Galapagos NV (GLPG NA)

Biotechnology

BERENBERG CAPITAL MARKETS

Pipeline is firing on all cylinders; PT up to €200

- **We are raising our price target to €200 (€140) and reiterating our Buy rating.** The Galapagos story continues its favorable trajectory. With the expanded Gilead collaboration providing $5.05bn of fresh funding for Galapagos to continue to execute on its high quality pipeline, we believe long-term value creation is likely to be driven by: 1) filgotinib, a selective JAK-1 inhibitor for in Phase II/III development for rheumatoid arthritis (RA), inflammatory bowel disease (IBD) (including Crohn's disease, CD, and ulcerative colitis, UC), and spondyloarthritis (SpA) (including ankylosing spondylitis (AS) and psoriatic arthritis, PsA); 2) GLPG1690, an autotaxin (ATX) inhibitor in Phase III development for idiopathic pulmonary fibrosis (IPF) (ISABELA program); and 3) GLPG1972, an ADAMTS-5 inhibitor in Phase II development for osteoarthritis (OA).
- **GLPG1690 the front runner among late stage, next generation IPF drugs.** We believe the recent halting of Biogen's BG00011 (STX-100) Phase IIb study places Galapagos in a race with FibroGen's pamrevlumab, which recently began enrolling its Phase III study (ZEPHYRUS). Key opinion leader (KOL) diligence points to high enthusiasm for GLPG1690; the Phase III design is favorable; the dosing, a once daily pill, is preferred to both standard of care, which are dosed multiple times per day, and pamrev, which is dosed as an intravenous infusion. We raise our peak sales estimate from $1.5bn to $2.0bn owing to favorable competitive dynamics. We also raise our probability of success assumption to 60% (from 50%) following Gilead's review of blinded safety data in ISABELA, which was part of its diligence for the expanded collaboration. Refer to pages 10-30 for our deep-dive analysis, including KOL viewpoints.
- **Filgotinib, if approved, may be viewed as the safest JAK on the market.** The European Medicines Agency (EMA) is currently reviewing the filgo filing in RA; the FDA is allowing a submission for RA in the U.S. prior to the full data release from MANTA (testicular tox study), which eliminates a key hurdle regarding the ability to file in the U.S. Meanwhile, Rinvoq, AbbVie's JAKi, recently became the third JAKi approved in RA by the FDA with a black box warning that includes blood clot language, which did not surprise us; however, the language is broad and could, we believe, indicate a class effect. If the FDA interprets filgo's data more favorably, this could be an area where filgo could separate; as it is, we think the Street expects a black box similar to the other JAKs for filgo. Another area of differentiation is dosing; if filgo is approved at a low and high dose, 100 mg and 200 mg, it could become the first and only JAKi for RA on the U.S. market with two approved doses. In all indications, we model peak un-risk adjusted sales of around $5bn; risk-adjusted our peak sales estimate is $3.6bn.
- **Model update and valuation.** We update our model for the expansion of the Gilead collaboration, for our increased confidence in Galapagos' pipeline, and our expectation of long-term value creation driven by continued execution. Our valuation is based on our SOTP and DCF. A key risk to our Buy thesis is the outcome of clinical data readouts.

Y/E 12/31, EURm	2017	2018	2019E	2020E	2021E
Sales	156	318	3,791	262	324
EBITDA	-86	-40	3,342	-275	-243
EBIT	-90	-45	3,331	-287	-256
Net profit	-116	-29	3,334	-284	-253
Y/E net debt (net cash)	-1,151	-1,291	-5,396	-5,138	-4,912
EPS (reported)	-2.34	-0.56	56.98	-4.48	-3.93
EPS (recurring)	-2.34	-0.56	56.98	-4.48	-3.93
CPS	23.27	24.77	92.24	81.05	76.28

Source: Company data, BCM estimates

September 10, 2019

BUY

Current price	Price target
EUR143.70	EUR200.00

09/09/2019 Amsterdam Close

Market cap (EURm)	8,407
Reuters	GLPG.AS
Bloomberg	GLPG NA

Changes made in this note

Rating:	Buy (no change)
Price target:	EUR200.00 (140.00)

Estimates changes

	2019E		2020E		2021E	
	old	Δ %	old	Δ %	old	Δ %
Sales	171	2121.0	261	0.5	330	-1.7
EBIT	-252	1420.0	-245	-17.0	-235	-9.1
EPS	-4.48	1372.0	-4.24	-5.7	-3.98	1.3

Source: BCM estimates

Share data

Shares outstanding (m)	59
Enterprise value (EURm)	3,011
Daily trading volume	60,269

Key data

Price/book value	1.5
Net debt/equity	-97.2%
CAGR sales 2019-2021	-70.7%
CAGR EPS 2019-2021	n.m.

Source: Thomson Reuters Datastream

See pages 44-46 for analyst certifications and important disclosures

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Biotechnology

BUY

September 10, 2019

Current price	Price target
EUR143.70	EUR200.00

09/09/2019 Amsterdam Close

Reuters	GLPG.AS
Bloomberg	GLPG NA
Market cap (EURm)	8,407
EV (EURm)	3,011
Trading volume	60,269
Free float	74.4%

Non-institutional shareholders

Gilead - 12.4%
Van Herk Investments - 9.9%

Business description

Galapagos is a biopharmaceutical company specializing in the discovery and development of small molecule medicines.

Share performance

High 52 weeks	EUR168.85
Low 52 weeks	EUR75.60

Performance relative to

	S&P 500	AEX
1mth	-10.7%	-13.4%
3mth	30.6%	31.1%
12mth	66.9%	65.1%

Investment thesis

- Filgotinib, a JAK1 inhibitor partnered with Gilead, has so far shown best-in-class safety and tolerability, and we estimate has the potential to deliver €4.5bn ($5bn) in peak sales. Risk-adjusted to 50-90%, depending on the indication, we value filgotinib at €62 per share.
- Galapagos' IPF fibrosis portfolio has shown good progress into Phase III development and, even on conservative estimates, is worth €30 per share, in our view.
- GLPG1972 and MOR106 recently showed encouraging progress into Phase II development. Risk-adjusted, we value these two programs at an additional €27 per share.
- Galapagos' platform is differentiated and has potential to generate many successful drugs over the long term. For now, we value the platform at €7 per share.
- Based on an SOTP valuation of the pipeline, our valuation of €200 per share offers solid upside potential, particularly as filgotinib for RA could soon be approved in the U.S. and EU, and as additional top-line data further validates the pipeline.

Profit and loss summary

EURm	2017	2018	2019E	2020E	2021E
Revenues	156	318	3,791	262	324
EBITDA	-86	-40	3,342	-275	-243
EBITA	-	-	-	-	-
EBIT	-90	-45	3,331	-287	-256
Associates contribution	-	-	-	-	-
Net interest	-	-	-	-	-
Tax	0	0	0	0	0
Minorities	0	0	0	0	0
Net income adj.	-116	-29	3,334	-284	-253
EPS reported	-2.34	-0.56	56.98	-4.48	-3.93
EPS adjusted	-2.34	-0.56	56.98	-4.48	-3.93
Year end shares	49	52	59	63	64
Average shares	49	52	59	63	64
DPS	-	-	-	-	-

Cash flow summary

EURm	2017	2018	2019E	2020E	2021E
Net income	-116	-29	3,334	-284	-253
Depreciation	4	5	11	12	13
Working capital changes	-13	20	-22	-10	-10
Other non-cash items	-23	-138	-67	36	39
Operating cash flow	-147	-142	3,257	-246	-211
Capex	-5	-10	-115	-12	-15
FCFE	-142	-132	3,372	-235	-197
Acquisitions, disposals	-	-	-	-	-
Other investment CF	-	-	-	-	-
Dividends paid	-	-	-	-	-
Buybacks, issuance	-	-	-	-	-
Change in net debt	-	-	-	-	-
Net debt	-1,151	-1,291	-5,396	-5,138	-4,912
FCF per share	-2.86	-2.53	57.63	-3.71	-3.06

Growth and margins

	2017	2018	2019E	2020E	2021E
Revenue growth	2.8%	103.9%	1092.7%	-93.1%	23.8%
EBITDA growth	-	-	-	-	-
EBIT growth	-	-	-	-	-
EPS adj growth	-	-	-	-	-
FCF growth	-	-	-	-	-
EBITDA margin	-	-	-	-	-
EBIT margin	-	-	-	-	-
Net income margin	-	-	-	-	-
FCF margin	-	-	-	-	-

Key ratios

	2017	2018	2019E	2020E	2021E
Net debt / equity	-113.8%	-106.3%	-97.2%	-96.9%	-96.6%
Net debt / EBITDA	-	-	-	-	-
Avg cost of debt	-	-	-	-	-
Tax rate	-	-	-	-	-
Interest cover	-	-	-	-	-
Payout ratio	-	-	-	-	-
ROCE	-	-	-	-	-
Capex / sales	-	-	-	-	-
Capex / depreciation	-	-	-	-	-

Valuation metrics

	2017	2018	2019E	2020E	2021E
P / adjusted EPS	-	-	-	-	-
P / book value	7.0	6.2	1.5	1.7	1.8
FCF yield	-	-	-	-	-
Dividend yield	-	-	-	-	-
EV / sales	17.7	9.1	0.8	15.2	13.4
EV / EBITDA	-	-	-	-	-
EV / EBIT	-	-	-	-	-
EV / FCF	-	-	-	-	-
EV / cap. employed	-	-	-	-	-

Source: Company data, BCM estimates

Key risks to our investment thesis

- The key risk to our thesis is disappointing clinical data readouts on important assets such as filgotinib (RA, IBD, PsA, AS), GLPG1690 (IPF), GLPG1972 (OA knee), and MOR106 (AtD).
- Additional risks to our thesis include: 1) drug development risk; 2) competitive risks, including if competitor products in development generate superior clinical data or if competitors conduct commercialization activities better than Galapagos or its partners; 3) government regulatory risk; 4) payer reimbursement risk; 5) pricing risk; 6) capital market risk; and 7) business development risk, among others.

