H.C.WAINWRIGHT&CO.

Company Update
Healthcare

May 23, 2019

Galapagos NV (GLPG)
Rating: Buy

Debjit Chattopadhyay
646-975-6991
dchattopadhyay@hcwresearch.com

Earl DeSouza
646-975-6990
edesouza@hcwresearch.com

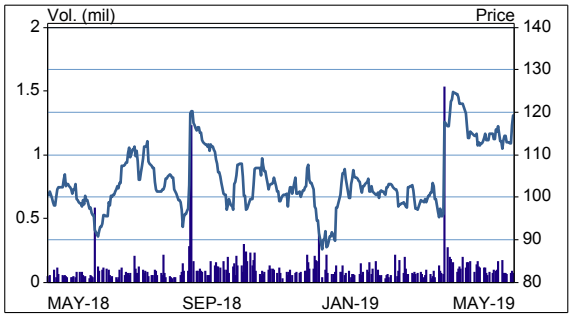
IPF in Vogue With Multiple Phase 3's: Overview and Perspectives

Stock Data	05/22/2019
Price	$119.21
Exchange	NASDAQ
Price Target	$150.00
52-Week High	$125.48
52-Week Low	$85.00
Enterprise Value (M)	$5,141
Market Cap (M)	$6,511
Shares Outstanding (M)	54.6
3 Month Avg Volume	124,687
Short Interest (M)	1.16
Balance Sheet Metrics	
Cash (M)	$1,369.6
Total Debt (M)	$0.0
Total Cash/Share	$25.08

Cash (M): Last reported cash balance during 1Q19 earnings was €1.22B.
General: Currency used is roughly 1 Euro to $1.12 US. Stock price is US$ as on NASDAQ

EPS (€) Diluted			
Full Year - Dec	2018A	2019E	2020E
1Q	€(0.73)	€(0.89)A	€(1.12)
2Q	€(0.42)	€(0.27)	€(1.14)
3Q	€0.27	€(1.17)	€(1.19)
4Q	€0.27	€(1.18)	€0.07
FY	€(0.56)	€(3.50)	€(3.37)

Revenue (€)			
Full Year - Dec	2018A	2019E	2020E
1Q	€44.8	€40.9A	€48.0
2Q	€57.0	€89.4	€48.0
3Q	€103.2	€43.0	€48.0
4Q	€112.8	€43.0	€118.8
FY	€317.8	€216.3	€262.8



IPF remains clinically and commercially important. With up to 40% of commercial opportunity untapped, discontinuation rates as high as 26%, and median survival of about 3.5 years, IPF is now the leading indication for lung transplantation worldwide. The hallmark of the disease is impaired healing after alveolar epithelial injury in the setting of a genetic predisposition. Moreover, IPF and its comorbidities have a severe impact on the quality of life of afflicted patients. Furthermore, the natural history of IPF is highly variable and unpredictable, ranging from: (1) accelerated decline with acute exacerbations; (2) slower stepwise downturn to slowly progressive disease; (3) combined pulmonary fibrosis and emphysema; (4) with pulmonary hypertension; and (5) familial pulmonary fibrosis. Hence, drug development has been challenging due to: (1) incomplete understanding of the disease pathogenesis; (2) unpredictable clinical course; (3) lack of validated biomarkers; (4) poor predictive value of animal models of lung injury; and (5) a need to commit to large clinical trials of long duration to obtain initial evidence of clinical efficacy. The approvals of two antifibrotic agents, pirfenidone and nintedanib, and their 2015 inclusion under clinical practice guidelines have provided some real-world relief with registry data suggesting improved survival in those treated with, versus without, antifibrotic treatments, regardless of baseline disease severity. However, tolerability remains a major concern with up to 21% of patients discontinuing pirfenidone on account of gastrointestinal and skin-related events and almost 27% of patients coming off nintedanib due to diarrhea. GLPG1690 is being evaluated in two identical Phase 3 studies, ISABELA 1 and 2. In a small Phase 2a FLORA study, conducted in 23 subjects with IPF, GLPG1690 exhibited a safety profile similar to placebo and demonstrated favorable effects on mean change from baseline in FVC at week 12 compared with placebo (25 mL vs –70 mL). GLPG1690 doses were selected based on efficacy, safety, tolerability, and PK/PD data, and are expected to allow plasma concentrations >80% inhibitory concentration of LPA to be attained for ≥60% of the dosing interval. Joining GLPG1690 in the Phase roster, is pamrevlumab [Fibrogen (FGEN; not rated)].

