic growth of China, which could adversely affect our ability to conduct business in China. The Chinese government continues to adjust economic policies to promote economic growth. Some of these measures benefit the overall Chinese economy, but may also have a negative effect on us. For example, our financial condition and results of operations in China may be adversely affected by government control over capital investments or changes in tax regulations. As the Chinese pharmaceutical industry grows and evolves, the Chinese government may also implement measures to change the structure of foreign investment in this industry. We are unable to predict the frequency and scope of such policy changes, any of which could materially and adversely affect FibroGen China s liquidity and access to capital and its ability to conduct business in China. Any failure on our part to comply with changing government regulations and policies could result in the loss of our ability to develop and commercialize our product candidates in China.

Risks Related to the Operation of Our Business

We may encounter difficulties in managing our growth and expanding our operations successfully.

As we seek to advance our product candidates through clinical trials and commercialization, we will need to expand our development, regulatory, manufacturing, commercialization and administration capabilities or contract with third

parties to provide these capabilities for us. As our operations expand and we continue to undertake the efforts and expense to operate as a public reporting company, we expect that we will need to increase the responsibilities on members of management and manage any future growth effectively. Our failure to accomplish any of them could prevent us from successfully implementing our strategy and maintaining the confidence of investors in our company.

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If we fail to attract and keep senior management and key personnel, in particular our chief executive officer, we may be unable to successfully develop our product candidates, conduct our clinical trials and commercialize our product candidates.

We are highly dependent on our chief executive officer, Thomas Neff, and other members of our senior management team. The loss of the services of Mr. Neff or any of these other individuals would be expected to significantly negatively impact the development and commercialization of our product candidates, our existing collaborative relationships and our ability to successfully implement our business strategy.

Recruiting and retaining qualified commercial, development, scientific, clinical and manufacturing personnel are and will continue to be critical to our success. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize product candidates. We may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the intense competition among numerous biopharmaceutical companies for similar personnel.

There is also significant competition, in particular in the San Francisco Bay area, for the hiring of experienced and qualified personnel, which increases the importance of retention of our existing personnel. If we are unable to continue to attract and retain personnel with the quality and experience applicable to our product candidates, our ability to pursue our strategy will be limited and our business and operations would be adversely affected.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing, manufacturing and commercialization of our product candidates. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in a product, negligence, strict liability or breach of warranty. Claims could also be asserted under state consumer protection acts. If we are unable to obtain insurance coverage at levels that are appropriate to maintain our business and operations, or if we are unable to successfully defend ourselves against product liability claims, we may incur substantial liabilities or otherwise cease operations. Product liability claims may result in:

termination of further development of unapproved product candidates or significantly reduced demand for any approved products;

material costs and expenses to defend the related litigation;

a diversion of time and resources across the entire organization, including our executive management;

product recalls, withdrawals or labeling restrictions;

termination of our collaboration relationships or disputes with our collaboration partners; and

reputational damage negatively impacting our other product candidates in development.

If we fail to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims, we may not be able to continue to develop our product candidates. We maintain product liability insurance in a customary amount for the stage of development of our product candidates. Although we believe that we have sufficient coverage based on the advice of our third party advisors, there can be no assurance that such levels will be sufficient for our needs. Moreover, our insurance policies have various exclusions, and we may be in a dispute with our carrier as to the extent and nature of our coverage, including whether we are covered under the applicable product liability policy. If we are not able to ensure coverage or are required to pay substantial amounts to settle or otherwise contest the claims for product liability, our business and operations would be negatively affected.

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Our business and operations would suffer in the event of computer system failures.

Despite the implementation of security measures, our internal computer systems, and those of our CROs, collaboration partners, and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, fire, terrorism, war and telecommunication and electrical failures. 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, ongoing or planned clinical trials 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 results 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 product candidates could be delayed.

Our headquarters and data storage facilities are located near known earthquake fault zones. The occurrence of an earthquake, fire or any other catastrophic event could disrupt our operations or the operations of third parties who provide vital support functions to us, which could have a material adverse effect on our business, results of operations and financial condition.

We and some of the third party service providers on which we depend for various support functions, such as data storage, are vulnerable to damage from catastrophic events, such as power loss, natural disasters, terrorism and similar unforeseen events beyond our control. Our corporate headquarters and other facilities are located in the San Francisco Bay Area, which in the past has experienced severe earthquakes and fires.

We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects.

If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, damaged critical infrastructure, such as our data storage facilities, enterprise financial systems or manufacturing resource planning and enterprise quality systems, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Furthermore, integral parties in our supply chain are operating from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events. If such an event were to affect our supply chain, it could have a material adverse effect on our business.

Risks Related to Our Common Stock

The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above your purchase price.

In general, pharmaceutical, biotechnology and other life sciences company stocks have been highly volatile in the current market. The volatility of pharmaceutical, biotechnology and other life sciences company stocks is sometimes unrelated to the operating performance of particular companies and biotechnology and life science companies stocks often respond to trends and perceptions rather than financial performance. In particular, the market price of shares of our common stock could be subject to wide fluctuations in response to the following factors:

results of clinical trials of our product candidates, including roxadustat and FG-3019;

the timing of the release of results of and regulatory updates regarding our clinical trials;

the level of expenses related to any of our product candidates or clinical development programs;

