

# FibroGen, Inc.

(FGEN - \$27.69)

**HOLD**

Price Target: \$25

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## Initiating HOLD: Complex Pathway Creates Higher Potential For Safety Risks; Cautious At Current Valuation

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FibroGen's two major development programs represent potential game-changing pioneering therapies that address vast commercial markets and its lead candidate - roxadustat - is entering large-scale Phase 3 clinical trials. We believe that the Company's progression into the P3 stage has served as a recent catalyst for its shares, considering the sizeable anemia market opportunity. While the success of roxadustat's Phase 2 program clearly supports the global P3 trials, we believe the potential clinical advantages may be offset by higher risk of adverse events as the HIF pathway is complex and goes beyond erythropoiesis. For these reasons, and considering the current valuation, we are cautious on FGEN shares. We are initiating coverage with a HOLD rating and a 12-month target price of \$25.

### HIGHLIGHTS

- Roxadustat Enters Global P3 Clinical Trials** – FGEN's lead candidate is entering global P3 clinical trials for the treatment of CKD-associated anemia, addressing the vast \$6B+ anemia market. In P2 clinical trials roxadustat demonstrated its ability to achieve and maintain Hb levels, along with potentially offering convenience of an all-oral regimen and safety advantages in comparison to erythropoiesis-stimulating agents (ESAs) - the current standard of care.
- The HIF Pathway Is Complex And Creates Elevated Safety Risk Concerns** – Roxadustat's mechanism of action is unique, involving the hypoxia-inducible factor prolyl hydroxylase inhibition (HIF-PHI). The HIF system is highly complex, operating in most mammalian cells, and is not restricted to erythropoiesis synthesis. The HIF pathway is also believed to be involved in the expression of over 100 genes which significantly elevates our concerns relating to safety risks. Consequently, we caution investors to be cognizant of these risks as roxadustat enters into its global P3 program that is comprised of approximately 7,300 subjects.
- FG-3019 Addresses Potential Multi-Billion Markets** – A second major development program is FG-3019 for fibrotic diseases and disorders. In Phase 2A studies, FG-3019 demonstrated its ability to reverse fibrosis and improve lung function in treating idiopathic pulmonary fibrosis (IPF). As Phase 2 programs advance, we remain cautiously optimistic that FG-3019 may emerge a potential treatment for fibrotic diseases, namely IPF. FG-3019 is also being evaluated as a treatment for pancreatic cancer and muscular dystrophy.
- Near-Term Events** – (i) initiation of enrollment of P3 studies of roxadustat in China in Q415; (ii) initiation of P2 studies of FG-3019 for Duchenne muscular dystrophy in Q415; (iii) completion of enrollment of three P3 studies of roxadustat in stable dialysis, incident-dialysis, and non-dialysis populations, respectively, by April 2016; (iv); interim results of P2 trials of FG-3019 in pancreatic cancer at ASCO GI in January 2016; (v) P2b results

Changes	Previous	Current
Rating:	--	HOLD
Price Target:	--	\$25
FY15E Rev. (M):	--	\$224.4
FY16E Rev. (M):	--	\$155.0
FY15E EPS:	--	(\$0.08)
FY16E EPS:	--	(\$1.04)

### Profile

Price:	\$27.69
Shares Out. (M):	68.8
Market Cap. (M):	\$1,903
Avg. Daily Vol.:	621,700
Insiders Own:	16.5%
Short Int.(M) / % of Float:	3.3/7%
Tan. Book Val. / Sh.:	\$4.20
Net Cash / Sh.:	\$5.82
Div / Yield:	\$0.00 / 0%

Rev. (M)	2015E	2016E	2017E
Mar	\$16.3A	--	--
Jun	\$120.6A	--	--
Sep	\$17.5	--	--
Dec	\$70.0	--	--
FY	\$224.3	\$155.0	\$210.0

EPS	2015E	2016E	2017E
Mar	(\$0.78)	--	--
Jun	\$0.83	--	--
Sep	(\$0.69)	--	--
Dec	\$0.45	--	--
FY	(\$0.08)	(\$1.04)	(\$1.01)
EBITDA	NM	NM	NM

Valuation	2015E	2016E	2017E
P/E	NM	NM	NM
EV/Sales	NM	NM	NM

### Management

CEO	Thomas B. Neff
CFO	Pat Cotroneo
CMO	Frank H. Valone, MD

### Company Description

Clean FibroGen, Inc. is a development stage biopharmaceutical company developing therapeutics for anemia and fibrosis-related diseases.

of FG-3019 for IPF in 2H16; and (vi) regulatory submission and conditional approval of roxadustat for CKD-related anemia in China in 2H16.

## INVESTMENT THESIS AND VALUATION

Our HOLD rating reflects our view that while the P2 clinical trials of roxadustat clearly support the global P3 program, the HIF system is highly complex, operating in most mammalian cells, and is not restricted to erythropoiesis synthesis. The HIF pathway is also believed to be involved in the expression of over 100 genes which significantly elevates our concerns relating to safety risks. Consequently, we caution investors to be cognizant of these risks as roxadustat enters into its global P3 program that is comprised of approximately 7,300 subjects. For these reasons, and considering the current valuation, we are HOLD rated on FGEN shares. Regarding FG-3019, we are cautiously optimistic considering its P2 status as a viable treatment for fibrotic diseases, namely idiopathic pulmonary fibrosis (IPF).

### VALUATION

Our 12-month target price is \$25, which is derived by valuing each product franchise independently. We use an extrapolation of peak sales; FibroGen's royalty stream or ownership interest in that franchise; adjusted by a probability of success assumption; and adjusted by applying an appropriate multiple of royalties or sales. The implied valuations are then discounted to present value using a 15% discount factor. The implied per share valuation is quotient of the implied present value of all franchises divided by shares outstanding.

	Peak Sales	FGEN Interest	Probability Success	FGEN Interest x Prob. Success	Multiple	Implied Valuation
Roxadustat, Global, ex-China, 22% Royalty	\$ 2,500,000,000	\$ 550,000,000	30%	\$ 165,000,000	15	\$2,475,000,000
Roxadustat, China, 50/50	\$ 1,000,000,000	\$ 500,000,000	30%	\$ 150,000,000	3	\$ 450,000,000
FG-3019, Wholly-Owned	\$ 2,000,000,000	\$2,000,000,000	30%	\$ 600,000,000	3	\$1,800,000,000

Program	Implied Valuation	Discount Factor	Years	Present Value
Roxadustat, Global, ex-China, 22% Royalty	\$ 2,475,000,000	15%	7	\$ 930,444,174
Roxadustat, China, 50/50	\$ 450,000,000	15%	5	\$ 223,729,531
FG-3019, Wholly-Owned	\$ 1,800,000,000	15%	8	\$ 588,423,193
Total Implied Present Value				\$1,742,596,898
Implied Present Value Per Share				\$ 25.35

## COMPANY OVERVIEW

FibroGen, Inc. is a development stage biopharmaceutical company with two key therapeutics in development for anemia and fibrosis-related diseases, respectively. The Company is headquartered in San Francisco, CA.