GLPG1690 inhibits autotaxin (ATX), an enzyme involved in the production of lysophosphatidic acid (LPA), implicated in IPF. The aberrant wound healing responses that result in fibrosis in IPF are thought to be at least partially mediated by lysophosphatidic acid (LPA). Levels of LPA and autotaxin (ATX), an enzyme involved in its production, are upregulated in patients with IPF. GLPG1690, is a first-in-class, small molecule ATX inhibitor. Galapgaos initiated ISABELA 1 and 2, evaluating GLPG1690 in two identically designed, Phase 3, international, randomized, double-blind, placebo-controlled studies being conducted in parallel. For details on the Phase 3 design, endpoints, and comparison vs. pamrevlumab refer to Exhibit 1. A deeper dive into Phase 1/2 results may be found in Pages 8 to 23.

Exhibit 1: Comparison of Galapagos and Fibrogen Phase 3 Studies

	Galapagos ISABELA 1 and ISABELA2	Fibrogen Phase 3
IPF diagnosis per ATS/ERS/JRS/ALAT	Yes	Yes
Placebo-controlled	Yes	Yes
Masking	Quadruple	Double
Enrollment n	1500	565
Randomization	1:1:1	3:2
Accepts patients currently taking OFEV or Esbriet	Yes	No
FVC window	≥45%	≥50% and ≤90%
DLCO	≥30%	≥30% and ≤90%
Dose	GLPG1690 200 or 600mg/day	30 mg/kg IV Q3W
Treatment duration	52 weeks	48 weeks
Primary Endpoint	Change in FVC from baseline	Rate of decline in FVC
Secondary Endpoints	FVC decline ≥10%	FVC decline ≥10%
Secondary Endpoints	All-cause mortality	All-cause mortality
Secondary Endpoints	Respiratory-related hospitalization	Respiratory-related hospitalization
Secondary Endpoints	St. George's Respiratory Questionnaire	St. George's Respiratory Questionnaire
Estimated Completion Date	December 2021	March 2023
Next update	ERA Sep 2019	NA

Source: FibroGen's (FGEN; not rated) and Galapagos' Phase 3 Trial Attributes from ClinicalTrials.gov.

Statistical analysis of ISABELA trials. An interim analysis based from a recent article, (*BMJ Open Resp Res 2019 doi:10.1136/bmjresp-2019-000422)*, to assess futility will be conducted when 25% of the patients from the two studies combined have completed 52 weeks of treatment. An IDMC would then review the interim results and make a recommendation to the sponsor, whom would remain blinded. The study will not be terminated early for positive interim efficacy results. To account for multiple testing with respect to the primary endpoint within each study, due to two dose comparisons being compared with placebo, a Bonferroni approach is to be applied to the alpha level with a focus on the higher dose. Using this approach, the GLPG1690 600 mg and 200 mg doses would be tested versus placebo at a 0.04 and 0.01 level, respectively. Within the article, the authors describe the statistical analysis plan for ISABELA trials. Here they note that a sample size of 250 per group will have 80% power to show a significant effect, assuming GLPG1690 600 mg has an effect ≥80 mL in the overall population. Furthermore, they provide the exact probabilities of observing statistically significant results based on predicted treatment differences, Exhibit 2. G600 and G200 are the two doses and the mLs denotes the treatment differences of the treatment groups with placebo. Assuming a standard deviation on a W52 decline in FVC of 275 mL, the probability that zero, one or two of the treatment comparisons with placebo will be statistically significant and the power for each scenario are provided in the table (Exhibit 2). Note, ISABELA clinical programs potentially reflect real-world patient dispositions, considering subjects in ISABELA 1 and 2 must have an FVC ≥45% predicted of normal, whereas predicted FVC was required to be ≥50% in the CAPACITY and INPULSIS studies, and 50%–90% in the ASCEND study and the planned Fibrogen Phase 3 study. In addition, unlike in CAPACITY and ASCEND, which excluded subjects aged >80 years, or in Fibrogen's study, there is no upper age limit in ISABELA 1 and 2. Furthermore, in contrast to previous Phase 3 IPF trials, in the ISABELA program GLPG1690 is being evaluated in conjunction with approved local SOC.