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results of clinical trials of our competitors products;

safety issues with respect to our product candidates or our competitors products;

regulatory actions with respect to our product candidates and any approved products or our competitors products;

fluctuations in our financial condition and operating results, which will be significantly affected by the manner in which we recognize revenue from the achievement of milestones under our collaboration agreements;

adverse developments concerning our collaborations and our manufacturers;

the termination of a collaboration or the inability to establish additional collaborations;

the publication of research reports by securities analysts about us or our competitors or our industry or negative recommendations or withdrawal of research coverage by securities analysts;

the inability to obtain adequate product supply for any approved drug product or inability to do so at acceptable prices;

disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;

the ineffectiveness of our internal controls;

our failure or the failure of our competitors to meet analysts projections or guidance that we or our competitors may give to the market;

additions and departures of key personnel;

announced strategic decisions by us or our competitors;

changes in legislation or other regulatory developments affecting our product candidates or our industry;

fluctuations in the valuation of the biotechnology industry and particular companies perceived by investors to be comparable to us;

sales of our common stock by us, our insiders or our other stockholders;

speculation in the press or investment community;

announcement or expectation of additional financing efforts;

announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;

changes in accounting principles;

activities of the government of China, including those related to the pharmaceutical industry as well as industrial policy generally;

performance of other United States publicly traded companies with significant operations in China;

terrorist acts, acts of war or periods of widespread civil unrest;

natural disasters such as earthquakes and other calamities;

changes in market conditions for biopharmaceutical stocks;

changes in general market and economic conditions; and

the other factors described in this Risk Factors section.

As a result of fluctuations caused by these and other factors, comparisons of our operating results across different periods may not be accurate indicators of our future performance. Any fluctuations that we report in the future may differ from the expectations of market analysts and investors, which could cause the price of our common

stock to fluctuate significantly. Moreover, securities class action litigation has often been initiated against companies following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management s attention and resources, and could also require us to make substantial payments to satisfy judgments or to settle litigation.

If securities or industry analysts do not continue to publish research or reports about our business, or if they change their recommendations regarding our stock adversely, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If one or more of the analysts who cover us downgrade our stock, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Our principal stockholders and management own a significant percentage of our stock and will be able to exercise significant influence over matters subject to stockholder approval.

As of February 28, 2015, our executive officers, directors and principal stockholders, together with their respective affiliates, owned approximately 16.5% of our common stock, including shares subject to outstanding options that are exercisable within 60 days after such date and shares issuable upon settlement of restricted stock units that will vest within 60 days after such date. Accordingly, these stockholders will be able to exert a significant degree of influence over our management and affairs and over matters requiring stockholder approval, including the election of our board of directors and approval of significant corporate transactions. The interests of this group may differ from those of other stockholders and they may vote their shares in a way that is contrary to the way other stockholders vote their shares. This concentration of ownership could have the effect of entrenching our management and/or the board of directors, delaying or preventing a change in our control or otherwise discouraging a potential acquirer from attempting to obtain control of us, which in turn could have a material and adverse effect on the fair market value of our common stock.

We are an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and for so long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies. Specifically, the JOBS Act:

- permits us to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced Management s Discussion and Analysis of Financial Condition and Results of Operations disclosure;

- eliminates the requirement to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;

removes the requirement to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board;

reduces disclosure obligations regarding executive compensation; and

exempts from the requirements of holding a non-binding stockholder advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

This Annual Report is based upon the reduced reporting burdens under the JOBS Act and we expect to continue at these reduced levels for so long as we are permitted under the JOBS Act. Specifically, we could be an emerging growth company for up to five years, although circumstances could cause us to lose that status earlier,

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including any of the following: if the market value of our common stock held by non-affiliates exceeds $700 million as of June 30 in any calendar year before that time or if we have total annual gross revenue of $1 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the end of such year or, if we issue more than $1 billion in non-convertible debt during any three-year period before that time, we would cease to be an emerging growth company immediately. If any investors find our common stock less attractive as a result, there may be a less active market for our common stock and our stock price may be more volatile.

In addition, Section 107 of the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. However, we chose to opt out of such extended transition period, and as a result, we will comply with new or revised accounting standards on the relevant dates that adoption of such standards is required for non-emerging growth companies. Our decision to opt out of the extended transition period for complying with new or revised accounting standards is irrevocable.

A significant portion of our total outstanding shares may be sold into the public market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

As of December 31, 2014, we had 59,046,296 shares of common stock outstanding. Sales of a substantial number of shares of our common stock in the public market could occur at any time after the expiration of the lock-up agreements entered into in connection with our initial public offering. These sales, or the market perception that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. 74.5% of our outstanding shares as of December 31, 2014 are restricted as a result of lock-up agreements or market stand off agreements but will be able to be sold, subject to any applicable volume limitations under federal securities laws with respect to affiliate sales, beginning on May 13, 2015. In addition, as of December 31, 2014, there were 14,426,853 shares subject to outstanding options, of which 10,695,104 shares were vested, 559,582 shares subject to outstanding restricted stock unit awards and 173,116 shares subject to outstanding warrants to purchase common stock that will become eligible for sale in the public market to the extent permitted by any applicable vesting requirements, the lock-up agreements and Rules 144 and 701 under the Securities Act of 1933, as amended (the Securities Act). We have registered all shares of common stock that we may issue under our employee benefit plans, including our 2005 Equity Incentive Plan and 2014 Equity Incentive Plan. Once these shares are issued in accordance with the terms of the plans, they can be freely sold in the public market upon issuance, subject to the lock-up agreements entered into in connection with our initial public offering (which we expect to expire on May 13, 2015) and the restrictions imposed on our affiliates under Rule 144.

Additional remedial measures that may be imposed in the proceedings instituted by the SEC against five China based accounting firms, including the Chinese affiliate of our independent registered public accounting firm, could result in our consolidated financial statements being determined to not be in compliance with the requirements of the Exchange Act.