FibroGen's lead candidate - roxadustat (FG-4592) - is an orally administered small molecule hypoxia-inducible factor prolyl hydroxylases inhibitor (HIF-PHI) in global P3 development for the treatment of anemia in patients with chronic kidney disease (CKD) in both the dialysis and non-dialysis populations.

The Company has partnered with AstraZeneca PLC (NYSE: AZN) and Astellas Pharma, Inc. (OTC: ALPMY), respectively, for the global development of roxadustat. These licensing agreements provide FibroGen with various non-contingent, development and regulatory funding for its anemia program that total up to \$2.5B. Thus far, FibroGen has received over \$800M from these alliances, along with equity investments from its license partners. Upon commercialization of roxadustat, FibroGen will also collect royalties from its partners based on roxadustat sales. The Company has also entered into a 50/50 partnership with AstraZeneca for the development and commercialization of roxadustat in China.

FibroGen is also developing a fully humanized monoclonal antibody - FG-3019 - for the treatment of various fibrotic diseases. FG-3019 is currently in P2 clinical trials for the treatment of idiopathic pulmonary fibrosis (IPF) and pancreatic cancer. The Company expects to initiate enrollment in P2 trials for the treatment of Duchenne muscular dystrophy (DMD) in 4Q 2015, and will investigate FG-3019 for the treatment of other fibrotic-based diseases and disorders in the future.

## LEAD CANDIDATE - ROXADUSTAT

### Roxadustat (FG-4592) – A Potential Pioneering Oral Therapy for Anemia

Roxadustat is in global Phase 3 trials for the treatment of anemia associated with CKD in both dialysis and non dialysis populations. roxadustat's mechanism of action is via a unique pathway, with Phase 2 clinical trials demonstrating its ability to achieve and maintain hemoglobin (Hb) levels. Its unique mechanism of action potentially offers numerous advantages over the standard of care, ESAs, as it: (i) is orally-administered; (ii) lowers hepcidin levels, and thereby improves iron availability such that its use in combination with orally-administered iron supplements attain comparable Hb levels as with IV-administered supplements; and (iii) has NOT been associated with elevating endogenous erythropoietin above normal physiologic levels experienced humans at high altitudes.

### The Current Standard of Care – Erythropoiesis-Stimulating Agent (ESAs)

The current standard of care for the treatment of anemia associated with CKD is erythropoiesis-stimulating agents (ESAs) such as Epogen®, Aranesp®, and Procrit®. ESA therapy has been commercially available since 1989. We estimate the global anemia market exceeds \$6 billion per annum, inclusive of iron, vitamin supplement, transfusions, and other treatments. ESAs are commonly used to treat anemia associated with: (i) chronic kidney disease (CKD) largely limited to the dialysis setting; (ii) surgery; (iii) cancer; (iv) HIV/AIDs; and (v) other conditions that involve severe anemia.

ESAs are recombinant-produced hormonal replacement therapies that are administered intravenously or by subcutaneous injection. ESAs elevate the body's

endogenous erythropoietin (EPO) levels, thereby stimulating production of red blood cells in the bone marrow. Patients receiving ESA therapy typically require IV-administered iron supplements as iron availability is necessary for hemoglobin (Hb) production and typically impaired in anemia populations.

ESA therapy is associated with increased risk of major adverse cardiovascular events, including myocardial infarctions, thrombosis, stroke, along with increased risk of cancer and death. Consequently, ESAs have a black box warning label, and their use is often restricted to patients with severe anemia.

#### **Roxadustat's Unique Mechanism of Action Involves the Complex HIF System**

Roxadustat is an orally administered small molecule hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI). This is a unique pathway that is differentiated to that of the standard of care that involves hormonal replacement therapies with recombinant-produced erythropoiesis-stimulating agents, ESAs.

In contrast to ESAs, roxadustat achieves EPO levels within or near the physiologic range typically experienced by people adapting to high altitudes where oxygen levels are low. Roxadustat's unique mechanism of action represents a potential pioneering treatment for anemia as it may prove to be more convenient and safer than ESA therapy. Roxadustat is orally administered, and in Phase 2 clinical trials has demonstrated its ability to achieve and maintain Hb levels, increase iron availability such that orally administered iron supplements are as efficacious as IV-administered iron supplements thereby supporting an all-oral treatment regimen for treating anemia, along with potentially offering a superior safety profile as these trials have not demonstrated cardiovascular risk in comparison to ESA therapy.

#### **The Hypoxia-Inducible Factor Prolyl Hydroxylase Inhibition (HIF-PHI) Explained**

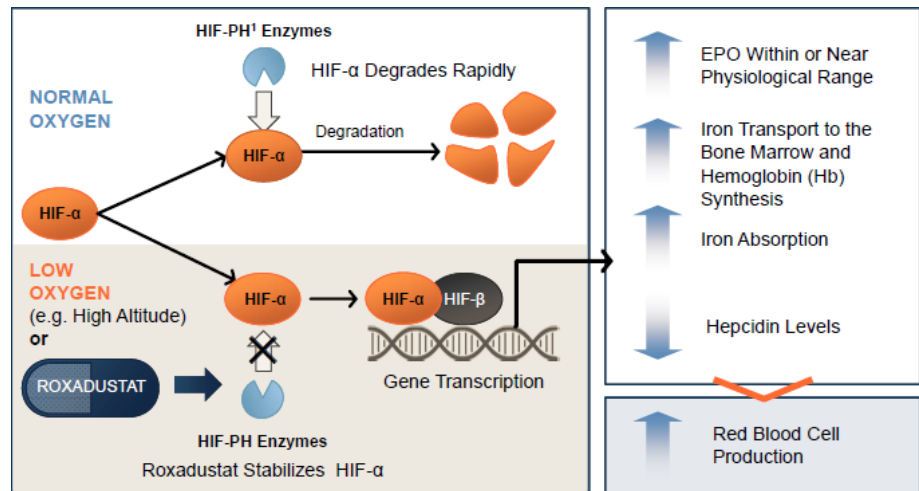
Roxadustat's mechanism of action is hypoxia-inducible factor prolyl hydroxylase inhibition (HIF-PHI) that stimulates erythropoiesis in a manner similar to the body's response to reduced oxygen levels as experienced at high altitudes. This response involves the regulation of numerous processes necessary for erythropoiesis, along with increasing iron availability and transport necessary for Hb production.

Hypoxia-inducible factor (HIF) is a transcription factor comprised of HIF-alpha and HIF-beta subunits that combine to form the HIF complex. In a normal oxygen environment (normoxia), the HIF-alpha subunit is rapidly degraded by prolyl hydroxylase (PH) enzymes, limiting formation of the necessary HIF complex needed for gene transcription to produce Hb.