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Perspective

Galapagos remains one of our best ideas within our SMID Therapeutics coverage universe. Following several calls with Galapagos management and KOLs, the expansion of the Gilead collaboration, the halting of a study for a key potential competitor in IPF, and the favorable filing news on filgotinib in the U.S. and EU, among other positive news for Galapagos, we increase our price target to €200 (from €140). Filgotinib, partnered with Gilead, is a key driver of the story, in our view, though progress on the rest of the portfolio, including GLPG1690, GLPG1972, as well as MOR106 for atopic dermatitis (AD) supports our valuation. With many potential positive events in H219 and beyond, Galapagos (GLPG) remains one of our best ideas within our coverage.

In this note, we highlight Galapagos' platform, given the value attributed to Galapagos' pipeline by Gilead, as well as GLPG1690 and filgotinib owing to the importance to our valuation and continued value creation for GLPG shares.

Estimate status

Our updated estimates reflect our increased confidence in Galapagos' pipeline programs following the closure of the expanded Gilead collaboration. On August 23, Gilead and Galapagos announced the closure of the global R&D collaboration agreement signed on July 14, 2019. The closure triggered an upfront license fee payment of $3.95bn (approximately €3.555bn, we estimate). In addition, Gilead made an equity investment in Galapagos of approximately $1.1bn (or approximately €960m, we estimate) by subscribing for new shares at a price of €140.59 per share, including issuance premium. Gilead now owns 13,589,686 ordinary shares of Galapagos (or 22% in total). The agreement also includes a 10-year standstill restricting Gilead's ability to seek to acquire Galapagos or increase its stake in Galapagos beyond 29.9% of GLPG's shares.

In addition, we increase our probability of success expectations on GLPG1690 to 70% from 50% and on GLPG1972 to 25% from 20% reflecting our increased confidence in these programs owing to: 1) the Gilead transaction in which Gilead had broad access to Galapagos' pipeline data, including blinded safety data in the ongoing Phase II and III studies for GLPG1972 and GLPG1690, respectively; and 2) additional KOL diligence on these programs.

We note that it is unclear what FactSet estimates include and do not include with respect to the Gilead transaction given that it only recently closed and not all estimates are likely to be updated for the upfront payment in Q319.

Exhibit 1: Our estimates reflect the Gilead transaction; we do not think all estimates on FactSet are updated

€ in millions, unless noted

	Q319E			2019E			2020E	
	BCM	FactSet		BCM	FactSet		BCM	FactSet
Filgotinib	0.0	0.0	Filgotinib	0.0	0.0	Filgotinib	5.9	9.5
Total revenues	**3,609.7**	**188.6**	**Total revenues**	**3,759.2**	**521.7**	**Total revenues**	**230.4**	**500.2**
Other income	7.5	8.5	Other income	31.7	29.6	Other income	31.7	30.3
Total revenues and other income	3,617.2	197.1	Total revenues and other income	3,790.9	551.3	Total revenues and other income	262.1	530.5
Gross profit	**3,617.2**	**415.7**	**Gross profit**	**3,790.9**	**640.7**	**Gross profit**	**242.1**	**578.8**
Gross margin	100.0%	210.9%	Gross margin	100.0%	116.2%	Gross margin	92.4%	109.1%
G&A	14.0	14.3	G&A	51.4	51.2	G&A	60.0	64.4
G&A margin	0.4%	7.3%	G&A margin	1.4%	9.3%	G&A margin	22.9%	12.1%
S&M	4.4	3.0	S&M	14.9	10.4	S&M	45.0	13.6
S&M margin	0.1%	1.5%	S&M margin	0.4%	1.9%	S&M margin	17.2%	2.6%
R&D	100.5	101.8	R&D	393.6	398.1	R&D	424.2	478.9
R&D margin	2.8%	51.6%	R&D margin	10.4%	72.2%	R&D margin	161.9%	90.3%
Operating profit (loss)	**3,498.3**	**68.4**	**Operating profit (loss)**	**3,331.0**	**101.9**	**Operating profit (loss)**	**(287.1)**	**(23.8)**
Non-operating income (expense)	0.5	(2.9)	Non-operating income (expense)	2.9	(6.4)	Non-operating income (expense)	2.9	(8.0)
IFRS EPS	**€ 56.30**	**€ 0.79**	**IFRS EPS**	**€ 56.98**	**€ 0.89**	**IFRS EPS**	**€ -4.48**	**€ -0.19**
Adjusted EPS	**€ 56.30**	**€ 1.31**	**Adjusted EPS**	**€ 56.98**	**€ 1.61**	**Adjusted EPS**	**€ -4.48**	**€ -0.25**
Shares o/s	62.1		Shares o/s	58.5		Shares o/s	63.4	

Source: FactSet, company filings, Berenberg Capital Markets

Gilead deal could generate substantial value

We think the deal is very favorable for both Galapagos and Gilead. Gilead gains access to a high quality pipeline and innovative small molecule R&D platform, as well as talent in the EU, while Galapagos gains funding that should enable it to dramatically expand and accelerate existing and future development programs, and shares the risk of funding expensive late stage programs.

Galapagos will fund and lead all discovery and development until the end of Phase II, after which Gilead will have the option to in-license the compound for $150m; Galapagos/Gilead will then co-develop the compound and share costs equally. Gilead will maintain option rights to Galapagos' programs through the 10-year term and for up to an additional three years thereafter for those programs that have entered clinical development prior to the end of the term. Galapagos will receive tiered royalties ranging from 20-24% on net sales of all Galapagos products licensed by Gilead.

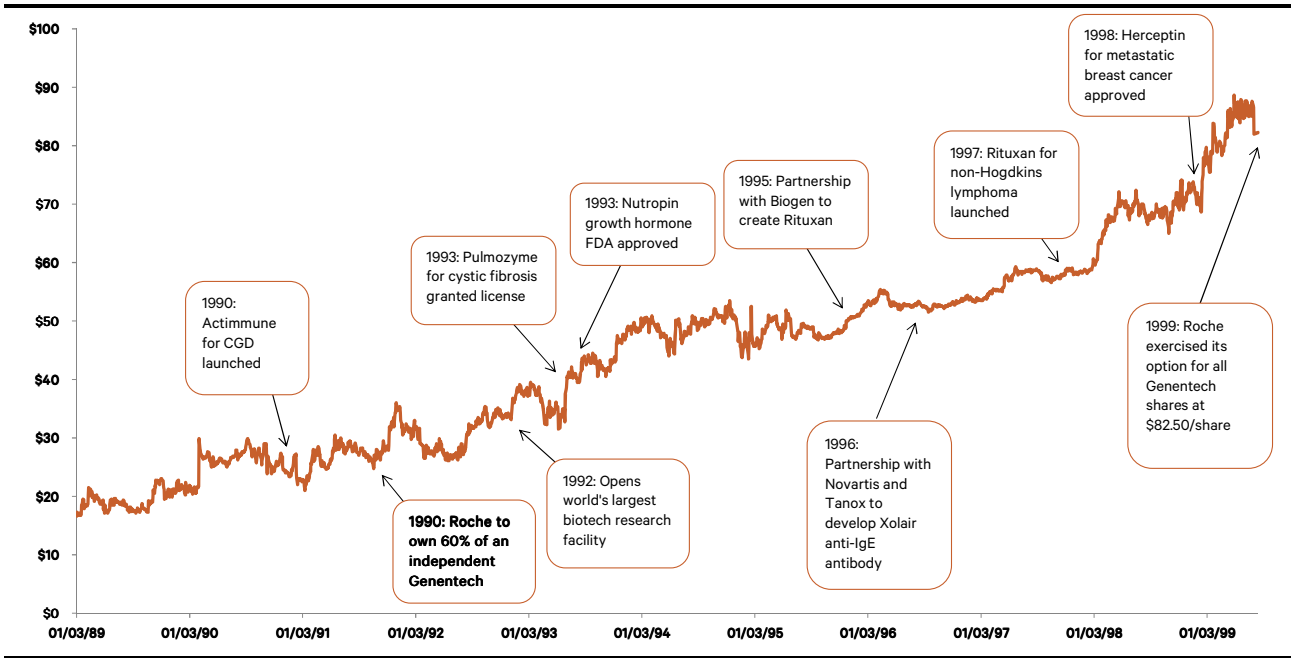
GLPG1690 (IPF, Phase III) terms: Galapagos will receive an additional $325m milestone fee if GLPG1690 is approved in the U.S. for treatment of idiopathic pulmonary fibrosis, possibly in 2022, we estimate. Galapagos retains commercial rights for the EU on GLPG1690.

GLPG1972 (OA, Phase II) terms: Gilead could in-license the compound after the Phase IIb study in osteoarthritis of the knee is completed in H220; additional milestones of $750m are possible. Galapagos is already partnered with Servier on for the EU on GLPG1972.