In late 2012, the SEC commenced administrative proceedings under Rule 102(e) of its Rules of Practice and also under the Sarbanes-Oxley Act of 2002 against the Chinese affiliates of the big four accounting firms, including PricewaterhouseCoopers Zhong Tian CPAs Limited, the Chinese affiliate of our independent registered public accounting firm. The Rule 102(e) proceedings initiated by the SEC relate to these firms failure to produce documents, including audit work papers, in response to the request of the SEC pursuant to Section 106 of the Sarbanes-Oxley Act of 2002, as the auditors located in China are not in a position lawfully to produce documents directly to the SEC because of restrictions under Chinese law and specific directives issued by the China Securities Regulatory Commission, or CSRC. The issues raised by the proceedings are not specific to our auditors or to us.

In January 2014, an administrative law judge reached an initial decision that the Chinese affiliates of the big four accounting firms should be barred from practicing before the SEC for a period of six months. In February

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2015, the Chinese affiliates of the big four accounting firms each agreed to a censure and to pay a fine to the SEC to settle the dispute and avoid suspension of their ability to practice before the SEC and audit U.S.-listed companies. The settlement required the firms to follow detailed procedures and to seek to provide the SEC with access to Chinese firms audit documents via the CSRC. If future document productions fail to meet specified criteria, the SEC retains authority to impose a variety of additional remedial measures on the firms depending on the nature of the failure.

We cannot predict if the SEC will further review the four firms compliance with specified criteria or if such further review would result in the SEC imposing additional penalties such as suspensions or commencing any further administrative proceedings. Although it does not play a substantial role (as defined under PCAOB standards) in the audit of our consolidated financial statements, if PricewaterhouseCoopers Zhong Tian CPAs Limited were denied, temporarily, the ability to practice before the SEC, our ability to produce audited consolidated financial statements for our company could be affected and we could be determined not to be in compliance with the requirements of the Exchange Act. Such a determination could ultimately lead to the delisting of our shares from the NASDAQ Global Select Market or deregistration from the SEC, or both, which would substantially reduce or effectively terminate the trading of our stock.

We are incurring significant compliance costs as a result of operating as a public company and our management is required to devote substantial resources to public company compliance programs.

As a newly public company, we are incurring significant legal, insurance, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, the listing requirements of The NASDAQ Stock Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We are currently and intend to continue to invest resources to comply with evolving laws, regulations and standards, and this investment will result in increased general and administrative expenses and may divert management s time and attention from product development activities. If our efforts to comply with new laws, regulations and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to practice, regulatory authorities may initiate legal proceedings against us and our business may be harmed. In the future, it may be more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These factors could also make it more difficult for us to attract and retain qualified members of our board of directors, particularly to serve on our audit committee and compensation committee, and qualified executive officers.

Specifically, in order to comply with the requirements of being a public company, we may need to undertake various actions, including implementing new internal controls and procedures and hiring new accounting or internal audit staff. The Sarbanes-Oxley Act requires that we maintain effective disclosure controls and procedures and internal control over financial reporting. We are continuing to develop and refine our disclosure controls and other procedures that are designed to ensure that information required to be disclosed by us in the reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC s rules and forms, and that information required to be disclosed in reports under the Exchange Act is accumulated and communicated to our principal executive and financial officers. Any failure to develop or maintain effective controls could adversely affect the results of periodic management evaluations. In the event that we are not able to demonstrate compliance with the Sarbanes-Oxley Act, that our internal control over financial reporting is perceived as inadequate, or that we are unable to produce timely or accurate financial statements, investors may lose confidence in our operating results and the price of our ordinary shares could decline. In addition, if we are unable to continue to meet these requirements, we may not be able to remain listed on The NASDAQ Stock Market.

We are not currently required to comply with the SEC s rules that implement Section 404 of the Sarbanes-Oxley Act, or Section 404, and are therefore not yet required to make a formal assessment of the effectiveness of our internal control over financial reporting for that purpose. We will be required to comply with certain of these

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rules, including the requirement of an annual management report on the effectiveness of our internal control over financial reporting, commencing with our annual report on Form 10-K for the fiscal year ending December 31, 2015. This assessment will need to include the disclosure of any material weaknesses in our internal control over financial reporting identified by our management or our independent registered public accounting firm. In addition, we will be required to have our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting beginning with our first annual report on Form 10-K following the date on which we are no longer an emerging growth company. To achieve compliance with Section 404 within the prescribed period, we will need to continue to dedicate internal resources, outside consultants and continue to execute a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our consolidated financial statements and we cannot assure you that there will not be material weaknesses or significant deficiencies in our internal controls in the future.

We may engage in future acquisitions that could disrupt our business, cause dilution to our stockholders and harm our business, results of operations, financial condition and cash flows and future prospects.

While we currently have no specific plans to acquire any other businesses, we may, in the future, make acquisitions of, or investments in, companies that we believe have products or capabilities that are a strategic or commercial fit with our present or future product candidates and business or otherwise offer opportunities for our company. In connection with these acquisitions or investments, we may:

issue stock that would dilute our existing stockholders percentage of ownership;

incur debt and assume liabilities; and

incur amortization expenses related to intangible assets or incur large and immediate write-offs.

We may not be able to complete acquisitions on favorable terms, if at all. If we do complete an acquisition, we cannot assure you that it will ultimately strengthen our competitive position or that it will be viewed positively by customers, financial markets or investors. Furthermore, future acquisitions could pose numerous additional risks to our operations, including:

problems integrating the purchased business, products or technologies, or employees or other assets of the acquisition target;

increases to our expenses;

disclosed or undisclosed liabilities of the acquired asset or company;

diversion of management s attention from their day-to-day responsibilities;

reprioritization of our development programs and even cessation of development and commercialization of our current product candidates;

harm to our operating results or financial condition;

entrance into markets in which we have limited or no prior experience; and

potential loss of key employees, particularly those of the acquired entity.

We may not be able to complete any acquisitions or effectively integrate the operations, products or personnel gained through any such acquisition.