However in low oxygen conditions, i.e. hypoxia, the PH enzymes are suppressed, allowing HIF-alpha to accumulate and combined with HIF-beta to form the HIF complex. This allows the HIF complex to initiate transcription of genes associated with the erythropoiesis process, along with promoting iron availability necessary for Hb production, and thereby fostering increased delivery of oxygen to tissues (Figure 1).

Roxadustat works by reversibly inhibiting the HIF-PH enzymes, and is administered by intermittent oral dosing, such that genes associated with the HIF pathway are not in a state of constant up regulation.

**Figure 1: Activates a Natural Pathway to Stimulate RBC Production**



<sup>1</sup>HIF-PH - hypoxia-inducible factor prolyl hydroxylase

Source: Company Reports

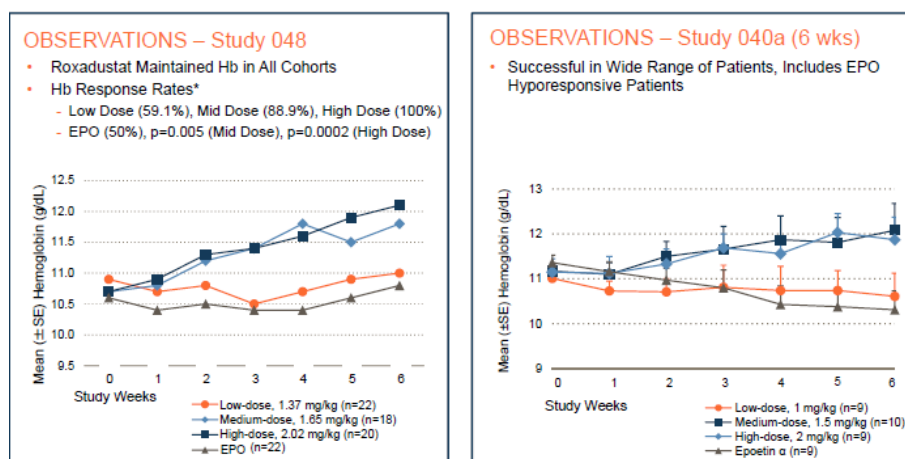
### Phase 2 Clinical Data Supports the Global Phase 3 Program

Phase 2 data demonstrate that roxadustat can: (i) achieve and maintain Hb levels in patients with CKD-associated anemia, with lower circulating EPO levels in comparison to ESA replacement therapies; (ii) mitigate the need for IV-administered iron supplements; (iii) achieve erythropoiesis in the presence of inflammation; (iv) and potentially offer a superior safety profile relative to ESA therapies that are associated with increased risk of cardiovascular events, cancer, and other risks. In Phase 2 trials, subjects receiving roxadustat did not observe increased risk of thromboembolic events. These studies also demonstrated that subjects receiving roxadustat demonstrated normal platelet counts, no change in blood pressure, improvements in HDL/LDL ratios, and reduction in total cholesterol levels.

### Roxadustat – Phase 2 Clinical Study Summary

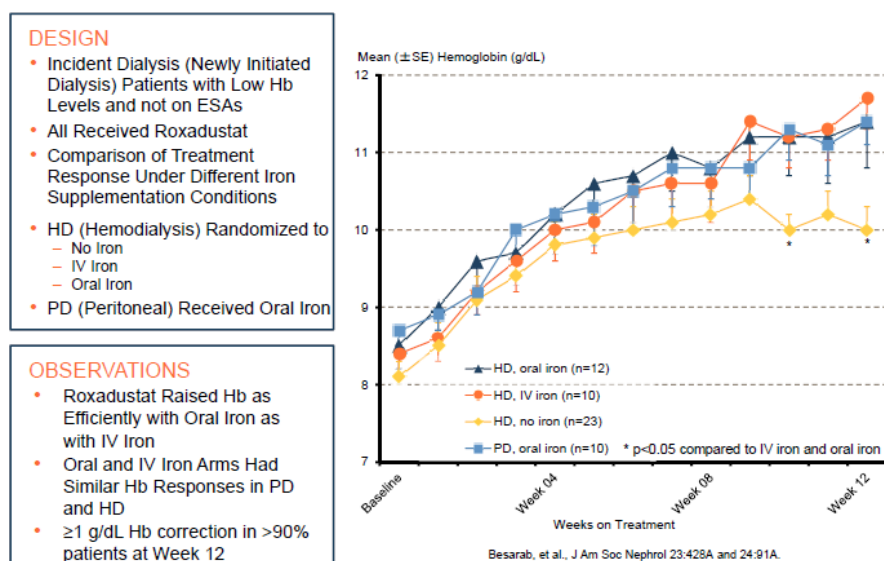
Roxadustat has been evaluated in a broad range of CKD patients, including patients on stable dialysis, incident dialysis, pre-dialysis patients, and ESA hypo-responders in various Phase 2 studies. In these studies, roxadustat achieved consistent dose-dependent hemoglobin (Hb) response and maintained Hb levels (Figure 2), reduced hepcidin levels, and thereby improving iron transport, and did NOT elevate endogenous erythropoietin above normal levels.

**Figure 2: Roxadustat - Demonstrated Ability to Achieve and Maintain Hb Levels**



FibroGen's Phase 2 studies also demonstrated roxadustat's ability to achieve hemoglobin (Hb) levels in combination with orally administered iron supplements that were comparable to levels achieved in combination with IV-administered iron (Figure 3). This is key, in our view, as it would offer clinicians *an all-oral regimen* for treating anemia that would address both the dialysis and the non dialysis CKD patient populations, if roxadustat receives regulatory clearance.

**Figure 3: Roxadustat - Raises Hb as Efficiently with Oral Iron as with IV Iron**



### Roxadustat: Carcinogenicity and Data Safety Monitoring Board Summary

Two separate two-year carcinogenicity safety studies of roxadustat have been completed, with no adverse findings. In July, the roxadustat safety monitoring board (DSMB) completed its review of data from Phase 3 programs, recommending that the studies proceed with any change in protocol. Thus far roxadustat has completed three DSMB reviews without any change in clinical protocol.



***HOWEVER - The HIF System Is Complex and Is Not Limited to the Erythropoiesis Process, Giving Rise to Our Concerns Regarding Safety Risk***

While there is optimism that the HIF-PHI pathway represents a potentially pioneering all-oral regimen for treating anemia with a superior safety profile relative to ESAs, the HIF pathway is highly complex. In low oxygen conditions there may be up to a 100-fold induction of EPO mRNA and proteins that induce erythropoiesis and iron transport. The HIF system has been associated with gene expression directly or indirectly in over 100 genes. The HIF pathway is a critical regulator of numerous systemic responses to hypoxia and is active in most mammalian cells.