History shows further upside for GLPG shares a strong possibility

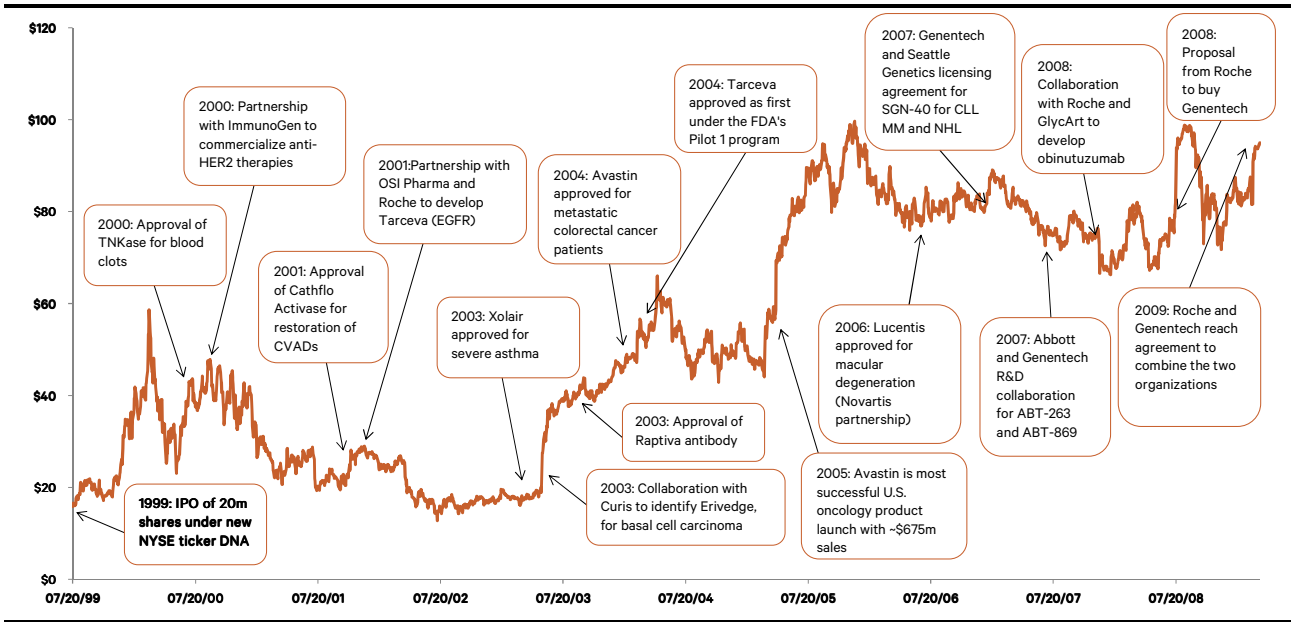
We think investors will be rewarded as further value in GLPG is unlocked. The Galapagos/Gilead expanded collaboration is unique; investors have typically compared it to Genentech/Roche (an acquisition over time, and a very successful collaboration), Chugai/Roche (structured similarly as Genentech), and Regeneron/Sanofi. Galapagos is maintaining a higher degree of control than Regeneron, and is more independent than Genentech or Chugai, so the comparisons are not precise. However, what we think is important is that much value can be generated *after* a collaboration such as these are expanded in a transformative manner. It should come as no surprise that further potential upside will continue to be data-driven and pipeline success-dependent; however, **we think the idea that potential upside is capped for GLPG shareholders by the expanded collaboration with Gilead is unfounded.**

Exhibit 2: From February 2, 1989 to June 4, 1999, the value of Genentech shares increased substantially



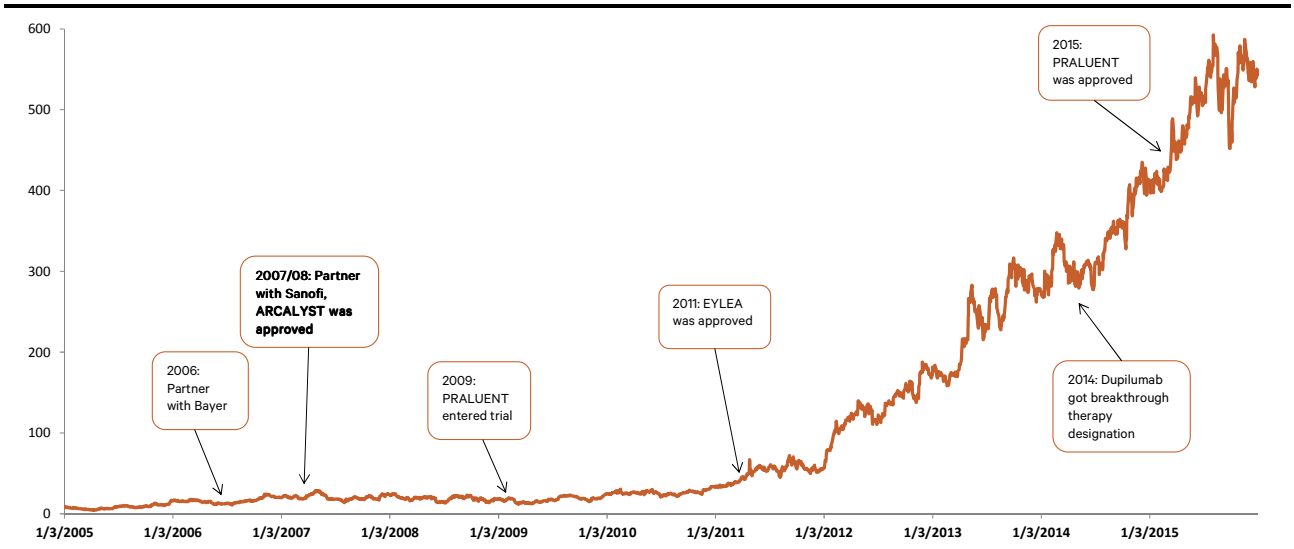
Source: FactSet, company filings, Berenberg Capital Markets

Exhibit 3: Additional value was generated for Genentech shareholders when Roche floated 20m new shares of Genentech



Source: FactSet, company filings, Berenberg Capital Markets

Exhibit 4: Regeneron shares increased robustly from 2008 to 2016



Source: FactSet, company filings, Berenberg Capital Markets

Galapagos has built one of the most robust pipelines worldwide

Galapagos' approach to R&D has potential to generate multiple blockbuster drugs. The human genome is made up of tens of thousands of genes, which code for the proteins that make up the human body. Nearly all chronic diseases and disorders are caused by a disruption in the normal function of certain proteins, according to Galapagos; the main goal of the industry is to discover and develop molecules that alter the activity of these proteins so that normal function returns and the cause of the disease is minimized or eliminated. One of the main obstacles in discovering new drugs is to understand exactly which of the body's thousands of proteins play a key role in a particular disease. Once these proteins are discovered, they become targets for drug design; finding these targets is one of the critical steps in the drug discovery process. **Galapagos' discovery platform focuses on target identification using primary human cells,** which Galapagos believes provides a good system to study the effect that a protein might have on the disease in the human body.

Galapagos takes advantage of the distinctive properties of adenoviruses. Adenovirus is the virus that causes the common cold and has the capability to infect almost every type of human cell. The adenoviruses that Galapagos works with have been engineered to act as a shuttle vehicle, allowing the delivery of specific pieces of DNA into human cells. Additionally, these viruses have been made replication incompetent, meaning they do not replicate in the human cell they infect, and so do not interfere with the processes in the cell. Galapagos engineered the viruses to carry small pieces of DNA, specific for individual human genes; when the virus enters the cell, this DNA piece leads to the production of a short sequence of RNA that is processed in the cell to become short interfering RNA (siRNA), which specifically interferes with the mRNA of the protein it was designed for. Thus, by using these viruses, Galapagos can cause the cells to block, or "knock-down," the production of a certain protein, mimicking what a small molecule drug does in the human body.

Galapagos built a collection with these adenoviruses, now in excess of 20,000 viruses, that addresses around 6,000 druggable genes. **The result has been the creation of one of the most dynamic and exciting drug pipelines worldwide: out of 43 pre-clinical candidates generated by Galapagos' R&D platform, 20 compounds have entered the clinic, of which 14 compounds have entered studies in patients, and of which 13 (out of 14) include novel mechanisms.**

Exhibit 5: Galapagos' differentiated platform: 14 compounds are currently being studied in patients, of which 13 represent novel mechanisms of action

Source: Galapagos, Berenberg Capital Markets

Galapagos' pipeline may contain multiple blockbuster drugs

We think the Galapagos story is likely to include more good news in H219 and beyond. Lead candidate filgotinib, in late stage development for various inflammatory conditions, acts on a target whose role in the specific disease was discovered by Galapagos using its discovery platform. Additional proof of the potential of Galapagos' small molecule platform approach could be achieved with success with GLPG1690 and MOR106, in Phase II development for atopic dermatitis (AD). The respective targets of autotaxin (ATX) and IL-17c were discovered by Galapagos for these diseases, according to Galapagos. Thus, we think the more success generated in late stage assets such as filgotinib, GLPG1690, and MOR106, the more value that we think will be attributed to Galapagos' platform.

In the Exhibits that follow, we present the next expected catalysts for Galapagos' pipeline, as well as our expectations for Galapagos' most advanced and important assets. We think Gilead's broad commercial expertise should increase the probability that our peak sales estimates could be achieved for each asset outlined below, if approved. **We estimate Galapagos could achieve sustainable profitability by 2022, all else being equal.**

Exhibit 6: Galapagos' high quality pipeline has many studies underway with potential to create value

Area	Therapy	Mechanism	Indication	Status
Inflammation	Filgotinib	Selective JAK1 inhibitor	Rheumatoid arthritis FINCH 1: MTX - IR FINCH 2: biologic - IR FINCH 3: MTX naïve	Phase III fully recruited Top-line data reported Q119 Top-line data reported Q418 Top-line data reported Q119
			Crohn's disease (CD) DIVERSITY 1	Phase III fully recruited H220
			Ulcerative colitis (UC) SELECTION 1	Phase III fully recruited
			Ankylosing spondylitis (AS) TORTUGA	Phase III ready Results published in *The Lancet*
			Psoriatic arthritis (PsA) EQUATOR	Phase III ready Results published in *The Lancet*
			Small bowel CD	Phase II recruiting
			Fistulizing CD	Phase II recruiting
			Sjögren's	Phase II top-line data expected by end of 2019
			Cutaneous lupus	Phase II top-line data expected by end of 2019
			Lupus nephropathy	Phase II no longer recruiting
			Uveitis	Phase II recruiting
	GLPG1972	ADAMTS-5 inhibitor	Osteoarthritis of the knee (OA knee) ROCCELLA	Phase II fully recruited Q319
	MOR106	IL-17C inhibitor	Atopic dermatitis (AtD) IGUANA (IV dose-ranging)	Phase II recruiting
			GECKO (subcutaneous)	Phase II initiated on April 23
	TOLEDO program	Undisclosed	Undisclosed	'3312 Phase I recruiting '3970 (second generation) Phase I study start H219
Fibrosis	GLPG1690	Autotaxin inhibitor	Idiopathic pulmonary fibrosis (IPF)/fibrosis ISABELA	Phase III enrolling (update by September possible)
			FLORA	Phase II results published in *The Lancet*
	GLPG1690	Autotaxin inhibitor	Systemic sclerosis (SSc) or scleroderma NOVESA	Phase II enrolling
	GLPG1205	GRP84 inhibitor	Idiopathic pulmonary fibrosis (IPF)/fibrosis PINTA	Phase II enrolling