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Provisions in our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current directors or management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- authorize blank check preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors pursuant to a resolution adopted by a majority of the total number of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed prior to the end of their term only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- require a supermajority vote of the holders of our common stock or the majority vote of our board of directors to amend our bylaws; and
- require a supermajority vote of the holders of our common stock to amend the classification of our board of directors into three classes and to amend certain other provisions of our certificate of incorporation.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

Moreover, because we are incorporated in Delaware, we are governed by certain anti-takeover provisions under Delaware law which may discourage, delay or prevent someone from acquiring us or merging with us whether or not it is desired by or beneficial to our stockholders. We are subject to the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, our amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

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

In general, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an ownership change is subject to limitations on its ability to utilize its pre-change net operating losses or tax credits, or NOLs or credits, to offset future taxable income. Our existing NOLs or credits may be subject to substantial limitations arising from previous ownership changes, and if we undergo an ownership change our ability to utilize NOLs or credits could be further limited by Section 382 of the Code. In addition, future changes in our stock ownership, many of which are outside of our control, could result in an ownership change under Section 382 of the Code. Our NOLs or credits may also be impaired under state law. Accordingly, we may not be able to utilize a material portion of our NOLs or credits. Furthermore, our ability to utilize our NOLs or credits is conditioned upon our attaining profitability and generating United States federal and state taxable income. As described above under Risks Related to our Financial Position and History of Operating Losses, we have incurred significant net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; thus, we do not know whether or when we will generate the United States federal or state taxable income necessary to utilize our NOLs or credits. A full valuation allowance has been provided for the entire amount of our NOLs and credits.

Our amended and restated certificate of incorporation designates the state or federal courts located in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that, subject to limited exceptions, the state and federal courts located in the State of Delaware will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated by-laws, or (4) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above. This choice of forum provision may limit a stockholder s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find these provisions of our amended and restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain and you may never receive a return on your investment.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future and investors seeking cash dividends should not purchase our common stock. We plan to retain any earnings to invest in our product candidates and maintain and expand our operations. Therefore, capital appreciation, or an increase in your stock price, which may never occur, may be the only way to realize any return on your investment.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

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ITEM 2. PROPERTIES

Our corporate and research and development operations are located in San Francisco, California, where we lease approximately 234,000 square feet of office and laboratory space with approximately 35,000 square feet subleased. The lease for our San Francisco headquarters expires in 2023. In addition, we have a leased facility located in South San Francisco, California, which was used as our corporate headquarters prior to moving to our current facility in 2008. The South San Francisco facility is approximately 106,000 square feet and is fully subleased. This lease and associated subleases expired in February 2015. We also lease approximately 67,000 square feet of office and manufacturing space in Beijing, China. Our lease in China expires in 2021. We believe our facilities are adequate for our current needs and that suitable additional or substitute space would be available if needed.

ITEM 3. LEGAL PROCEEEDINGS

We are not currently a party to any material legal proceedings.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

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PART II

ITEM 5. MARKET FOR REGISTRANT S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information for Common Stock

Our common stock has been listed on the NASDAQ Global Select Market (NASDAQ) since November 14, 2014, under the symbol FGEN. Prior to our initial public offering, there was no public market for our common stock.

The following table sets forth for the indicated periods the high and low closing sales prices of our common stock as reported on the NASDAQ.

	Fourth Quarter 2014 (1)
High	$ 31.48
Low	$ 20.10

(1) Beginning on November 14, 2014

Stock Price Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return for our common stock since November 14, 2014, which is the date our common stock first began trading on the NASDAQ Global Select Market, to two indices: the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The graph assumes an initial investment of $100 on November 14, 2014, in our common stock, the stocks comprising the NASDAQ Composite Index, and the stocks comprising the NASDAQ Biotechnology Index. The stockholder return shown in the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.

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The above Stock Price Performance Graph and related information shall not be deemed soliciting material or to be filed with the Securities and Exchange Commission, nor shall such information be incorporated by reference into any future filing under the Securities Actor Exchange Act, except to the extent that we specifically incorporate it by reference into such filing.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Stockholders

As of February 28, 2015, there were 989 registered stockholders of record for our common stock. The actual number of stockholders includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees, and accordingly is greater than the number of registered holders. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Use of Proceeds from Initial Public Offering of Common Stock

On November 13, 2014, our Registration Statement on Form S-1, as amended (Reg. Nos. 333-199069 and 333-200189) was declared effective in connection with the initial public offering of our common stock, pursuant to which we sold 9,315,000 shares at a price to the public of $18.00 per share. Goldman, Sachs & Co., Citigroup Global Markets Inc., and Leerink Partners LLC acted as joint book-running managers of the initial public offering, and RBC Capital Markets, LLC, Stifel, Nicolaus & Company, Incorporated, and William Blair & Company, L.L.C. acted as co-managers. AstraZeneca, one of our collaboration partners, agreed to purchase from us concurrently with the closing of our initial public offering in a private placement shares of our common stock with an aggregate purchase price of $20.0 million at a price per share equal to the initial public offering price. The initial public offering and concurrent private placement closed on November 19, 2014, as a result of which we received net proceeds of approximately $171.8 million, after deducting underwriting discounts and commissions of $11.7 million and offering expenses of $4.1 million. Upon the closing of our initial public offering, all outstanding shares of our convertible preferred stock automatically converted into 33,919,954 shares of common stock. Upon the closing of our initial public offering, 958,996 shares of FibroGen Europe convertible preferred stock were converted into shares of FibroGen common stock.

There has been no material change in the planned use of proceeds from our initial public offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act on November 14, 2014.