The HIF system operates in many cell types and is not limited to erythropoiesis, with activity shown in genes encoding glycolytic and lactate dehydrogenase enzymes, along with glucose transporters and multiple enzymes associated and responsible for shifting metabolism to anaerobic glycolysis in hypoxic conditions. Simply put, many genes that are induced by HIF-1a have been cited as being expressed at higher levels in cancer cells than in normal tissue including genes that promote glucose uptake, lactate production, while decreasing cell respiration.

Source: Cell Death and Differentiation (2008) 15, 621-627; A Weidemann and R S Johnson

***The HIF System is Complex with Advantages Possibly Offset by Safety Risk***

The potential advantages of HIF-PHIs for the treatment of anemia could prove to be offset by safety risks that have yet to be elucidated. Clearly, Phase 2 data support the large-scale Phase 3 study of roxadustat in treating CKD-associated anemia; however, the complexity and breadth of the HIF system's activity, beyond erythropoiesis and iron transport, may give rise to unanticipated adverse events in Phase 3 trials and beyond.

Source: Cell Death and Differentiation (2008) 15, 621-627; A Weidemann and R S Johnson

**Partnerships with AstraZeneca and Astellas Pharma**

In 2013 FibroGen entered into an agreement with AstraZeneca that provided the latter with development and commercial rights of roxadustat for the treatment of anemia associated with CKD in all major markets except those covered by an existing agreement with Astellas. In 2006, FibroGen entered into a licensing agreement with Astellas Pharma, that provided Astellas with development and marketing rights to roxadustat for the treatment of anemia in Japan, the E.U., the Commonwealth of Independent States (CIS), Middle East, and South Africa.

Under the terms of these agreements, FibroGen receives upfront non-contingent, development, regulatory, and commercial milestone payments, that could total up to \$2.5 billion. Thus far, FibroGen has received over \$800 million from its partners. The Company also received equity investment from its partners, totaling \$101 million. Furthermore, upon commercialization FibroGen will receive sales royalties from its partners as described below (Figure 4).

FibroGen and AstraZeneca have also entered into a 50/50 partnership relating to the development and commercialization of roxadustat in China. Under the terms of this agreement, FibroGen will share equally with AstraZeneca all development, regulatory, marketing and related expenses, along with profits, associated with commercialization in China.

AstraZeneca will pay sales royalties to FibroGen in the low-to-mid 20%'s of net sales to transfer price upon the commercialization of roxadustat in the U.S. and RoW markets (excluding China and markets covered by the licensing agreement with Astellas.) This partnership also includes a development cost cap of \$116.5 million, after which AstraZeneca will fully fund development. FibroGen anticipates to

achieve the cap in Q4 2015, with \$33.1 million remaining as of June 30, 2015. Astellas Pharma will pay sales royalties in the low 20% of net sales to transfer price for sales in Japan, the E.U., the CIS, Middle East, and South Africa.

**Figure 4: Roxadustat - Summary of Agreements with AstraZeneca and Astellas**

		Astellas	AstraZeneca	Cash Received To
	\$ Millions	Japan, EU, ETC.	U.S., CHINA, ROW	Date
Payments To FibroGen	Equity Investment In Fibrogen	\$81	\$20	\$101
	Upfront, Non-Contingent	\$360	\$402	\$360 + \$220
	Development & Regulatory Milestones	\$543	\$571	\$223
	Commercial Milestones	\$15	\$653	\$0
	Potential Total Payments	\$999	\$1,646	\$803 of \$2,544
Royalty Rates	Low 20% (Astellas); Low-Mid 20% (AstraZeneca) Net Sales Royalty / Transfer Price			
Development Funding	Fibrogen Ex-China Costs Capped at \$116.5 Million. (Cost Share <50% of Planned CKD Anemia Development Costs)			
Launch Funding	Commercialization Costs Covered by Partners in All Territories Ex-China FibroGen + AstraZeneca 50/50 Partnership in China			

Source: Company Reports and LSCM Estimates

### Roxadustat: Global Phase 3 Clinical Programs

FibroGen has multiple Phase 3 global clinical trials in progress, targeting total enrollment of 7,300 subjects with anemia associated with CKD in both the dialysis and pre-dialysis CKD patient populations (Figure 5). Enrollment is ongoing and progressing smoothly. Of these trials, three are being conducted by FibroGen comprising 2,100 subjects. FibroGen expects to achieve full enrollment in its three programs, which evaluate roxadustat in non dialysis CKD, incident-dialysis CKD, and stable dialysis CKD, by March/April 2016.

**Figure 5: Roxadustat - Global Phase 3 Programs**

STUDY NUMBER	COMPARATOR	RANDOM-IZATION	N	STUDY LOCATIONS	CHINA	EUROPE	US	STUDY SPONSOR
PHASE 3 STUDIES TO SUPPORT REGULATORY APPROVAL								
<b>Stable Dialysis</b>								
CL-613 <sup>1</sup>	Epoetin α/Darbe	376/200/174	750	EU, MEA <sup>3</sup>		36+ wks	52+ wks	Astellas
FG-064 <sup>1</sup>	Epoetin α	1:1	Up to 750	US+/-Global		36+ wks	52+ wks	FibroGen
FG-806	Epoetin α	2:1	300	China	26-52 wks			FibroGen
<b>Incident Dialysis</b>								
FG-063 <sup>1</sup>	Epoetin α	1:1	Up to 750	Global		36+ wks	52+ wks	FibroGen
<b>Incident and Stable Dialysis</b>								
AZ-002	Epoetin α	1:1	1425	Global			52+ wks	AstraZeneca
<b>Non-Dialysis</b>								
FG-060*	Placebo	2:1	Up to 600	US, LA <sup>2</sup> , APAC <sup>3</sup>		36+ wks	52+ wks	FibroGen
CL-0608*	Placebo	2:1	450-600	EU, MEA <sup>4</sup>		36+ wks	52+ wks	Astellas
FG-808	Placebo	2:1	150	China	26-52 wks			FibroGen
AZ-001	Placebo	1:1	~2,600	Global			52+ wks	AstraZeneca
<b>EUROPEAN REIMBURSEMENT STUDY</b>								
CL-0610	Darbepoetin	2:1	570	EU, MEA		36+ wks	N/A	Astellas

<sup>1</sup> Plan to support US regulatory approval with 7 studies (4 DD and 3 NDD); 5 of which (3DD and 2 NDD, highlighted) will also be used in the European package that contains a total of 8 studies (3 DD and 3 NDD)

<sup>2</sup> LA - Latin America; <sup>3</sup> APAC - Asia-Pacific; <sup>4</sup> MEA - Middle East & Africa

Source: Company Reports

**Study '060 /ANDES (Non Dialysis Population):** ANDES is a multicenter, randomized, double-blind, placebo-controlled study of the safety and efficacy of roxadustat for the treatment of anemia in CKD patients not on dialysis. A total of up to 600



subjects will be randomized, 2:1, to receive either roxadustat (apx. 400 subjects, weight-based oral dosing of 70mg or 100mg, three times a week (TIW)) or placebo (apx. 200 subjects, TIW) in a double-blind methodology. Enrollment for ANDES will include the U.S., Latin America, and the Asia-Pacific region. The primary endpoint of ANDES is the efficacy of roxadustat in achieving Hb correction and maintenance over 52 weeks. Secondary endpoints include: (i) effect on patients' outcomes reports; (ii) change in serum lipid levels; (iii) effect on blood pressure; (iv) occurrence of rescue therapy (i.e., IV-administered iron therapy, blood transfusion, etc.), and others endpoints.