Note: IR = inadequate response; MTX = methotrexate; FINCH = Phase III program evaluating filgotinib in rheumatoid arthritis (RA); DIVERSITY = Phase III program evaluating filgotinib in Crohn's disease (CD); SELECTION = Phase III program evaluating filgotinib in ulcerative colitis (UC) patients; EQUATOR = Phase II trial with filgotinib in psoriatic arthritis (PsA) patients; TORTUGA = Phase II trial with filgotinib in patients with ankylosing spondylitis (AS); ROCCELLA = global Phase II trial together with collaboration partner Servier, investigating GLPG1972/S201086 in osteoarthritis (OA) patients; IGUANA = Phase II trial together with partners MorphoSys and Novartis investigating MOR106 in AtD patients; ISABELA = Phase III program investigating GLPG1690 in IPF patients; FLORA = a double-blind, placebo-controlled exploratory Phase IIa trial with GLPG1690 in up to 24 IPF patients, which generated top-line data in August 2017; NOVESA = Phase II trial with GLPG1690 in patients with systemic sclerosis (SSc) or scleroderma; PINTA = Phase II trial of GPR84 inhibitor GLPG1205 in IPF patients
Source: Company filings, Berenberg Capital Markets

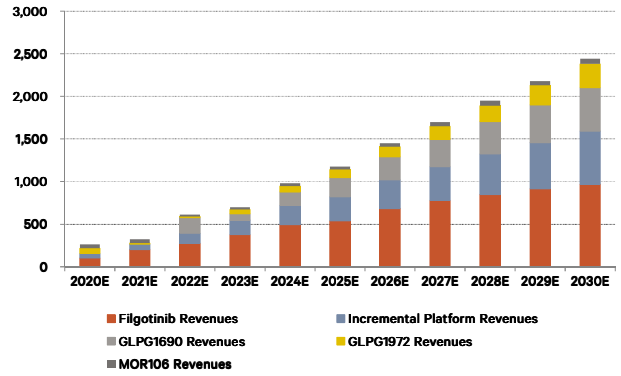
Exhibit 7: 2020 is lining up to be a transformational year, with important studies enrolling and generating top-line data, and with potential approval of Galapagos' first drug (filgotinib in RA)

Program	H119	H219	2020
Filgotinib	• FINCH 1 top-line wk 24 • FINCH 3 top-line wk 24 • FINCH 2 manuscript publication	• Sjögrens PoC topline • CLE PoC topline • Phase III PsA start • Filings for approval in RA	• Phase III AS start • Potential approval in RA in the U.S. and EU
Fibrosis	• First dosing NOVESA SSc GLPG1690 • ATS (possibly ISABELA poster) GLPG1690	• PINTA recruited • ERS • ACS (structure)	• 25% enrollment for futility analysis (GLPG1690)
GLPG1972	• OARSI symposium	• ROCCELLA recruited	ROCCELLA top-line
MOR106	• GECKO Phase II start/IND opening • Japan study start	• S.C. bridging top-line	• IGUANA top-line
Earlier programs	• Start Phase I GLPG3312 (first generation TOLEDO), GLPG2534, GLPG3121	• Top-line GLPG3312, GLPG2534, GLPG3121 • Start GLPG3970 Phase I • Start PoC GLPG3312 in IBD	• TBA

Source: Company filings, Berenberg Capital Markets

Exhibit 8: Galapagos annual revenues could exceed €2bn by 2030E

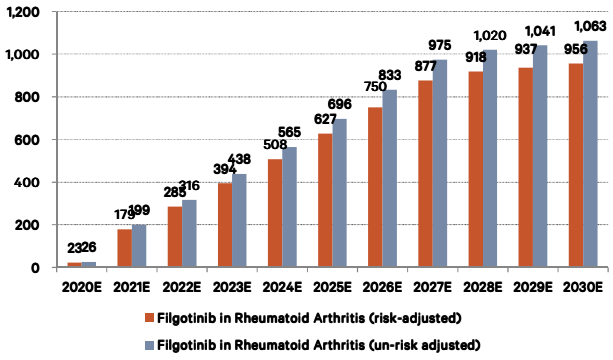
€ in millions



Source: Company filings, BCM estimates

Exhibit 9: We think filgotinib has blockbuster potential in RA

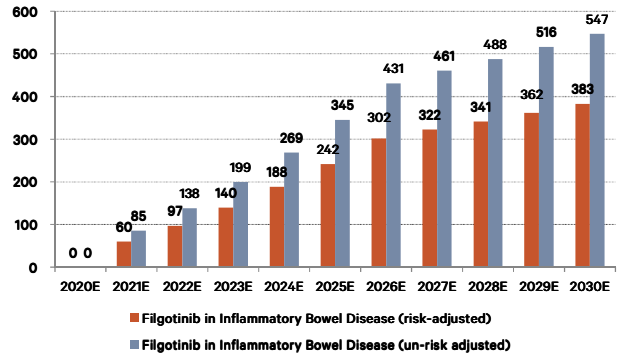
€ in millions



Source: Company filings, BCM estimates

Exhibit 10: Our filgotinib estimates in IBD could be conservative; competitive dynamics could impact uptake

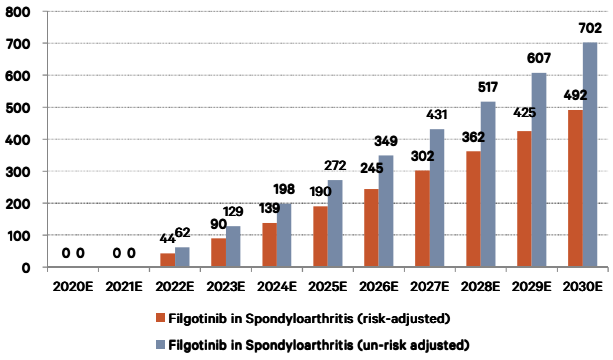
€ in millions



Note: IBD includes ulcerative colitis and Crohn's disease (UC and CD)
Source: Company filings, BCM estimates

Exhibit 11: Filgotinib has generated strong data so far in PsA and AS, pointing to very strong sales potential long term

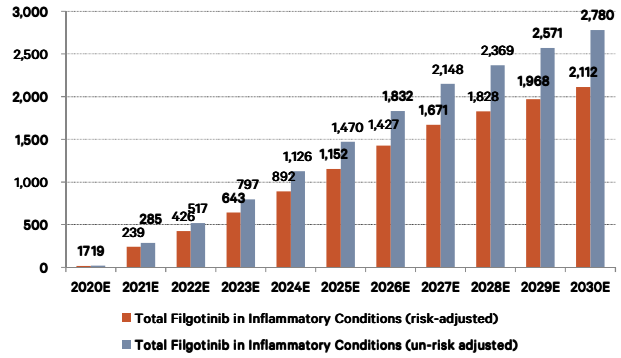
€ in millions



Note: PsA = psoriatic arthritis; AS = ankylosing spondylitis
Source: Company filings, BCM estimates

Exhibit 12: Total filgotinib sales in all indications could reach nearly €2.8bn worldwide by 2030E, if approved

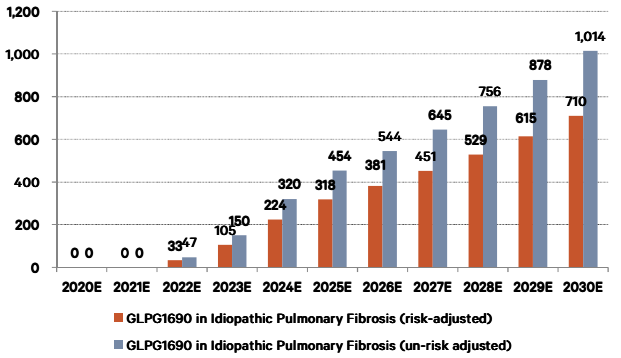
€ in millions



Source: Company filings, BCM estimates

Exhibit 13: GLPG1690 also has blockbuster potential, if approved; by 2030E we estimate sales could reach €1bn worldwide

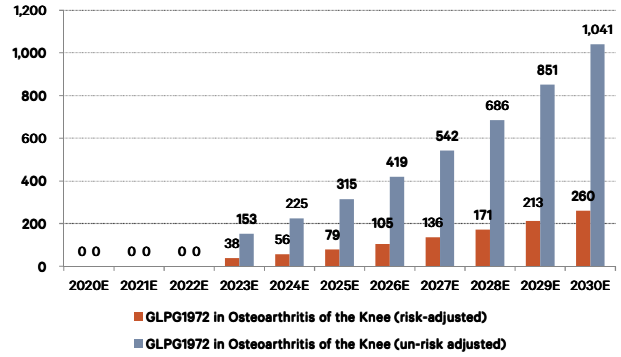
€ in millions



Source: Company filings, BCM estimates

Exhibit 14: GLPG1972 in OA knee alone could become a blockbuster; additional indications would be incremental