Recent Sales of Unregistered Securities

2005 Stock Plan From January 1, 2014 through November 12, 2014 we granted options under our 2005 Stock Plan to purchase an aggregate of 2,264,667 shares of our common stock to employees, consultants and directors, having exercise prices ranging from $13.75 to $14.58 per share. Of these grants, options to purchase an aggregate of 94,300 shares of common stock were cancelled without being exercised in 2014. During the period from January 1, 2014 through December 31, 2014, an aggregate of 540,242 shares of our common stock were issued upon the exercise of

stock options from the 2005 Stock Plan, at exercise prices between $2.00 and $14.58 per share, for aggregate proceeds of approximately $1.7 million.

2014 Equity Incentive Plan From November 13, 2014 through December 31, 2014 we granted options under our 2014 Equity Incentive Plan to purchase an aggregate of 1,734,916 shares of our common stock to employees,

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consultants and directors, having exercise prices ranging from $18.00 to $28.42 per share. From January 1, 2014 through December 31, 2014, we also granted 560,278 restricted stock units. Of these grants, options to purchase an aggregate of 22,232 shares of common stock were cancelled without being exercised in 2014. During the period from January 1, 2014 through December 31, 2014, no shares of our common stock were issued upon the exercise of stock options from the 2014 Equity Incentive Plan.

The offers, sales and issuances of the securities described above were exempt from registration under Rule 701 promulgated under the Securities Act in that the transactions were under compensatory benefit plans as provided under Rule 701. Appropriate legends were affixed to the securities issued in these transactions. Shares of common stock to be issued pursuant to awards (including options) under our 2005 Stock Plan and 2014 Equity Incentive Plan were registered on a Registration Statement on Form S-8, filed with the SEC on November 18, 2014.

Private Placement On November 19, 2014, we sold and issued 1,111,111 shares of our common stock to AstraZeneca at the initial public offering price of $18.00 per share in a private placement offering for aggregate gross proceeds of $20 million pursuant to a common stock purchase agreement dated as of October 20, 2014. The private placement offering closed concurrently with the closing of our initial public offering. The sale and issuance of shares of common stock in the private placement was made in reliance on Rule 506 promulgated under the Securities Act and was made without general solicitation or advertising. AstraZeneca represented that it was an accredited investor with access to information about us sufficient to evaluate the investment and that the common stock being acquired constituted restricted securities. Appropriate legends were affixed to the securities issued in the private placement.

Conversion of FibroGen Europe Stock On November 19, 2014, upon the closing of our initial public offering, 958,996 shares of our common stock were issued upon the exchange of outstanding shares of FibroGen Europe convertible preferred stock pursuant to exchange option agreements and related elections to exchange. The issuance of shares of common stock in the exchange was deemed to be exempt from registration under the Securities Act in reliance upon Section 4(a)(2) of the Securities Act or Rule 506 or Regulation S promulgated thereunder, with each exchanging stockholder representing that it had access to information about us sufficient to evaluate the investment. Appropriate legends were affixed to the securities issued in the exchange.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

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ITEM 6. SELECTED FINANCIAL DATA

The following selected consolidated financial data as of December 31, 2014, 2013 and 2012 and for the years ended December 31, 2014, 2013 and 2012 is derived from our audited consolidated financial statements. Our historical results are not necessarily indicative of the results to be expected in the future. The selected consolidated financial data should be read together with Part II, Item 7: Management s Discussion and Analysis of Financial Condition and Results of Operations and in conjunction with the consolidated financial statements, related notes, and other financial information included elsewhere in this Annual Report.

	Years Ended December 31,		
	2014	2013	2012
	(in thousands)		
Result of Operations			
Revenue:			
License and milestone revenue	$ 117,191	$ 94,961	$ 62,845
Collaboration services and other revenue	20,410	7,209	3,088
Total revenue	137,601	102,170	65,933
Operating expenses:			
Research and development (1)	150,794	85,710	74,222
General and administrative (1)	36,909	24,409	18,934
Total operating expenses	187,703	110,119	93,156
Loss from operations	(50,102)	(7,949)	(27,223)
Total interest and other, net	(9,402)	(6,994)	(5,448)
Loss before income taxes	(59,504)	(14,943)	(32,671)
Benefit from income taxes			100
Net loss	$ (59,504)	$ (14,943)	$ (32,571)
Net loss per share basic (2)	$ (3.17)	$ (1.13)	$ (2.48)
Net loss per share diluted (2)	$ (3.17)	$ (1.13)	$ (2.48)
Weighted-average number of common shares used in net loss per share basic (2)	18,775	13,186	13,128
Weighted-average number of common shares used in net loss per share diluted (2)	18,775	13,186	13,128

(1) Stock-based compensation expense is included in our results of operations as follows (in thousands):

	Years Ended December 31,		
	2014	2013	2012

Research and development	$ 10,893	$ 1,925	$ 2,277
General and administrative	7,805	1,519	2,284
Total stock-based compensation expense	$ 18,698	$ 3,444	$ 4,561

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(2) See Note 10 to our consolidated financial statements appearing elsewhere in this Annual Report for a description of the method used to calculate basic and diluted net loss per share of common stock.