**Study '063 /HIMALAYAS (Incident-Dependent Population):** HIMALAYAS is a global, multicenter, open-label, randomized, active-controlled study of the safety and efficacy of roxadustat in the treatment of anemia in incident-dialysis patients, compared to epoetin alfa. A total of up to 750 subjects will be randomized, 1:1, to receive either roxadustat (apx. 375 subjects, orally dosed, TIW) or epoetin alfa (apx. 375 subjects, dosed per the package insert). The minimum treatment period for the study is 52 weeks, up to a maximum of three years after the last patient is randomized. The primary endpoint of HIMALAYAS is the mean change in Hb levels from baseline at week from week 28 to week 52. Secondary endpoints include: (i) proportion of patients achieving Hb response during the first 24 weeks; (ii) average use of IV-administered iron therapy; (iii) change in LDL level; (iv) effect on blood pressure, and other endpoints.

**Study '064 /SIERRAS (Stable Dialysis Population):** Study '064 (SIERRAS) is a global, multicenter, open-label, randomized, active-controlled study of the efficacy of roxadustat in the maintenance of anemia in patients with CKD on stable dialysis, compared to epoetin alfa. A total of up to 750 subjects will be randomized, 1:1, to receive either roxadustat (apx. 375 subjects, orally dosed, TIW) or epoetin alfa (apx. 375 subjects, IV-administered, TIW). The primary endpoint of SIERRAS is defined as each subject's (Hb) change from baseline to the average Hb level achieved during the evaluation periods of week 28 to week 52. Secondary endpoints include: (i) average use of IV-administered iron therapy; (ii) change in serum lipid levels; (iii) effect on blood pressure, and other endpoints.

### ASTRAZENECA SPONSORED PHASE 3 PROGRAMS

**AZ-001 (Non Dialysis Population):** Study AZ-001 is a global, multicenter, randomized, double-blind, placebo-controlled study that evaluates the safety and efficacy of roxadustat for the treatment of anemia in CKD patients not on dialysis. A total of up to 2,600 subjects will be randomized, 1:1, to receive either roxadustat (apx. 1,300 subjects, orally dosed, TIW) or placebo (apx. 1,300 subjects, orally dosed, TIW). The primary endpoint of Study AZ-001 is major adverse cardiovascular events (MACE). Secondary endpoints include: (i) mean change in Hb from baseline to end of treatment; (ii) timing and incident of rescue therapy; (iii) change in estimated glomerular filtration rates (eGFR); (iv) change in anemia symptoms; (v) adverse events; and other endpoints.

**AZ-002 (Stable Dialysis Population):** Study AZ-002 is a global, multicenter, randomized, open-label, active-controlled study of the safety and efficacy of roxadustat in the treatment of anemia in CKD patients on dialysis, compared to epoetin alfa. A total of up to 1,425 subjects will be randomized, 1:1, to receive either roxadustat (orally dosed, three times weekly (TIW)) or epoetin alfa (IV or subcutaneous injection, TIW). The primary endpoint of Study AZ-002 is major adverse cardiovascular events (MACE). Secondary endpoints include: (i) mean change of Hb from baseline; (ii) timing and incidence of rescue therapy; (iii) changes in self-reported health status; (iv) adverse events, and other endpoints.

### PHASE 3 PROGRAMS IN CHINA

FibroGen is developing roxadustat in China with AstraZeneca in a 50/50% partnership. The Company expects to initiate enrollment in two Phase 3 clinical programs during Q4 2015, studying roxadustat in both non dialysis and stable dialysis patient populations. FibroGen anticipates regulatory submission of roxadustat in China in 2016.

### ASTELLAS PHARMA SPONSORED PHASE 3 PROGRAMS

**CL-0608 /ALPS (Non Dialysis Population):** ALPS is a multicenter, randomized, double-blind, placebo-controlled, study and efficacy of roxadustat for the treatment of anemia in CKD patients not on dialysis. A total of up to 600 subjects will be recruited in the U.S., E.U., Middle East, and Africa, randomized, 1:1, to receive roxadustat (orally dosed, TIW) or placebo (orally dosed, TIW) for a treatment period of 52 to 104 weeks. The primary endpoint of ALPS is Hb response to roxadustat versus placebo. Secondary endpoints include: (i) maintenance of Hb levels; (ii) changes in LDL-C; (iii) blood pressure changes; (iv) incidence of rescue therapy, and other endpoints.

**CL-613 /Pyrenees (Stable Dialysis):** Pyrenees is a randomized, open-label, active-controlled study evaluating the safety and efficacy of roxadustat in the maintenance of treatment of anemia in patients with CKD on stable dialysis, compared to epoetin alfa/darbepoetin alfa. A total of up to 750 subjects will be randomized, to receive roxadustat (apx. 376 subjects, orally dosed), epoetin alfa (apx. 200 subjects, IV or subcutaneous dosed) or darbepoetin alfa (apx. 174 subjects, IV or subcutaneous dosed) for 104 weeks. Pyrenees' primary endpoint is Hb change from baseline to the average Hb of weeks 28 to 36 without rescue therapy. Secondary endpoints include: (i) Hb response without rescue therapy; (ii) change in LDL-C from baseline; (iii) mean monthly IV-administered iron use; (iv) blood pressure effect, and other endpoints.

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## FG-3019 –POTENTIAL BLOCKBUSTER FOR FIBROTIC DISEASES

### FG-3019 - Addresses Multiple Fibrotic Diseases

#### Currently in Phase 2 for Idiopathic Pulmonary Fibrosis (IPF) and Pancreatic Cancer

FG-3019 represents a potential breakthrough therapy, addressing various fibrotic diseases and disorders. FG-3019 is a monoclonal antibody therapy that inhibits connective tissue growth factor. FG-3019 has demonstrated its potential to reverse and suppress the progression of fibrosis in Phase 2a studies involving patients with idiopathic pulmonary fibrosis (IPF). FG-3019 has also demonstrated its potential ability to improve survival in patients with locally advanced and metastatic pancreatic ductal adenocarcinoma in a Phase 2 dose-escalation study.