Exhibit 2: Probability of Success in ISABELA Trials Based on Difference in FVC

	0 significant %	1 significant %	2 significant %	Powering %
G600-80 mLs G200-80 mLs	6.8	23.4	69.9	93.2
G600-80 mLs G200-60 mLs	10.1	46.9	43.0	89.9
G600-80 mLs G200-20 mLs	11.5	84.4	4.1	88.5
G600-80 mLs G200-0 mLs	11.2	88.0	0.7	88.8
G600-90 mLs G200-60 mLs	5.1	51.1	43.8	94.9
G600-90 mLs G200-60 mLs	95.2	4.5	0.3	4.8

Source: BMJ Open Resp Res 2019.

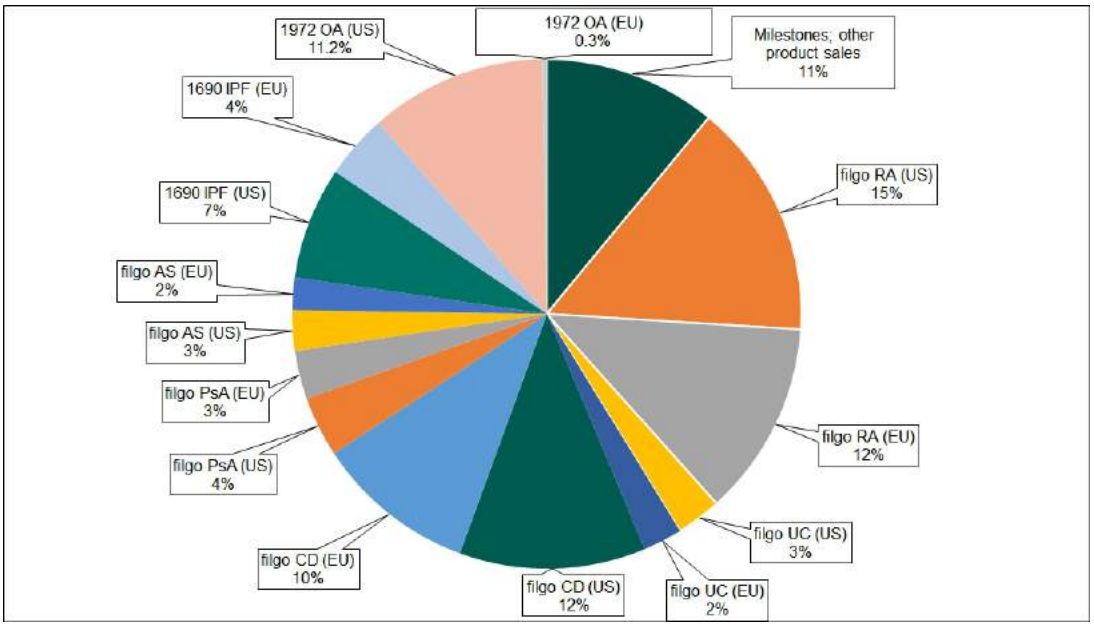
GLPG1690 and pamrevlumab have differing MOAs allowing expanded patient population for '1690. Lysophosphatidic acid (LPA) has been found in bronchoalveolar lavage fluid and exhaled breath condensate of IPF subjects. LPA acts as a signaling molecule through LPAR which couples to G-proteins. GLPG1690 inhibits autotaxin, the enzyme that produces LPA. LPA is a completely distinct target from that of the approved drugs Esbriet and OFEV which target VEGF, FGF, PDGF, and TGF-β signaling pathways. Pamrevlumab is a mAb targeting CTGF, which is regulated by many factors, including TGF-β, EGFR, and PDGF, the same targets as OFEV and Esbriet. Thus we would expect that pamrevlumab may have similar efficacy to OFEV and Esbriet, and in the 52-week Phase 2 clinical trial, and this is what was observed, however it lacked the significant nausea and vomiting which usually accompanies OFEV and Esbriet, perhaps due to the difference in delivery method (IV vs. oral). In the short 12-week study of GLPG1690, no AEs were noted and efficacy was superior to OFEV and Esbriet at a similar time point, however the study is much to short to support a strong conviction. The importance of the distinct mechanism is the opportunity for combination therapy with OFEV or Esbriet for '1690. This is reflected in the design of the ISABELA1 and 2 trials in that patient currently taking OFEV or Esbriet are permitted, whereas in the trial of pamrevlumab, these patients are excluded. Interestingly, from the small Phase 2 study of 103 patients in IPF, Fibrogen reported standard deviations (SD) of 24 and 31 mLs for placebo and treatment groups, respectively, probably due to due to the use of quantitative high-resolution computed tomography (qHRCT) scans, that is also being used in the pamrevlumab Phase 3 program. The SD in the Fibrogen study was one-tenth those reported in the OFEV and Esbriet trials, which averaged 285 mL. Galapagos has published a study using a qHRCT method known as Functional Respiratory Imaging (FRI), but has not indicated the use of this in the ISABELA trials.