	2014	As of December 31, 2013	2012
		(in thousands)	
Balance Sheet Data:			
Cash and cash equivalents	$ 165,455	$ 76,332	$ 38,872
Short-term and long-term investments	158,633	61,833	82,630
Working capital	135,484	106,164	29,125
Total assets	483,528	296,952	265,588
Deferred revenue	70,206	36,649	5,764
Lease financing obligations	97,221	96,809	92,902
Product development obligations	16,465	18,257	17,152
Senior Preferred Stock		168,436	168,436
Junior Preferred Stock		136,313	136,313
Accumulated deficit	(322,283)	(262,779)	(247,836)
Total stockholders equity (deficit)	221,405	(88,708)	(73,952)
Non-controlling interests	19,271	27,875	27,700
Total equity (deficit)	240,676	(60,833)	(46,252)

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ITEM 7. MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes and other financial information included in Item 15 of this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business, international operations and product candidates, includes forward-looking statements that involve risks and uncertainties. You should review the Risk Factors section of this Annual Report beginning on page 100 for a discussion of important factors that could cause our actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a research-based, biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutics to treat serious unmet medical needs. We have capitalized on our extensive experience in fibrosis and hypoxia-inducible factor, or HIF, biology to generate multiple programs targeting various therapeutic areas. Roxadustat, or FG-4592, is an oral small molecule inhibitor of HIF prolyl hydroxylases, or HIF-PHs, in Phase 3 clinical development for the treatment of anemia in chronic kidney disease, or CKD. FG-3019 is our monoclonal antibody in Phase 2 clinical development for the treatment of idiopathic pulmonary fibrosis, or IPF, pancreatic cancer and liver fibrosis. We have taken a global approach with respect to our product candidates, and this includes development and commercialization of product candidates in the People s Republic of China, or China.

Roxadustat, the first HIF-PH inhibitor to enter Phase 3 clinical development, acts by stimulating the body s natural pathway of erythropoiesis, or red blood cell production. Roxadustat represents a new paradigm for the treatment of anemia in CKD patients, and has the potential to offer a safer, more effective, more convenient and more accessible therapy than the current therapies available for anemia in CKD, such as injectable erythropoiesis stimulating agents, or ESAs, used in approximately 80% of U.S. DD-CKD patients and up to 15% of U.S. NDD-CKD patients under the care of nephrologists at initiation of dialysis as of 2012. We, along with our collaboration partners Astellas Pharma Inc., or Astellas, and AstraZeneca AB, or AstraZeneca, have designed a global Phase 3 program to support regulatory approval of roxadustat in both NDD-CKD and DD-CKD patients in multiple geographies.

FG-3019 is our fully-human monoclonal antibody that inhibits the activity of connective tissue growth factor, or CTGF, a critical common element in the progression of fibrosis and associated serious diseases. We are currently conducting an open-label Phase 2 trial in IPF; a randomized, double-blind placebo-controlled Phase 2 trial in IPF; an open-label Phase 2 trial in pancreatic cancer; and a randomized, double-blind, placebo-controlled Phase 2 trial in liver fibrosis. To date, we have retained exclusive worldwide rights for FG-3019.

We are also currently pursuing our corneal implant FG-5200 for treatment of corneal blindness resulting from partial thickness corneal damage in China.

To date, our operations have been primarily funded by net proceeds from the sale of convertible preferred stock and common stock of FibroGen, Inc. and sales of preferred stock in our majority-owned subsidiaries as well as equity investments from our collaboration partners and upfront payments, milestone payments and net research and development payments from our collaboration partners.

On November 10, 2014, we effected a 1-for-2.5 reverse split of our common stock. Upon the effectiveness of the reverse stock split, (i) every 2.5 shares of outstanding common stock were combined into one share of common stock,

(ii) the number of shares of common stock for which each outstanding option or warrant to purchase

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common stock is exercisable was proportionally decreased on a 1-for-2.5 basis, (iii) the exercise price of each outstanding option or warrant to purchase common stock was proportionately increased on a 1-for-2.5 basis, (iv) the exchange ratio for each share of outstanding FibroGen Europe share of stock which is exchangeable into our common stock was proportionately reduced on a 1-for-2.5 basis, and (v) the conversion ratio for each share of outstanding preferred stock which is convertible into our common stock was proportionately reduced on a 1-for-2.5 basis. All of the share numbers, share prices, and exercise prices have been adjusted, on a retroactive basis, to reflect this 1-for-2.5 reverse stock split. We paid cash in lieu of any fractional shares to which a holder of common stock would otherwise be entitled as a result of the reverse stock split. The par value per share and the authorized number of shares of common stock and preferred stock were not adjusted as a result of the reverse stock split.

On November 19, 2014, we closed the initial public offering of our common stock. In our initial public offering, we sold 9,315,000 shares of our common stock at a public offering price of $18.00 per share. Net proceeds from our initial public offering and concurrent private placement were approximately $171.8 million, after deducting underwriting discounts and commissions of $11.7 million and offering expenses of $4.1 million. AstraZeneca, one of our collaboration partners, agreed to purchase from us concurrently with the closing of our initial public offering in a private placement shares of our common stock with an aggregate purchase price of $20.0 million at a price per share equal to the initial public offering price. Upon the closing of our initial public offering, all outstanding shares of our convertible preferred stock automatically converted into 33,919,954 shares of common stock. Upon the closing of our initial public offering, 958,996 shares of FibroGen Europe convertible preferred stock were converted into shares of our common stock. Our proceeds from the sale of the common stock sold in the concurrent private placement were $20.0 million.

Since inception and through December 31, 2014, we have incurred a total of $918.4 million in research and development expenses, a majority of which relates to the development of roxadustat, FG-3019 and other HIF-PH inhibitors. We expect to continue to incur significant expenses and operating losses over at least the next several years and we expect our research and development expenses to continue to increase in the future as we advance our product candidates through clinical trials and expand our product candidate portfolio. We will not generate revenue based on product sales unless and until we or one of our partners successfully complete development of and obtain regulatory approval for one or more of our product candidates, which we expect will take a number of years and is subject to significant uncertainty. In addition, we expect to incur significant expenses relating to seeking regulatory approval for our product candidates. We also anticipate increased expenses related to audit, legal, regulatory and tax-related services associated with operating as a public reporting company. We consider the active management and development of our clinical pipeline to be crucial to our long-term success. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time consuming. Except for $116.5 million, of which $46.8 million had been incurred as of December 31, 2014, all currently planned development and commercialization costs for roxadustat for the treatment of anemia in CKD in the United States, Europe, Japan and all other markets outside of China are paid by Astellas and AstraZeneca. All development and commercialization costs for roxadustat in China will be shared equally, and AstraZeneca will pay for all of our commercialization costs until profitability and AstraZeneca will recoup such costs out of product sales, if any. Any termination of any of our collaboration agreements would require us to fund the further development and commercialization of roxadustat in the affected territory or pursue another collaboration, which we may be unable to do, either of which could have an adverse effect on our business and operations.