FG-3019 is a fully humanized monoclonal antibody that inhibits the activity of connective tissue growth factor (CTGF). Elevation of CTGF is common in chronic fibrotic and tissue proliferation disorders that promotes excessive scarring, often leading to organ failure. FG-3019 is currently in Phase 2 clinical studies for the treatment of idiopathic pulmonary fibrosis (IPF) and pancreatic cancer. The Company was recently cleared by the FDA to begin Phase 2 clinical studies of FG-3019 for Duchenne muscular dystrophy (DMD) - a rare and fatal genetic disease that afflicts approximately 1 in every 3,500 newborn males. FibroGen will also continue to evaluate FG-3019 for the treatment of other fibrotic based diseases and disorders.

**FG-3019: A Potential Breakthrough for Treating Idiopathic Pulmonary Fibrosis**

Idiopathic pulmonary fibrosis (IPF) is a progressive, chronic, and fatal disease, characterized by a declining lung function caused by thickening of the interstitium - the interstitial space between the alveoli and the bloodstream. IPF afflicts over 125,000 people in the U.S., with new cases and deaths per year at approximately 45,000 and 40,000, respectively.

FG-3019 is a promising breakthrough therapy for the treatment of IPF. At the American Thoracic Society conference held in May 2014, FibroGen released supporting efficacy and safety data involving the first cohort of its Phase 2a clinical trial of subjects who received 48 weeks of FG-3019 therapy, along with patients in the first cohort that continued therapy for two years. After 48 weeks, 36% (12 of 33) of subjects who received FG-3019 witnessed improved fibrosis as measured by high resolution computed tomography (HRCT), with an additional 2 subjects demonstrating stable fibrosis, equating to 42% (14 of 33) witnessing improved or stabilized fibrosis in the first cohort. Change in forced vital capacity (FVC) also correlated with changes in fibrosis at 48 weeks. FG-3019 was well tolerated, with no severe adverse event attributed to administration of FG-3019. The study demonstrated reversal of lung fibrosis and improved lung function (Figure 6), making it the first human trial to demonstrate reversal of fibrosis.

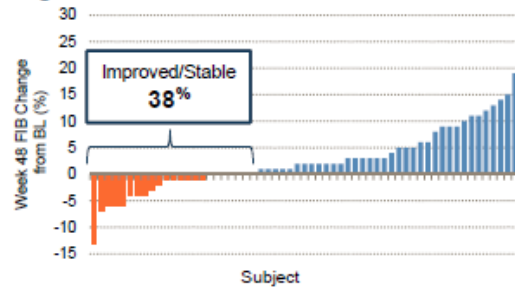
At the 18<sup>th</sup> International Colloquium of Lung and Airway Fibrosis (ICLAF) conference held in September 2014, FibroGen released the full data set from its clinical study of patients with idiopathic pulmonary fibrosis treated with FG-3019 for 48 weeks. This study supported the safety and efficacy of FG-3019. This was an open-label, dose-escalation study that evaluated safety and efficacy of FG-3019 administered at doses of 15 mg/kg (Cohort 1 and Cohort 1-EX) and 30 mg/kg (Cohort 2 and Cohort 2-EX) every three weeks for 45 weeks, and every three weeks thereafter. 74 subjects completed 24 weeks, and 66 subjects completed 48 weeks of treatment. Assessment of fibrosis was measured by HRCT.

After 24 weeks of treatment 23% (17 of 74) of subjects who received FG-3019 witnessed improved fibrosis as measured by HRCT. After 48 weeks improved fibrosis was witnessed by 24% (16 of 66) of subjects receiving FG-3019 treatment. Changes in fibrosis also correlated with improvements in forced vital capacity (FVC). Subjects with stable or improved fibrosis had improved pulmonary function as measured by FVC. FG-3019 was well tolerated in treated patients, with adverse events observed consistent with that seen in the general IPF patient population. The study's results are quite encouraging, in our view, as no therapy has demonstrated reversal of fibrosis in human trials.

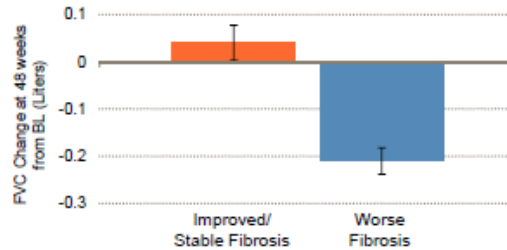
**Figure 6: Reversal of Lung Fibrosis in Phase 2A IPF Study**

**Phase 2A IPF Clinical Trial**

**Reversal of Lung Fibrosis by  
High Resolution CT at Week 48**



**Improved / Stable Fibrosis Correlates  
with Improved Lung Function**



Source: Company Reports

**FG-3109: Phase 2 Idiopathic Pulmonary Fibrosis Study '067**

FibroGen is conducting a randomized, placebo-controlled, Phase 2 trial evaluating FG-3019 in slowing progression lung function loss in subjects with IPF over 48 weeks.

**FG-3019 - Phase 2 - Study '067** is a multi-center, double-blind, randomized, placebo-controlled study that evaluates the safety and efficacy of FG-3019. The primary endpoint of this study is to evaluate FG-3019 in slowing the progression of FVC loss. Secondary endpoints include: (i) change in pulmonary fibrosis score at week 24, Week 48, and thereafter. The Company is currently enrolling patients in the U.S., Canada, South Africa, and plans to open additional sites in Eastern Europe, India, Australia, and New Zealand this year.

FibroGen is also exploring the possibility of expansion of this study wherein it may add a group of subjects receiving approved therapies such as Ofev™ and/or Esbriet®. Since FG-3019's activity is through CTGF inhibition and as existing therapies work through different pathways, there is optimism that efficacy of combining therapies would be additive.

**FG-3019: Pancreatic Cancer**

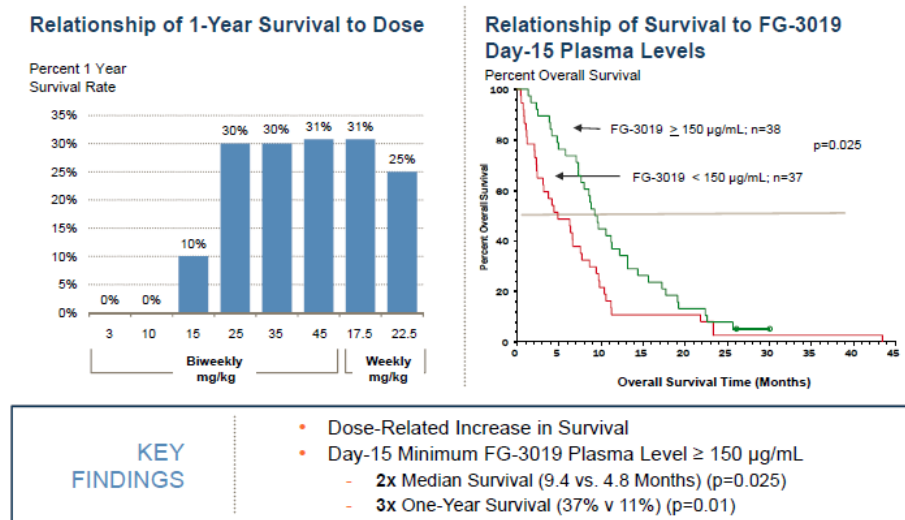
Recent clinical data from a Phase 2 open-label, single-arm, dose-escalation study demonstrated improvements in survival using FG-3019 in combination with gemcitabine and erlotinib (Tarceva®) versus the gemcitabine plus erlotinib regimen (Figure 7).