Exhibit 3: No Changes in Driver Programs in Catalyst Calendar 2019

Program	Indication	Phase and Milestone	Timing	Impact on Stock
Filgotinib	Rheumatoid Arthritis	FINCH 2, Completed, Manuscript Publication	1H19	+
Filgotinib	Ulcerative Colitis	SELECTION Phase 3 Recruited	1H19	+
'1972	Osteoarthritis	Presentation at OARSI	1H19	+
Mor106	Atopic Dermatitis	GECKO Phase 2 start	1H19	+
'1690	Systemic Sclerosis	Phase 2 start	1H19	+
'3312, '2534, '3121	Inflammation	Phase 1 start	1H19	+
Filgotinib	Rheumatoid Arthritis	FDA, EMA filings for RA approval	2H19	+++
Filgotinib	Sjogren's	Phase 2 PoC topline	2H19	++
Filgotinib	Cutaneous Lupus Erythematosus	Phase 2 PoC topline	2H19	++
Filgotinib	Psoriatic Arthritis	Phase 3 Start	2H19	+
GLPG1205	Idiopathic Pulmonary Fibrosis	PINTA Phase 2 recruited	2H19	+
GLPG1205	Idiopathic Pulmonary Fibrosis	ACS Conference	2H19	+
GLPG1972	Osteoarthritis	ROCELLA Phase 2b recruited	2H19	+
Mor106	Atopic Dermatitis	IGUANA Phase 2 topline	2H19	+++
Mor106	Atopic Dermatitis	Japan study start	2H19	+
Mor106	Atopic Dermatitis	SQ bridging topline	2H19	+++
Mor106	Atopic Dermatitis	GECKO Phase 2 recruited	2H19	+
'3312, '2534, '3121	Inflammation	Topline data	2H19	++
'3970	Inflammation	Phase 1 start	2H19	+
'3312	Inflammatory Bowel Disease	Phase 1 start	2H19	+

Source: Galapagos Earnings Presentation April 26, 2019.

Exhibit 4: Weighted Contribution of Individual Disease Segments to Target



Source: H.C. Wainwright & Co. estimates.