The actual probability of success for each of our product candidates and clinical programs, and our ability to generate product revenue and become profitable, depends upon a variety of factors, including the quality of the product candidate, clinical results, investment in the program, competition, manufacturing capability, commercial viability, and our and our partners ability to successfully execute our development and commercialization plans. For a description of the numerous risks and uncertainties associated with product development, see Risk Factors .

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Financial Operations Overview

Revenue

Our revenue to date has been generated primarily from our collaboration agreements with Astellas Pharmaceuticals Inc., or Astellas, and AstraZeneca AB, or AstraZeneca. The following tables summarize the sources of our revenue for the years ended December 31, 2014, 2013 and 2012:

	Year Ended December 31,		
	2014	2013	2012
	(in thousands)		
Astellas-Related party:			
License	$ 14,452	$ 9,826	$ 12,845
Milestone		12,500	50,000
Collaboration Services	3,535	3,335	2,275
Total Astellas	$ 17,987	$ 25,661	$ 65,120
AstraZeneca:			
License	$ 102,739	$ 72,635	$
Collaboration Services	16,820	3,843	
Total AstraZeneca	$ 119,559	$ 76,478	$
Other	55	$ 31	$ 813
Total Revenue	$ 137,601	$ 102,170	$ 65,933

Under our revenue recognition policy, license revenue includes amounts from upfront, non-refundable license payments and amounts allocated pursuant to the relative selling price method from other consideration received (other than substantive milestone payments) during the periods. This revenue is generally recognized as deliverables are met and services are performed. Milestone revenue includes payments from milestones which are deemed to be substantive in nature and is recognized in its entirety in the period in which the milestone is achieved. License and milestone revenues represented 85%, 93% and 95% of total revenues for the years ended December 31, 2014, 2013 and 2012, respectively.

Collaboration services include co-development services, manufacturing of clinical supplies, committee services and information sharing. Collaboration services revenues are recognized over the non-contingent performance period, ranging from 36 to 65 months. Other revenues consist of royalty payments received, which are recorded on a monthly basis as they are reported to us, and have been included with collaboration services and other revenue in the Consolidated Statements of Operations, as they have not been material for each of the years ended December 31, 2014, 2013 and 2012. Collaboration services and other revenues represented 15%, 7% and 5% of total revenues for the years ended December 31, 2014, 2013 and 2012, respectively.

We have not generated any revenues based on the sale of FDA approved products. In the future, we may generate revenue from product sales and from collaboration agreements in the form of license fees, milestone payments,

reimbursements for collaboration services and royalties on product sales. We expect that any revenues we generate will fluctuate from quarter to quarter as a result of the uncertain timing and amount of such payments and sales.

Collaboration Agreements

Our current and future research, development, manufacturing and commercialization efforts with respect to roxadustat and our other product candidates currently in development depend on funds from our collaboration agreements with Astellas and AstraZeneca as described below.

In June 2005, we entered into a collaboration agreement with Astellas for roxadustat for the treatment of anemia in Japan (Japan Agreement).

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In April 2006, we entered into a collaboration agreement with Astellas for roxadustat for the treatment of anemia in Europe, the Commonwealth of Independent States, the Middle East, and South Africa (Europe Agreement).

In July 2013, we entered into a collaboration agreement with AstraZeneca for roxadustat for the treatment of anemia in the U.S. and all territories not previously licensed to Astellas, except China (US/RoW Agreement).

In July 2013, through our China subsidiary and related affiliates, we entered into a collaboration agreement with AstraZeneca for roxadustat for the treatment of anemia in China (China Agreement).

For more detailed discussions on the accounting for these agreements, see Note 3 to the consolidated financial statements. In addition, see Business Collaborations for a more detailed description of our collaboration agreements.

Total cash consideration received through December 31, 2014 and potential cash consideration, other than development cost reimbursement, transfer price payments, royalties and profit share, pursuant to our existing collaboration agreements are as follows:

	Cash Received Through December 31, 2014	Additional Potential Cash Payments	Total Potential Cash Payments
		(in thousands)	
Astellas-Related party:			
Japan Agreement	$ 52,593	$ 120,000	$ 172,593
Europe Agreement	410,000	335,000	745,000
Total Astellas	462,593	455,000	917,593
AstraZeneca:			
US/RoW Agreement	192,000	1,057,000	1,249,000
China Agreement	28,200	348,500	376,700
Total AstraZeneca	220,200	1,405,500	1,625,700
Total	$ 682,793	$ 1,860,500	$ 2,543,293

These collaboration agreements also provide for reimbursement of certain fully burdened research and development costs as well as direct out of pocket expenses.

Research and Development Expenses

Research and development expenses consist of third party research and development costs and the fully-burdened amount of costs associated with work performed under collaboration agreements. Research and development costs include employee-related expenses for research and development functions, expenses incurred under agreements with clinical research organizations, or CROs, other clinical and preclinical costs and allocated direct and indirect overhead costs, such as facilities costs, information technology costs and other overhead. Research and development costs are expensed as incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites.