The study showed a dose-related improvement in survival, identifying a FG-3019 blood levels of 150 micrograms/mL (Cmin) or higher being necessary to achieve sufficient blockage of CTGF to improve survival in subjects with advanced pancreatic cancer. For subjects at or above the Cmin, median survival was 9.4 months versus 4.8 months for those below the Cmin threshold. The best results were shown in patients with the highest level of FG-3109 blood plasma concentrations, accompanied by the lowest baseline CTGF blood plasma levels, with median survival being 11.2 months, and 45% of subjects surviving over 1 year. At the lowest dose of FG-3019 no patients survived for one year, while at the highest doses approximately 30% of patients survived for one year. We note that the median survival of the pivotal gemcitabine plus erlotinib clinical trial was 6.2 months.

FibroGen continues to enroll patients in its ongoing open label Phase 2 program, targeting enrollment of 40 subjects. This study will evaluate the safety and efficacy of FG-3019 in combination with gemcitabine and nab-paclitaxel versus the chemotherapy regimen alone, with the goal of showing the potential for conversion of non-operable patients to operable status. Management will review the preliminary data, including biopsies, to determine if trial expansion is warranted.

**Figure 7: Dose-Dependent Survival In Advance Pancreatic Cancer**

**FG-3019 Combined with Gemcitabine and Erlotinib (n=75)**



Source: Company Reports

### Phase 2 - Study '069

Study '069 is a multi-center, open label, randomized study that is evaluating gemcitabine and nab-paclitaxel with and without FG-3019 in the treatment of advanced unresectable pancreatic cancer, targeting enrollment of 40 subjects. The primary outcome of Study '069 is safety through 28 days following last dose, assessment of treatment-emergent adverse events and discontinuation due to adverse events. Secondary endpoints include: (i) the proportion of subjects that achieve RO resection; (ii) surgical safety with respect to complications; (iii) tumor response rates; and (iv) overall survival rates. We anticipate interim data to be presented at the American Society of Clinical Oncology Gastrointestinal (ASCO GI) symposium in January 2016.

**FG-3019: Duchenne Muscular Dystrophy (DMD)**

Recently, the FDA completed the review of FG-3019 IND for the treatment of DMD, allowing clinical trials in humans to proceed. The Company plans to initiate a multi-site Phase 2 program of FG-3019 of DMD in non-ambulatory patients, beginning in the Q4 2015. The rationale for FG-3019 use as a therapeutic for DMD is based upon data that demonstrate elevated CTGF suppresses the ability for muscles to regenerate along with promoting fibrosis.

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**MANAGEMENT**

**Thomas B. Neff, CEO** – Mr. Neff founded FibroGen, Inc. in 1993, and serves as its Chairman and Chief Executive Officer. Prior to FibroGen, Mr. Neff founded Pharmaceutical Partners I and Pharmaceutical Partners II - the predecessor to Royalty Pharma – which invested in drug royalties. Mr. Neff was also the founder and a general partner of Three Arch Bay Health Science Fund, a privately held investment vehicle that invested in emerging biomedical and related companies. Mr. Neff also has significant investment banking experience, including holding senior level positions with Lazard Freres & Company, and Paine Webber Incorporated. He serves as a director on the board of Kolltan Pharmaceuticals, which was spun out of Yale University. Mr. Neff received a Bachelor of Arts degree from Claremont McKenna College with concentrations in molecular biology and government studies. Mr. Neff studied economics and finance at the University of Chicago Graduate School of Business, and was a Fellow of the Thomas J. Watson Foundation.

**Pat Cotroneo, CFO** – Mr. Cotroneo is FibroGen's Chief Financial Officer and has held this role since 2008. He joined the Company in 2000 in the role of Controller. Prior to this, Mr. Cotroneo served as Controller at both SyStemix, Inc., and Genetic Therapy, Inc. (Novartis subsidiaries) from 1993 to 2000. He has public accounting experience with Deloitte & Touche, and received a Bachelors in Science degree from the University of San Francisco.

**Frank H. Valone, M.D., Chief Medical Officer** – Mr. Valone serves as FibroGen's Chief Medical Officer, having held this role since 2008. Dr. Valone has over 15 years of expertise in the biotechnology industry in leadership roles overseeing preclinical and clinical development, medical and regulatory affairs governance, and quality assurance and quality controls programs. Prior to this, Dr. Valone served as Senior Vice President of Medical Affairs of Bayhill Therapeutics, where he was responsible for clinical, regulatory, development, toxicology and safety, and related affairs, from 2003 to 2008. Dr. Valone's industry experience also includes serving as Executive Vice President of Clinical Development and Regulatory Affairs of Titan Pharmaceuticals Inc. (2002 – 2003), and Chief Medical Officer and Senior Vice President of Clinical and Regulatory Affairs of Dendreon Corporation (1994 to 2002). Dr. Valone served as Clinical Associate Professor, Department of Medicine, at Stanford University from 1995 to 2001. From 1991 through 1996 Dr. Valone held various roles at the Dartmouth-Hitchcock Medical Center – including Adjunct Professor of Medicine, and Norris Cotton Cancer Center – including Professor of Medicine. From 1982 to 1991, Dr. Valone held various roles at the University of California, San Francisco and the San Francisco VA Medical Center, including Associate and Chief of Hematology and Oncology, respectively. Dr. Valone has a Bachelor of Arts degree from Hamilton College, and received an M.D. from Harvard Medical School. His post-doctoral training was completed at Brigham and Womens Hospital in Internal Medicine/Allergy and Rheumatology and at Dana-Farber Cancer Institute in Medical Oncology.



**K. Peony Yu, M.D., Vice President of Clinical Development** – Dr. Yu serves as the Company's Vice President of Clinical Development, having held this role since 2008. Prior to this, Dr. Yu was Vice President of Clinical Research at Anesiva, Inc., where she was responsible for management of clinical research, clinical operations, medical affairs, and statistics and data management for all clinical programs, including the development and approval of Zingo – a drug-device combination for pain management. Prior to Anesiva, Dr. Yu was Director, Clinical Development, at ALZA Corporation – a division of Johnson & Johnson. Dr. Yu has been directly involved several successful NDA submissions with the FDA, along with the European regulatory authorities. Prior to ALZA, Dr. Yu held key clinical development roles at Pain Therapeutics, Inc., and Elan Pharmaceuticals. Dr. Yu received both an M.D. and Bachelors of Science degree from University of California, Davis, and completed residency training at Stanford Medical School.