Valuation and risks to our investment thesis. Our 12-month, $150 price target on shares of Galapagos is derived from a 13-year DCF-based, sum-of-the-parts analysis. Our DCF is driven by: beta of 1.34, terminal growth rate of -3.0%, risk premium of 4.93%, calculated WACC of 9.3%, and tax rate of 20% beginning in FY 2025. Filgotinib (66%), GLPG1690 (11%), GLPG1972 (11%) together make up 88% of our value, with the remainder derived from the probability-adjusted, filgotinib-associated milestone payments. For filgotinib, we assume POS in the range of: 75% (upped from 65% previously) for RA based on the FINCH 1 and 3 clinical updates released post close on March 28, 2019, 65% for UC, and 60% for CD, PsA and AS each, whereas for '1690 and '1972, we assign a 35% and 10% POS, respectively. Note, filgotinib, in our view, did not materially underperform upadacitinib in the FINCH 1 and 3 studies, which we assigned a low probability outcome due to its competitive profile, along with our $2.9B in 2027 sales estimate for the RA segment. Other key risks include: emergence of safety concerns, clinical risks, regulatory risks, and financial risks. Furthermore, regulatory and commercial strategy for filgotinib is under the control of partner, Gilead, not an established player in autoimmune indications. Hence, Gilead may not be able to drive rapid adoption of filgotinib, especially if the overall profile is relatively undifferentiated from AbbVie's upadacitinib, in our view. Hence, our estimates could be negatively impacted if AbbVie successfully leverages its market positioning with Humira during the launch of upadacitinib, which is likely to be a year ahead of filgotinib. The next two value drivers for Galapagos are GLPG1690 and GLPG1972 programs, both of which are high-risk, high-reward programs given the checkered history of drug development of each target. Hence, there are significant clinical risks associated with these programs, which we believe are adequately reflected in our POS assumptions.

Valuation: Galapagos (GLPG) Discounted Cash Flow (DCF) Analysis

		Discounted Cash Flow Analysis	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	TV
Ticker	GLPG															
Period	2028E	EBIT (000s €)	€ (209,626)	€ (202,209)	€ (226,466)	€ (64,638)	€ 144,949	€ 620,171	€ 1,024,744	€ 1,573,758	€ 1,821,395	€ 1,948,535	€ 2,025,401	€ 2,036,434	€ 2,046,447	
Beta est	1.34	*% growth*	*367.8%*	*-3.5%*	*12.0%*	*-71.5%*	*-324.2%*	*327.9%*	*65.2%*	*53.6%*	*15.7%*	*7.0%*	*3.9%*	*0.5%*	*0.5%*	
Risk-free rate (R_F)(10 yr yield)	2.65%	*Tax rate*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	
Risk premium (R_p)	4.93%	EBIT*(1-t)	(209,700)	(202,209)	(226,466)	(64,638)	144,949	620,171	819,795	1,259,006	1,457,116	1,558,828	1,620,321	1,629,147	1,637,157	
Cost of equity (KE)	9.3%	Capital expenditures	(5,853)	(6,000)	(6,600)	(7,260)	(7,986)	(8,785)	(9,663)	(10,629)	(11,692)	(12,862)	(14,148)	(15,562)	(17,119)	
Cost of debt (K_D)	0.0%	*% growth*	*-43.7%*	*2.5%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	
Terminal growth rate	-3.0%	Depreciation	11,008	12,000	12,600	13,230	13,362	13,496	13,631	13,767	13,905	14,044	14,184	14,326	14,469	
Terminal value (% of total value)	46.3%	*% growth*	*162.7%*	*9.0%*	*5.0%*	*5.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	*1.0%*	
Shareholder equity	6,829,892	Change in non-cash working capital	(11,774)	(20,862)	(7,377)	(16,245)	(2,530)	17,025	44,523	82,363	118,093	160,142	198,398	240,768	279,303	
Debt outstanding	0	*% growth*	*-61.9%*	*77.2%*	*-64.6%*	*120.2%*	*-84.4%*	*-773.0%*	*161.5%*	*85.0%*	*43.4%*	*35.6%*	*23.9%*	*21.4%*	*16.0%*	
Total capital	6,829,892	**Free cash flow to the firm**	**(181,065)**	**(163,347)**	**(199,889)**	**(27,903)**	**168,827**	**625,427**	**798,566**	**1,201,040**	**1,364,620**	**1,425,592**	**1,450,255**	**1,418,268**	**1,389,442**	**11,047,286**
Equity/cap	100.0%	*Discount factor*	*1.00*	*0.92*	*0.84*	*0.77*	*0.70*	*0.64*	*0.59*	*0.54*	*0.49*	*0.45*	*0.41*	*0.38*	*0.35*	
Debt/cap	0.0%	**Present value of cash flows**	**(181,065)**	**(149,508)**	**(167,455)**	**(21,395)**	**118,484**	**401,741**	**469,499**	**646,301**	**672,114**	**642,659**	**598,389**	**535,613**	**480,272**	**3,495,074**
WACC (calculated)	9.3%	**Value of firm**	**7,540,722**													
WACC (applied)	9.3%	Debt	0													
Shares outstanding	56,220	**Value of equity**	**7,540,722**													
		Value per share ($)	**$ 150.00**													