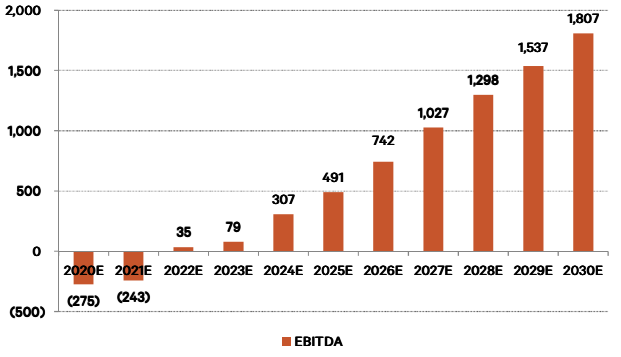
€ in millions



Source: Company filings, BCM estimates

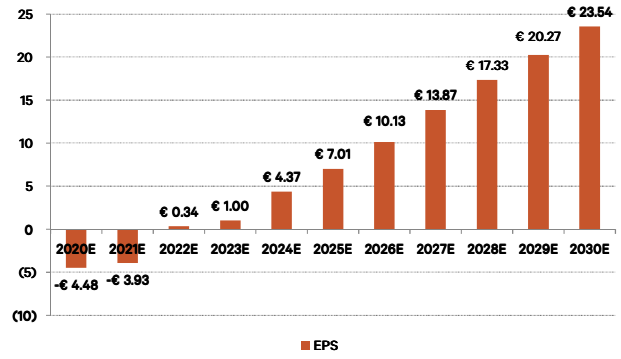
Exhibit 15: We estimate Galapagos will generate sustainably positive EBITDA beginning in 2022E

€ in millions



Source: Company filings, BCM estimates

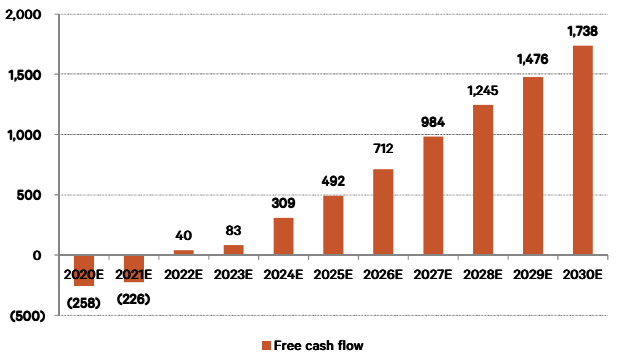
Exhibit 16: Galapagos' EPS growth should accelerate in 2022E-2030E



Source: Company filings, BCM estimates

Exhibit 17: Free cash flow should also build over the next decade

€ in millions



Source: Company filings, BCM estimates

GLPG1690 could generate peak sales of $2bn

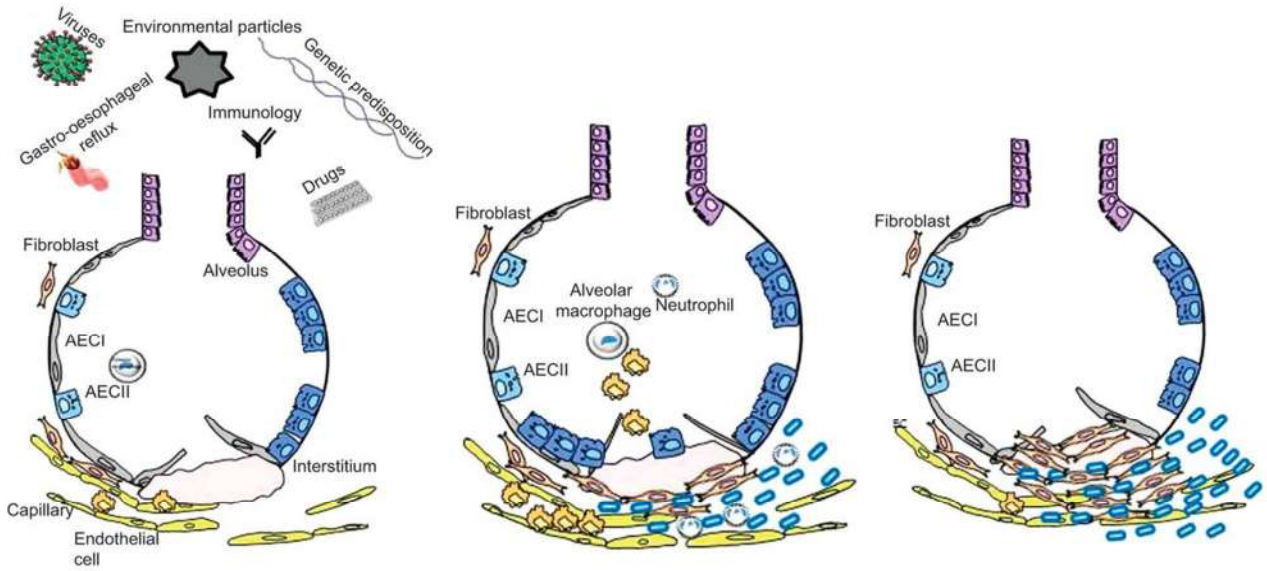
GLPG-1690 is an oral, potential first-in-class compound in Phase III development for idiopathic pulmonary fibrosis (IPF).

Background. IPF is a specific form of chronic, progressive fibrosing interstitial pneumonia of unknown cause occurring in adults. Treatment options are limited. The prognosis of people with IPF is similar to that of stage one and two non-small cell lung cancer with a median survival, from diagnosis, of less than three years; people die on average seven years prematurely.

The exact cause of IPF remains unknown. Pulmonary fibrosis is the end stage of several diffuse parenchymal lung diseases (DPLDs), characterized by excessive matrix deposition and destruction of the lung architecture, finally leading to respiratory insufficiency. The most common form of pulmonary fibrosis, idiopathic pulmonary fibrosis (IPF), is a progressive disease with a five-year survival rate of only 20%, reflecting the lack of effective therapies. There is still no unifying mechanism that can explain all lung fibrogenesis, and it is likely that multiple factors play a role.

Pulmonary fibrosis is regarded as a disease caused by repeated subclinical injury leading to epithelial damage and subsequent destruction of the alveolar-capillary basement membrane. This process initiates the infiltration of fibrotic cells and the activation of (myo)fibroblasts. In pulmonary fibrosis the normal resolution of inflammatory and mesenchymal cells through apoptosis and phagocytosis is dysregulated. This results in the destruction of the normal lung architecture and loss of function. In IPF this process leads to death with a median time of three years after diagnosis. These processes are summarized in the Exhibit below. For additional information, see here, here, here, and here.

Exhibit 18: Progression of fibrosis



Injury:
Epithelial damage
Endothelial damage
Destruction of alveolar capillary basement membrane
Vascular leak
Platelet activation
Fibrin clot activation

Epithelial-fibroblastic interaction:
Release of profibrotic cytokines; (myo)fibroblast recruitment, proliferation and differentiation
Provisional matrix formation
Angiogenesis
Defective re-epithelialization

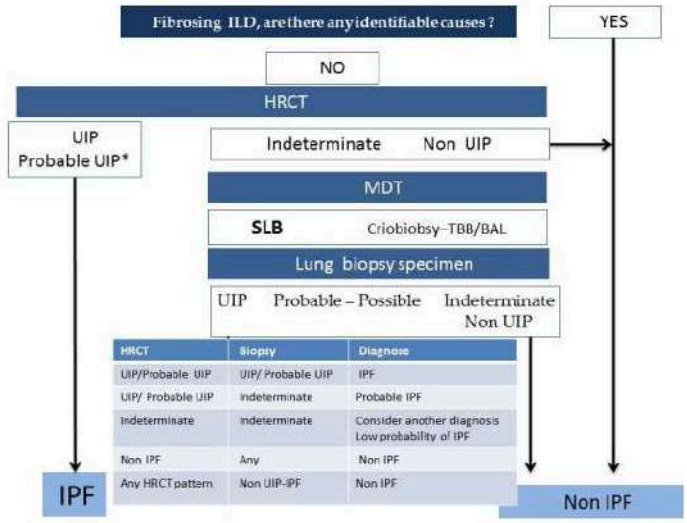
Aberrant repair and fibrosis:
Exaggerated extracellular matrix accumulation
Lack of matrix degradation
Progressive lung remodeling
Honeycomb changes

Note: AEC = alveolar epithelial cell
Source: European Respiratory Journal, Berenberg Capital Markets

Diagnosis guidelines rely on process of elimination, imaging, and sometimes biopsies. The collaborative effort between the American Thoracic Society (ATS), European Respiratory Society (ERS), Japanese Respiratory Society (JRS), and Latin American Thoracic Society (ALAT) led to published diagnostic guidelines in 2011 and updated guidelines in 2018. Previously defined patterns of usual interstitial pneumonia (UIP) were refined to

patterns of UIP, probable UIP, indeterminate for UIP, and alternate diagnosis. For patients with newly detected interstitial lung disease (ILD) who have a high-resolution computed tomography scan pattern of probable UIP, indeterminate for UIP, or an alternative diagnosis, conditional recommendations were made for performing bronchoalveolar lavage (BAL) and surgical lung biopsy; because of a lack of evidence, no recommendation was made for or against performing transbronchial lung biopsy or lung cryobiopsy. In contrast, for patients with newly detected ILD who have a high-resolution computed tomography scan pattern of UIP, strong recommendations were made against performing surgical lung biopsy, transbronchial lung biopsy, and lung cryobiopsy, and a conditional recommendation was made against performing BAL. Additional recommendations included a conditional recommendation for multidisciplinary discussion and a strong recommendation against measurement of serum biomarkers for the sole purpose of distinguishing IPF from other ILDs. Further details can be found here and here.

Exhibit 19: Flow chart of diagnostic procedure



Note: MDT = multidisciplinary team; SLB = surgical lung biopsy; TBB = transbronchial forceps biopsy; BAL = bronco alveolar lavage
**Patient with "probable UIP pattern" in high-resolution computed tomography (HRCT) and clinical high suspicion of IPF (patient over 60 years, smoking history, and unknown etiology do not require biopsy).*
Source: Medical Sciences, Multidisciplinary Digital Publishing Institute (MDPI)

IPF is considered a rare, sporadic disease. According to the National Institutes of Health, around 100,000 people in the U.S. have IPF, with 30,000-40,000 new cases diagnosed each year. According to GlobalData, IPF affects approximately 200,000 patients in the U.S. and Europe, and this population is expected to increase in part owing to improved diagnosis. Furthermore, according to GlobalData, prevalence is expected to increase with the aging population. See here.