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The following table summarizes our research and development expenses incurred during the years ended December 31, 2014, 2013 and 2012:

Product Candidate	Phase of Development	Year Ended December 31, 2014	2013	2012
		(in thousands)		
Roxadustat	Phase 3	$ 83,806	$ 43,620	$ 36,631
FG-3019	Phase 2	25,505	20,103	16,607
FG-6874	Phase 1	3,067	1,979	3,410
FG-5200	Preclinical	4,311	3,154	2,428
Other research and development expenses		34,105	16,854	15,146
Total research and development expenses		$ 150,794	$ 85,710	$ 74,222

The program-specific expenses summarized in the table above include costs we directly attribute to our product candidates. We allocate research and development salaries, benefits, stock-based compensation and other indirect costs to our product candidates on a program-specific basis, and we include these costs in the program-specific expenses. The largest component of our total operating expenses has historically been our investment in research and development activities, including the clinical development of our product candidates. Since inception and through December 31, 2014, we have incurred a total of $918.4 million in research and development expenses, a majority of which relates to the development of roxadustat, FG-3019 and other HIF-PH inhibitors. We expect our research and development expenses to continue to increase in the future as we advance our product candidates through clinical trials and expand our product candidate portfolio. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time consuming. We consider the active management and development of our clinical pipeline to be crucial to our long-term success. The actual probability of success for each product candidate and clinical program may be affected by a variety of factors, including the safety and efficacy data of the product candidate, investment in the program, competition, manufacturing capability and commercial viability. Furthermore, we have entered into collaborations with third parties to participate in the development and commercialization of our product candidates, and we may enter into additional collaborations in the future. In situations in which third parties have control over the preclinical development or clinical study process for a product candidate, the estimated completion dates are largely outside of our control. We are unable to forecast with any degree of certainty which of our product candidates, if any, will be subject to collaborations in the future or how such arrangements would affect our development plans or capital requirements. As a result of the uncertainties discussed above, we are unable to determine the duration and completion costs of our research and development projects, or when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates.

The duration, costs and timing of clinical studies and development of our product candidates will depend on a variety of factors. For example, if the FDA, EMA or another regulatory authority were to require us to conduct clinical studies beyond those that we currently anticipate will be required, or if we experience significant delays in enrollment in any of our clinical studies, we could be required to expend significant additional financial resources and the time to the completion of clinical development would be extended.

We intend to identify additional partnerships to further develop product candidates other than roxadustat, which may offset a portion of our research and development expenses through reimbursement from potential partners. Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of expenses incurred or when, or if, we will be able to achieve sustained profitability.

General and Administrative Expenses

General and administrative expenses consist primarily of employee-related expenses for executive, operational, finance, legal, compliance and human resource functions. Other general and administrative expenses include

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facility-related costs and professional fees, accounting and legal services, other outside services, recruiting fees and expenses associated with obtaining and maintaining patents.

For the years ended December 31, 2014, 2013 and 2012, we incurred $36.9 million, $24.4 million and $18.9 million, respectively, in general and administrative expenses.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research and development and potential commercialization of our product candidates. We also anticipate increased expenses, including exchange listing and Securities and Exchange Commission requirements, director and officer insurance premiums, legal, audit and tax fees, regulatory compliance programs and investor relations costs associated with being a public company. Additionally, if and when we believe the first regulatory approval of one of our product candidates appears likely, we anticipate an increase in payroll and related expenses as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of our product candidates.

Interest and Other, Net

Interest Expense

In connection with our long-term lease for our corporate headquarters in San Francisco, California, which was entered into in September 2006, and the lease for our pilot plant located in Beijing Yizhuang Biomedical Park, or BYBP, which was entered into in February 2013, we recognized an asset for costs of constructing the building shells of $50.8 million and $3.1 million, respectively for these facilities and recorded a corresponding lease financing obligation. In addition, we recorded $32.5 million in reimbursements for tenant improvements in the San Francisco location and $0.5 million in rent reimbursements for BYBP.

As the monthly lease payments are made, we record interest expense and an increase or reduction in the corresponding lease financing obligation for any amounts allocated to or deficiencies being applied to the principal value of these obligations.

Interest expense includes payments made for imputed interest related to the facility lease financing obligations for the San Francisco and China properties (see Note 8 to the consolidated financial statements) and interest related to The Technology Development Center of the Republic of Finland, or TEKES, product development obligations (see Note 6 to the consolidated financial statements).

Interest Income

Interest income represents interest earned on our cash, cash equivalents and investments.

Other Income (Expense)

Other income (expense) relates to foreign currency transaction gains (losses) and remeasurement of certain monetary assets and liabilities in non-functional currency of our subsidiaries using exchange rates in effect at the end of the period into the functional currency as well as realized gains (losses) on sales of investments.

Sublease Income

We sublease approximately 34,400 square feet of space within our corporate headquarters facility to certain subtenants on a short-term basis. These subleases include invoices for base rent and reimbursement of various expenses. Sublease income is included as an offset to our facilities expenses for both general and administrative and research and development expenses. For the years ended December 31, 2014, 2013 and 2012, we had sublease income of $5.0 million, $4.5 million and $4.3 million, respectively.

In addition, we had a leased facility located in South San Francisco, California, covering approximately 106,000 square feet of space that was fully subleased. This lease and associated subleases expired in February 2015.

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Results of Operations

	Years ended December 31,		
	2014	2013	2012
	(in thousands)		
Revenue:			
License and milestone revenue	$ 117,191	$ 94,961	$ 62,845
Collaboration services and other revenue	20,410	7,209	3,088
Total revenue	137,601	102,170	65,933
Operating expenses:			
Research and development	150,794	85,710	74,222
General and administrative	36,909	24,409	18,934
Total operating expenses	187,703	110,119	93,156
Loss from operations	(50,102)	(7,949)	(27,223)
Total interest and other, net	(9,402)	(6,994)	(5,448)
Loss before income taxes	(59,504)	(14,943)	(32,671)
Benefit from income taxes			100
Net loss	$ (59,504)	$ (14,943)	$ (32,571)