Source: H.C. Wainwright & Co. estimates.

IPF Background and Clinical Characteristics

- **Progressive accumulation of collagen scar tissue in lungs causing irreversible loss of lung function**
- **Cause poorly understood**
- **Five-year survival rates between 20% to 30%**
- **Mouse model not reliable**
- **Honeycombing of lungs noted in CT scan**
- **Reduction in Forced Vital Capacity (FVC)**
- **Reduction in oxygen diffusion rates (DlCO)**
- **Resting oxygen desaturation**

Source: UpToDate, Inc. 2019

Clinical and Commercial Need in IPF

- Two approved anti-fibrotic therapies designed to slow lung scarring, and hence, halt rapid progression, with significant GI-tract AEs
  - Esbriet® (Pirfenidone) by Roche (RHHBY; not rated), oral medication taken three times daily
  - OFEV® (Nintedanib) by Boehringer Ingelheim (private); oral medication taken twice daily
- GLPG1690, an autotaxin inhibitor, is currently in Phase 3
  - In the FLORA Phase 2a trial, patients on treatment with GLPG1690 showed improvement in forced vital capacity (FVC) at 12 weeks, with an encouraging safety profile
- Pamrevlumab, a monoclonal antibody targeting CTGF intends to initiate a Phase 3 trial soon
  - In the PRAISE Phase 2 pamrevlumab signfiicnatly reduced change in FVC from baseline and had an acceptable safety profile