The standard of care (SOC) treatments are blockbuster drugs

Only two novel therapies are approved for treatment of IPF. The official ATS/ERS/JRS/ALAT clinical practice guidelines were last updated in 2015. Notably, the guidelines shifted pirfenidone, Roche/Genentech's Esbriet, approved by the FDA in 2014, from a conditional recommendation against use based on low confidence in effect estimates to conditional recommendation for use. Nintedanib, Boehringer's Ofev, approved by the FDA in 2014, received a conditional recommendation for use in the updated guidelines. Other treatments, such as warfarin and the combination of prednisone + azathioprine + N-acetylcysteine moved from a conditional recommendation against use to a strong recommendation against use. Sildenafil, a PDE5 inhibitor, was not addressed in the 2011 guideline, though in the updated guidance received a conditional recommendation against use. See the Exhibit 20 and here for additional details.

Ofev and Esbriet, generated combined sales of $1.9bn in 2017, with approximately 74% of sales being in the U.S. FactSet consensus estimates point to Esbriet peaking at around $1.2bn in 2020-2021E. Galapagos estimates the market of approved IPF drugs could reach

$5bn by 2025, which appears feasible to us based on the current market size, growth in the market, and novel drugs in development that have shown promise in IPF treatment. We discuss the competitive landscape in the next section of this report, and include further details from KOL conversations in the section that follows.

Exhibit 20: The only therapies approved that have shown improvement in disease progression are nintedanib and pirfenidone

Agent	2015 Guideline	Comments	2011 Guideline	Comments
New and revised recommendations				
Anticoagulation (warfarin)	Strong recommendation against use	Moderate confidence in effect estimates	Conditional recommendation against use	Very low confidence in effect estimates
Combination prednisone + azathioprine + N-acetylcysteine	Strong recommendation against use	Low confidence in effect estimates	Conditional recommendation against use	Low confidence in effect estimates
Selective endothelin receptor antagonist (ambrisentan)	Strong recommendation against use	Low confidence in effect estimates	Not addressed	Not addressed
Imatinib, a tyrosine kinase inhibitor with one target	Strong recommendation against use	Moderate confidence in effect estimates	Not addressed	Not addressed
Nintedanib, a tyrosine kinase inhibitor with multiple targets	Conditional recommendation for use	Moderate confidence in effect estimates	Not addressed	Not addressed
Pirfenidone (mechanism has not been established)	Conditional recommendation for use	Moderate confidence in effect estimates	Conditional recommendation against use	Low confidence in effect estimates
Dual endothelin receptor antagonists (macitentan, bosentan)	Conditional recommendation against use	Low confidence in effect estimates	Strong recommendation against use	Moderate confidence in effect estimates
Phosphodiesterase-5 inhibitor (sildenafil)	Conditional recommendation against use	Moderate confidence in effect estimates	Not addressed	Not addressed
Unchanged recommendations				
Antacid therapy	Conditional recommendation for use	Very low confidence in effect estimates	Conditional recommendation for use	Very low confidence in effect estimates
N-acetylcystein monotherapy	Conditional recommendation against use	Low confidence in effect estimates	Conditional recommendation against use	Low confidence in effect estimates
Antipulmonary hypertension therapy for IPF-associated pulmonary hypertension	Reassessment of the previous recommendation was deferred		Conditional recommendation against use	Very low confidence in effect estimates
Lung transplantation: single vs. bilateral lung transplantation	Formulation of a recommendation was deferred		Not addressed	Not addressed

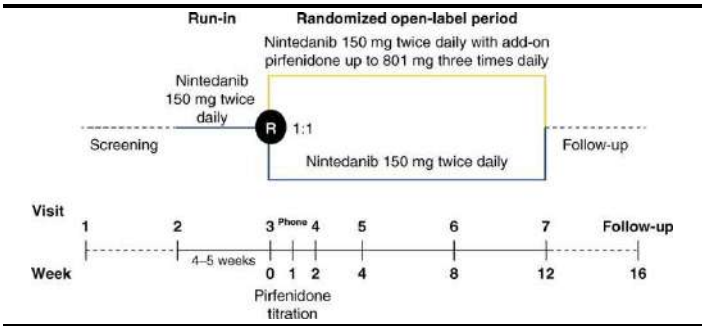
Source: American Thoracic Society Documents, Berenberg Capital Markets

INJOURNEY trial points to good potential for combination therapy

With the availability of two antifibrotic drugs, it is expected that combination therapy is likely to be the future of treatment of IPF, similar to the management of other chronic progressive diseases, such as pulmonary arterial hypertension and several types of cancer. Nintedanib and pirfenidone have pleiotropic effects and are thought to target different aspects of the fibrotic cascade, suggesting that therapy with both drugs may provide additive or even synergistic effects, resulting in a greater improvement in outcomes than either monotherapy. However, given the overlapping adverse event profiles of nintedanib and pirfenidone, data on potential additive adverse events and the overall benefit/risk ratio of combined therapy are needed.

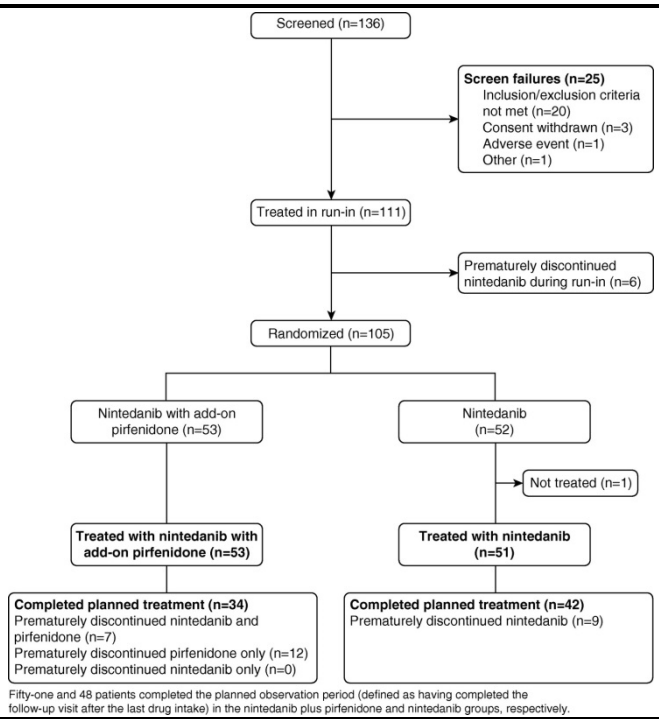
In the open-label randomized INJOURNEY trial, treatment with nintedanib with add-on pirfenidone had a manageable safety and tolerability profile in patients with IPF, in line with the adverse profiles of the individual drugs. Plasma trough concentrations of nintedanib were similar when it was administered alone or with add-on pirfenidone. **Decline in FVC over 12 weeks appeared to be less in patients treated with nintedanib with add-on pirfenidone than with nintedanib alone.** See here for further details.

Exhibit 21: INJOURNEY trial design



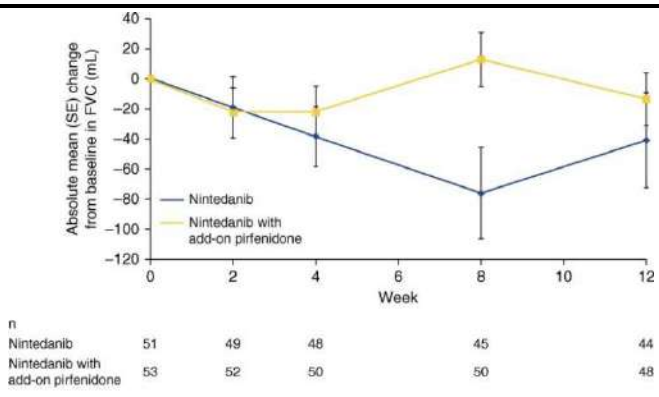
Source: ATS

Exhibit 22: INJOURNEY patient disposition



Source: ATS

Exhibit 23: IPF combo treatment = FVC stabilization?



Source: ATS

"When I meet with an IPF patient, I'm staring at death"

Clinicians want more effective and safer drugs for IPF. The SOC treatments for IPF, pirfenidone and nintenadib, slow the inevitable decline in lung function as measured by forced vital capacity (FVC) for patients. However, according to one key opinion leader (KOL) we recently spoke to, these drugs are not good enough; the KOL's morbid description, quoted above, reflects the inevitable end for all IPF patients, according to the KOL: either a lung transplant or death. The KOL noted high enthusiasm for GLPG1690, with many patients requesting it.

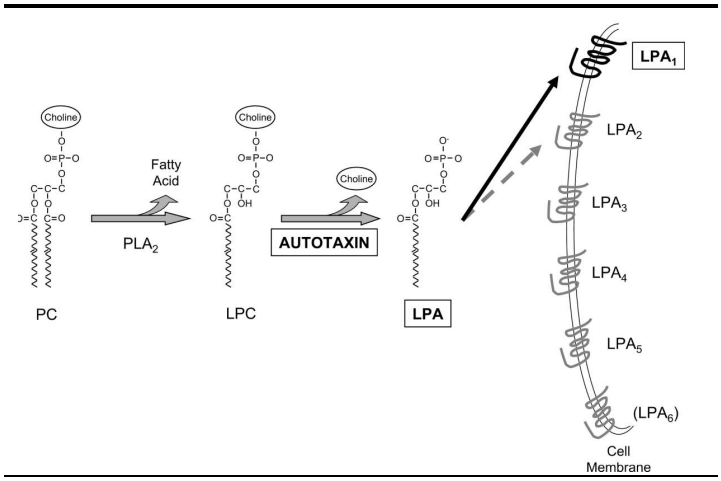
Galapagos/Gilead's '1690 in Phase III; interim analysis expected 2021

GLPG1690 is a potent and selective inhibitor of autotaxin (ATX)

Autotaxin in pathophysiology and pulmonary fibrosis. ATX was first identified as an autocrine motility-stimulating factor, isolated from the supernatant of highly metastatic melanoma cells. Its cDNA cloning revealed that ATX was homologous to ectonucleotide pyrophosphatase-phosphodiesterase 1 (ENPP1), possessing phosphodiesterase activity *in vitro;* ATX was thus classified as ENPP2 in the ENPP (1–7) protein family, being the only secreted and not transmembrane member. In addition, several years later it was discovered that ATX is identical to the long elusive plasma lysoPLD, and is now considered responsible for the synthesis of the majority of extracellular lysophosphatidic acid (LPA).