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## RISKS

An investment in FibroGen, Inc., involves risk.

- **Clinical and Regulatory Hurdles** – The Company's success is predicated upon its ability to advance its lead compounds through human clinical trials that demonstrate safety and efficacy such that the Company attains the necessary marketing clearances from regulating agencies in multiple jurisdictions.
- **Reimbursement and Payor Risk** – The Company must garner funding from various entitlement programs, insurance carriers, private payors, and other funding sources.
- **Safety Risk** – Any safety risks associated with any of its products that arise at any time represent a risk to performance.
- **Sales, Marketing, and Distribution** – Impairment of the Company's or its license partners' ability to sell, market, or distribute its products represent risk to performance.
- **Manufacturing and Supply Chain** – Impairment of the Company's or its license partners to procure or produce compliant finished products represent a risk to performance.
- **Competition, Generics and Biosimilars, and Pricing** – Competition from existing therapies, generics, biosimilars, and/or low adoption of its branded products represent a risk to performance. The Company's success is predicated on broad commercial acceptance of its products.
- **Future Capital Needs** – The Company may need to raise capital to support development and commercialization of its products; its ability to raise sufficient funding represents a risk.
- **Intellectual Property** – The Company's success also depends on its ability to enforce its intellectual property. Litigation and defense expenses associated with enforcing its intellectual property also represent a risk to the Company's performance.

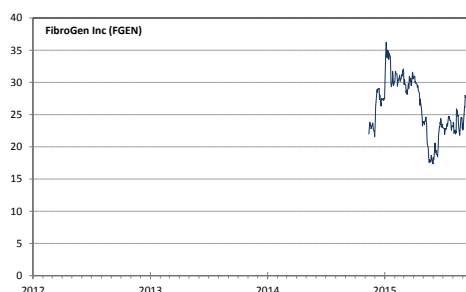
## FINANCIAL MODEL

### FibroGen, Inc.

(# in \$1,000s, except per share data)

	<u>Q1 2015A</u>	<u>Q2 2015A</u>	<u>Q3 2015E</u>	<u>Q4 2015E</u>	<u>FY 2014A</u>	<u>FY 2015E</u>	<u>FY 2016E</u>	<u>FY 2017E</u>	<u>FY 2018E</u>	<u>FY 2019E</u>	<u>FY 2020E</u>
License, Milestone Revenue	11,506	106,879	7,500	60,000	117,191	185,885	120,000	175,000	150,000	150,000	200,000
Collaboration and Other	4,792	13,671	10,000	10,000	20,410	38,463	35,000	35,000	35,000	30,000	30,000
Royalty Revenue	-	-	-	-	-	-	-	-	-	35,000	100,000
Sales Revenue, Roxadustat (China), FG-3019	-	-	-	-	-	-	-	-	2,500	50,000	125,000
Total Revenue	16,298	120,550	17,500	70,000	137,601	224,348	155,000	210,000	187,500	265,000	455,000
Cost of Goods Sold									500	10,000	18,750
Research & Development Exp.	50,539	51,555	53,250	25,000	150,794	180,344	135,000	150,000	185,000	220,000	255,000
General & Administrative Exp.	10,482	9,680	10,250	11,000	36,909	41,412	85,000	125,000	150,000	185,000	215,000
Total Operating Expense	61,021	61,235	63,500	36,000	187,703	221,756	220,000	275,000	335,000	405,000	470,000
Income from Operation (Loss)	(44,723)	59,315	(46,000)	34,000	(50,102)	2,592	(65,000)	(65,000)	(147,500)	(140,000)	(15,000)
Interest Expense	(2,758)	(2,762)	(2,750)	(2,750)	(11,108)	(11,020)	(12,500)	(12,500)	(12,500)	(12,500)	(12,500)
Interest and Other Income, Net	843	707	925	800	1,706	3,275	2,250	2,000	1,500	1,000	1,000
Income before Tax (Loss)	(46,638)	57,260	(47,825)	32,050	(59,504)	(5,153)	(75,250)	(75,500)	(158,500)	(151,500)	(26,500)
Income Tax Benefit, (Tax)	271	(205)	265	(150)		181	-	-	-	-	-
Net Income	(46,367)	57,055	(47,560)	31,900	(59,504)	(5,334)	(75,250)	(75,500)	(158,500)	(151,500)	(26,500)
<b>EPS</b>	<b>\$ (0.78)</b>	<b>\$ 0.83</b>	<b>\$ (0.69)</b>	<b>\$ 0.45</b>	<b>\$ (3.17)</b>	<b>\$ (0.08)</b>	<b>\$ (1.04)</b>	<b>\$ (1.01)</b>	<b>\$ (2.07)</b>	<b>\$ (1.93)</b>	<b>\$ (0.33)</b>
Average Shares Outstanding	59,197	68,752	69,250	71,000	18,775	67,050	72,500	74,500	76,500	78,500	80,500
<b>Royalty Revenue</b>	<u>Q1 2015A</u>	<u>Q2 2015A</u>	<u>Q3 2015E</u>	<u>Q4 2015E</u>	<u>FY 2014A</u>	<u>FY 2015E</u>	<u>FY 2016E</u>	<u>FY 2017E</u>	<u>FY 2018E</u>	<u>FY 2019E</u>	<u>FY 2020E</u>
Roxadustat (AZN, ex-China and Astellas licensing)	-	-	-	-	-	-	-	-	-	25,000	75,000
Roxadustat (Astellas)	-	-	-	-	-	-	-	-	-	10,000	25,000
Total Royalties	-	-	-	-	-	-	-	-	-	35,000	100,000
Roxadustat, China Sales									2,500	25,000	75,000
FG-3019 Sales									-	25,000	50,000
TTL Sales									2,500	50,000	125,000

## IMPORTANT DISCLOSURES



Initiate: September 23, 2015 – Rating: HOLD - Price Target: \$25

Source: Thomson ONE

## RATINGS DEFINITION

**BUY** rated stocks are expected to generate greater than 10% returns during the next 12 months. **HOLD** rated stocks are expected to generate returns of 0% to 10% during the next 12 months. **SELL** rated stocks are expected to generate negative returns over the next 12 months and generally do not have a price target.

Information on our valuation methodology and risks can be found in the “Investment Thesis & Valuation” and “Risks” sections above.

## RATINGS DISTRIBUTION

(as of September 21, 2015)

Rating	All Covered Companies (%)	Investment Banking Clients (%)
BUY	86.8%	8.9%
HOLD	13.2%	0.0%
SELL	0.0%	0.0%

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