Five high-affinity LPA receptors have been definitively established and designated LPA1 to LPA5; a lower-affinity receptor is likely to join the LPA receptor family as LPA6. LPA signaling specifically through LPA1 has pro-fibrotic effects on epithelial cells, endothelial cells, and fibroblasts, promoting epithelial cell apoptosis, inducing vascular leak, and directing fibroblast recruitment, proliferation, and persistence. LPA–LPA2 signaling may also have pro-fibrotic effects, inducing activation of latent TGF-β by lung epithelial cells, although LPA signaling through LPA2 on leukocytes may serve to prevent excess innate immune activation after tissue injury.

Exhibit 24: The autotaxin-LPA-LPA1 pathway

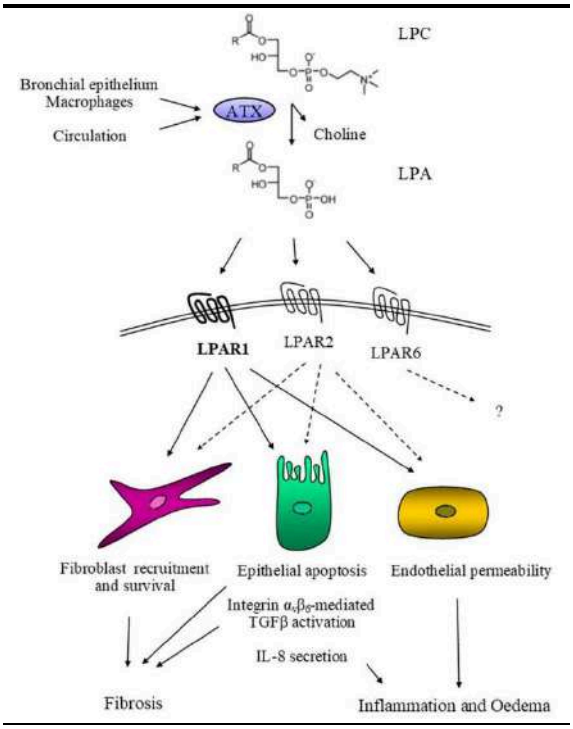


Source: American Journal of Respiratory Cell and Molecular Biology, ATS

Generation of lysophosphatidic acid (LPA) by ATX, and LPA signaling through LPA1; both are required for bleomycin-induced pulmonary fibrosis in mice, and both have been implicated in the pathogenesis of IPF in humans. The majority of LPA *in vivo* appears to be produced by conversion of phospholipids such as phosphatidylcholine (PC) to lysophospholipids such as lysophosphatidylcholine (LPC) through the action of phospholipase A2 (PLA2) family members, followed by the conversion of these lysophospholipids to LPA through the lysophospholipase D activity of ATX. LPA activates its cognate receptors LPAR1, possibly LPAR2, and hypothetically LPAR6, activating the corresponding G-protein-mediated signal transduction cascades. As a result, LPA induces epithelial apoptosis, the initiating pathogenetic event in modeled pulmonary fibrosis and possibly IPF. LPA also induces IL-8 secretion from epithelial cells, promoting inflammation, while it also stimulates endothelial permeability, thus promoting pulmonary

edema. Moreover, LPA stimulate the αvβ6-mediated TGFβ activation leading to the activation and trans-differentiation of pulmonary fibroblasts, for which LPA is additionally a pro-survival and chemotactic factor. See here and here for further details.

Exhibit 25: ATX's mode of action in pulmonary fibrosis



Source: Frontiers in Medicine

GLPG1690 selectively inhibits ATX, with *ex vivo* human plasma LPA release assays indicating a half maximal inhibitory concentration (IC50) of approximately 100 nM. In preclinical studies, GLPG1690 has demonstrated efficacy in a mouse bleomycin-induced pulmonary fibrosis model (therapeutic setting): GLPG1690 was superior to pirfenidone and similar to nintedanib in reducing the Ashcroft fibrotic score and collagen content. See here and here for details.

A first-in-human study demonstrated that GLPG 1690 was well tolerated after administration of single doses up to 1500 mg and multiple doses up to 1000 mg once daily for 14 days. There was a reduction in plasma LPA C18:2 levels following administration of GLPG1690, reaching a maximum of approximately 90% reduction from baseline; the decrease in LPA C18:2 was rapid, with higher doses providing a more sustained effect. Reduction in LPA C18:2 was also apparent in the pooled placebo group, only in the MAD part of the study; however, this was highly variable, and there was clear separation between placebo and GLPG1690 (even at the lowest dosage) in effects on LPA C18:2. These results indicate that GLPG1690 inhibited ATX effectively. After 14 days of GLPG1690 administration, plasma LPA C18:2 was reduced at predose by at least 70% for all doses; for GLPG1690 600 mg once daily and 1000 mg once daily, this finding indicates that GLPG1690 concentration remained at a level capable of inhibiting ATX for at least 24 hours post dose and that once-daily dosing is sufficient. LPA C18:2 returned toward baseline 48 hours post dose for all doses, demonstrating that the inhibition of ATX by GLPG1690 is reversible. Treatment emergent adverse events (TEAEs) experienced by subjects were at most moderate in severity; the most common TEAE was headache, which was considered at least possibly related to GLPG1690. **Importantly, no dose-limiting toxicities were identified during the study.** See here for details.

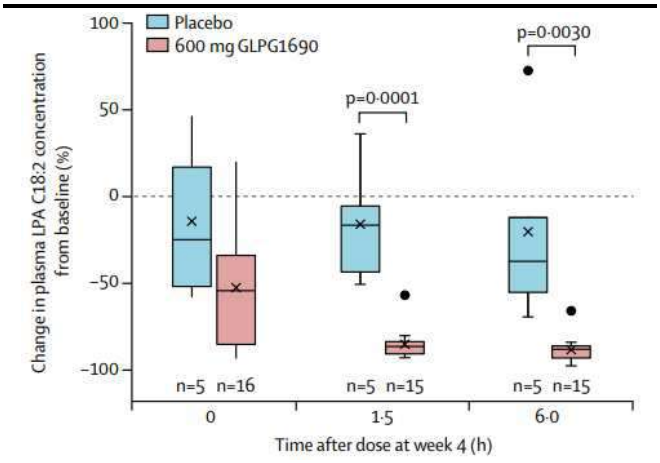
GLPG1690 generated compelling Phase IIa data in the FLORA study

A Phase IIa study (FLORA) in 23 patients with IPF demonstrated that GLPG1690 was well tolerated, reduced plasma LPA C18:2 levels, and stabilized forced vital capacity (FVC) after 12 weeks of treatment. FLORA was a randomized double-blind placebo-controlled Phase IIa study conducted in 17 centers in Italy, Ukraine, and the UK. Eligible patients were

40 years or older, non-smokers, not taking pirfenidone or nintedanib, and had a centrally confirmed diagnosis of IPF. Patients were randomized 1:3 to receive placebo or 600 mg oral GLPG1690 once daily for 12 weeks. The primary outcomes were safety (adverse events), tolerability, pharmacokinetics, and pharmacodynamics. Spirometry was assessed as a secondary outcome.

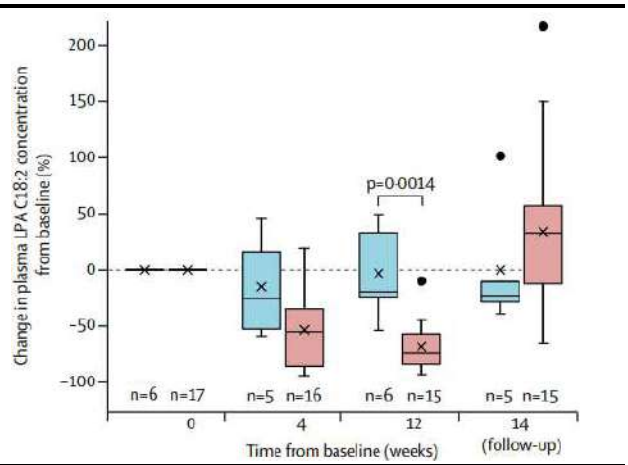
Pharmacodynamic analyses showed that concentrations of LPA C18:2 in plasma decreased after administration of GLPG1690 at the week 4 and week 12 visits and that they returned to baseline concentrations at the follow-up visit. Reductions of LPA C18:2 concentrations were seen with GLPG1690 in observed cases at week 4 (maximum percentage reduction from baseline 35.5% for placebo and 89.4% for GLPG1690, p=0.0008) and with area under the effective-time curve over 6 h (104.1% for placebo and 496.0% for GLPG1690, p=0.0007).

Exhibit 26: Change in LPA C18:2 concentrations in plasma from baseline demonstrates GLPG1690 is performing as designed



Source: The Lancet

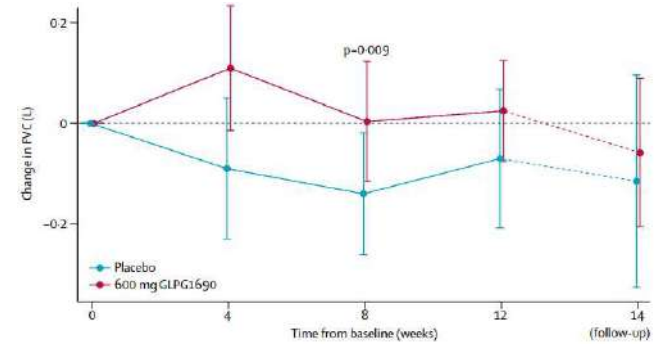
Exhibit 27: In the observed-case analysis, changes from baseline were significant at week 12



Source: The Lancet

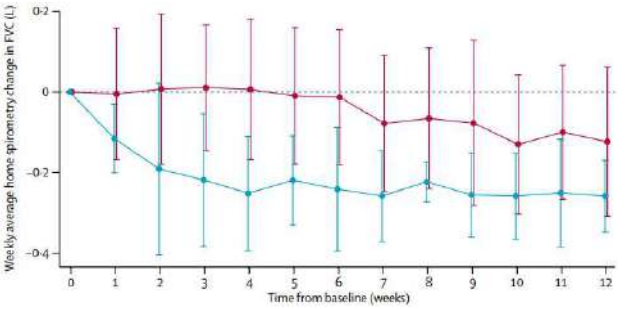
Mean forced vital capacity (FVC) decreased over the 12 week treatment period in the placebo group but remained similar to or greater than baseline values in the GLPG1690 treatment group (mean −70 mL [95% CI −208 to 68] in the placebo group and 25 mL [−75 to 124] in the GLPG1690 group with LOCF). Results from the observed-case analysis were similar with mean FVC −87.5 mL [95% CI −345 to 170] for placebo and +8 mL [−101 to 116] for GLPG1690. The overall patterns of change in FVC assessed by spirometry at home were similar to those seen with study center spirometry testing.

Exhibit 28: Spirometry results from study center visits



Note: placebo group n = 6 and GLPG1690 n=17; changes were not significant at Weeks 4 (p=0.13) and 12 (p=0.3)
Source: The Lancet

Exhibit 29: Spirometry results from measurements at home

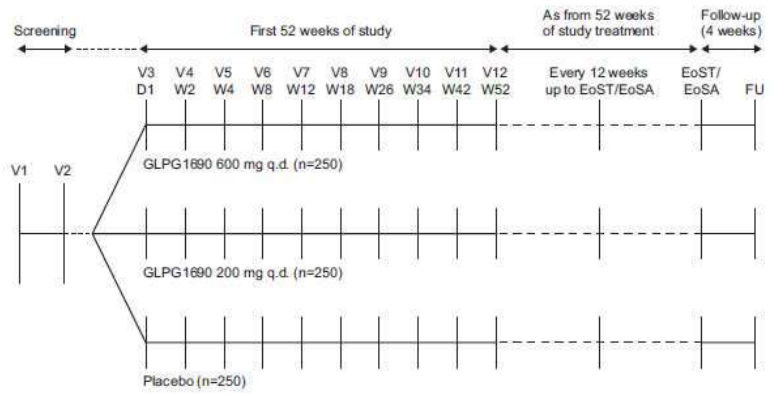


Note: placebo group n=6 and GLPG1690 group n=16
Source: The Lancet

GLPG1690 Phase III (ISABELA 1 and 2) program update expected in Q419

Following the encouraging FLORA results, in 2018 Galapagos announced the design of a worldwide Phase III program, ISABELA, based on feedback from the FDA and EMA. The ISABELA Phase III program consists of two identically designed trials, ISABELA 1 and 2, and intends to enroll a total of 1,500 IPF patients combined. A significant proportion of the patients will be enrolled at sites in the U.S. and EU. The program is intended to support application for a broad label in IPF in both the New Drug Application (NDA) and Market Authorization Application (MAA) submissions in the U.S. and EU, respectively. Patients will continue on their standard of care, including pirfenidone and nintedanib, and will be randomized to one of two doses of GLPG1690 or placebo.

Exhibit 30: Design of the ISABELA 1 and 2 studies



Note: D = day; EoSA = end-of-study assessment; EoST = end-of-study treatment; FU = follow-up; qd = once daily; V = visit; W = week
Source: BMJ

The primary endpoint will be the rate of decline in FVC (in ml) until week 52. Secondary assessments will include respiratory-related hospitalizations, mortality, quality of life, safety and tolerability. The first patient dosing was announced in December 2018. The primary and safety analyses will be performed on the full analysis set (all randomized subjects who received at least one dose of study drug). The primary time point is week 52; analyses conducted at the end of the studies are secondary or supportive.

An interim analysis to assess futility will be conducted when a reasonable number of subjects (e.g., 25% from the two studies combined) have completed 52 weeks of treatment. An independent data monitoring committee (IDMC) will review the interim analysis results and make a recommendation to Galapagos, who will remain blinded. The study will not be terminated for early positive interim efficacy results. We anticipate Galapagos to provide an update on the timing for the interim analysis either on the Q319 earnings conference call or at the R&D Day in November.

Given favorable competitive dynamics, which we discuss in further detail in the next sections of this report, we think it is possible that the ISABELA program could enroll ahead of schedule, setting up a potential interim analysis in H220 rather than H121. We provide further perspective on FVC changes and pivotal study design of ISABELA later in this report as well.

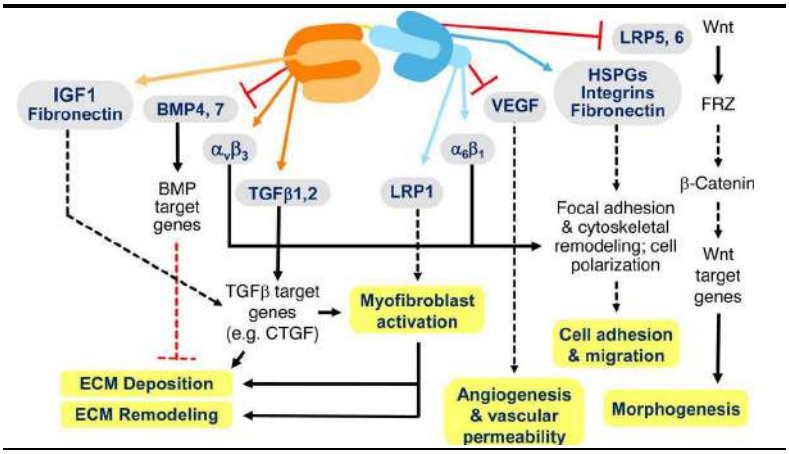
FibroGen's pamrev also in Phase III: completion expected by 2023

Pamrevlumab is an anti-connective tissue growth factor monoclonal antibody

Connective tissue growth factor (CTGF) is a matricellular protein with very complex biology. CTGF modulates cellular responses to the extracellular matrix (ECM). CTGF interacts with a variety of molecules, including cytokines and growth factors, receptors and matrix proteins. These interactions alter signal transduction pathways, either positively or negatively, which results in changes in cellular responses. CTGF has been shown to modulate many signaling pathways leading to cell adhesion and migration, angiogenesis, myofibroblast activation, and extracellular matrix deposition and remodeling, which together lead to tissue remodeling and fibrosis. It has been reported in the literature that inhibition of CTGF expression by siRNA prevents CCl_4-induced liver fibrosis and can

reverse fibrosis when administered after significant collagen deposition is observed. In patients with IPF, CTGF expression is increased in bronchoalveolar lavage (BAL) fluid and in lung tissue, specifically type II alveolar epithelial cells and interstitial fibroblasts. In animal models of lung fibrosis, targeting CTGF diminishes fibrosis.

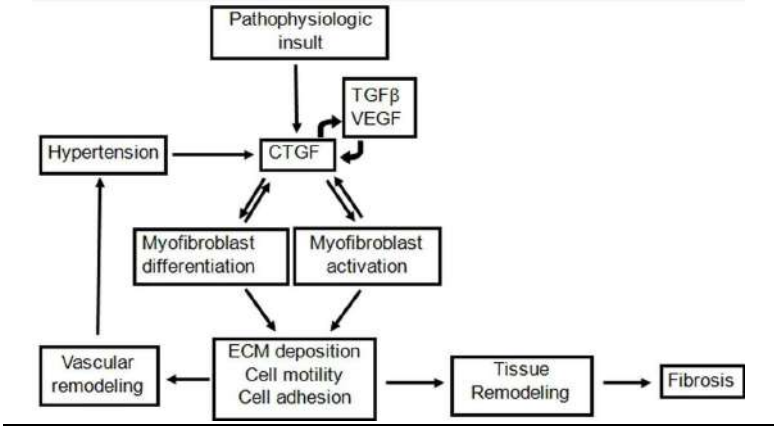
Exhibit 31: CTGF affects multiple signaling pathways and processes important in pathophysiology



Source: Fibrogenesis and Tissue Repair

Many different stimuli can induce expression of CTGF, which then promotes formation of myofibroblasts by modulating differentiation of other cells, including epithelial cells (EMT, epithelial to mesenchymal transition), resident fibroblasts or recruited fibrocytes (bone-marrow-derived, circulating mesenchymal stem cells). CTGF also promotes activation of the myofibroblasts and stimulates ECM deposition and tissue remodeling. Remodeling in the vasculature can produce local hypertension that induces the expression of more CTGF, resulting in a positive feedback loop. Other positive feedback loops result from cytokines whose expression may be stimulated by CTGF, that in turn induce the expression of CTGF. See here, here, here, here, here, and here for additional details.

Exhibit 32: CTGF is a central mediator of tissue remodeling and fibrosis



Source: Fibrogenesis and Tissue Repair

FibroGen was founded in 1993 to discover and develop drugs for fibrosis

FibroGen began studying CTGF shortly after its discovery. FibroGen's accumulated discovery efforts indicate that CTGF is a critical common element in the progression of serious diseases associated with fibrosis. From FibroGen's library of human monoclonal antibodies that bind to different parts of the CTGF protein and block various aspects of CTGF biological activity, FibroGen selected pamrevlumab. FibroGen holds exclusive worldwide rights to pamrevlumab. FibroGen believes that pamrevlumab blocks CTGF and inhibits its central role in causing diseases associated with fibrosis.