Given the Unmet Clinical Need, IPF Is an Active Area of Pharma Investment

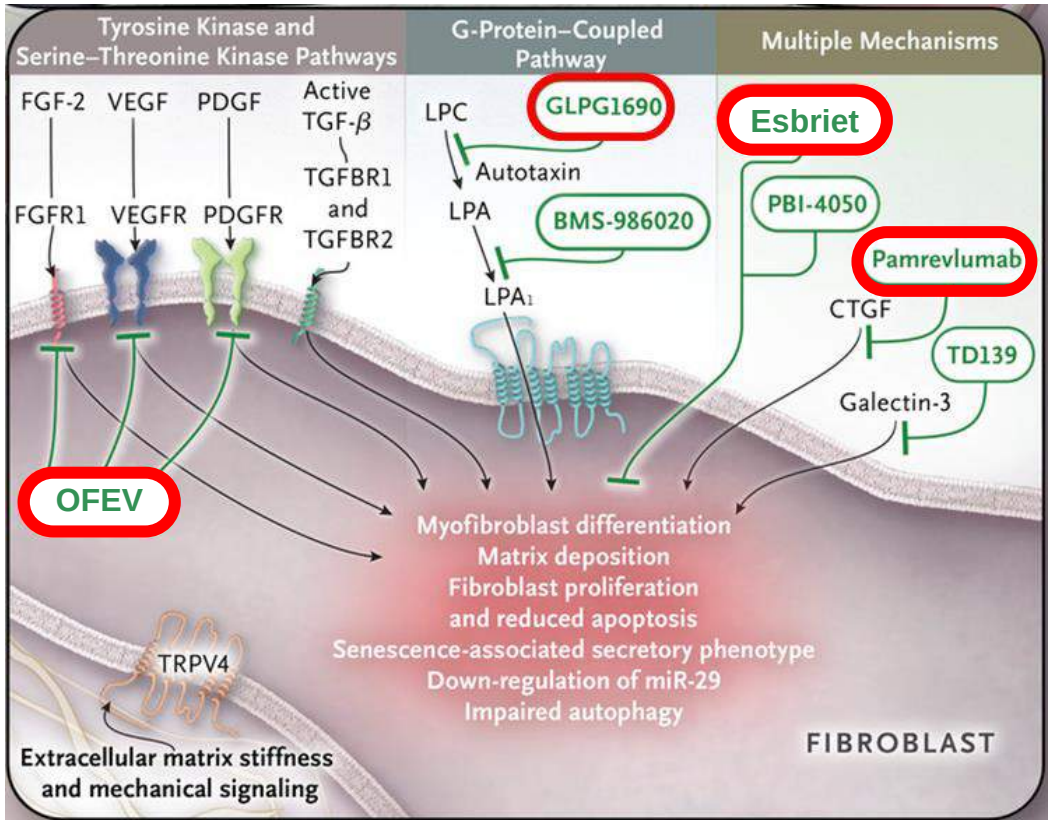
Esbriet is a small molecule that inhibits TGFβ

OFEV is a small molecule that blocks the tyrosine kinase activity of PDGFR, FGFR, and VEGFR

GLPG1690 inhibits autotaxin mediated production of lysophosphatidic acid

Pamrevlumab inhibits CTGF

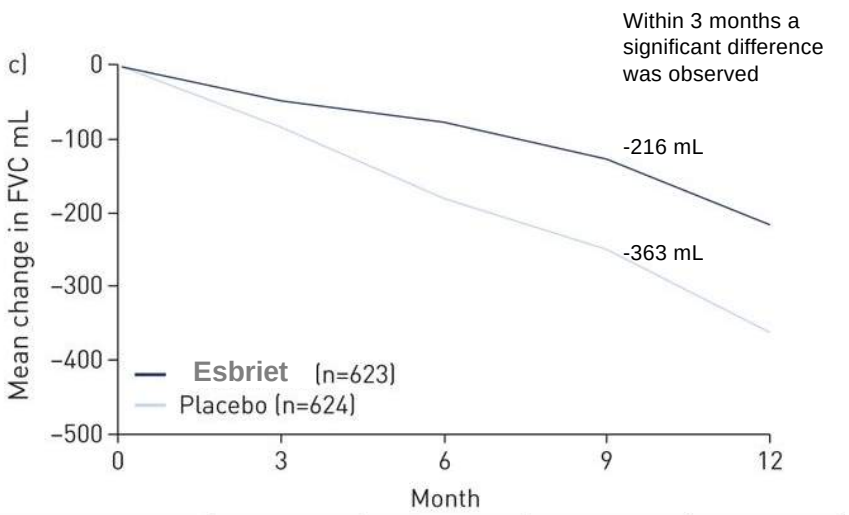
OFEV & Esbriet inhibit similar pathways which impinge on the target of pamrevlumab, but GLPG1690 acts via a novel mechanisms potentially allowing for additive benefit



Source: N Engl J Med 2018 (378) http://doi.org/10.1056/NEJMra1705751.

Lessons From the Esbriet Clinical Program—Clinically Meaningful Impact on Rate of Disease Progression

- **Approved based on pooled analysis of three Phase 3 studies**
- **Pooled analysis reflected outcomes from a total of 623 IPF patients treated with 2,403 mg/day Esbriet vs. 624 patients on placebo**
- **Patients were 40 to 80 years old**
- **DlCO >35% and FVC >50% of predicted**
- **52-weeks measured mean change in FVC in mLs primary endpoint**

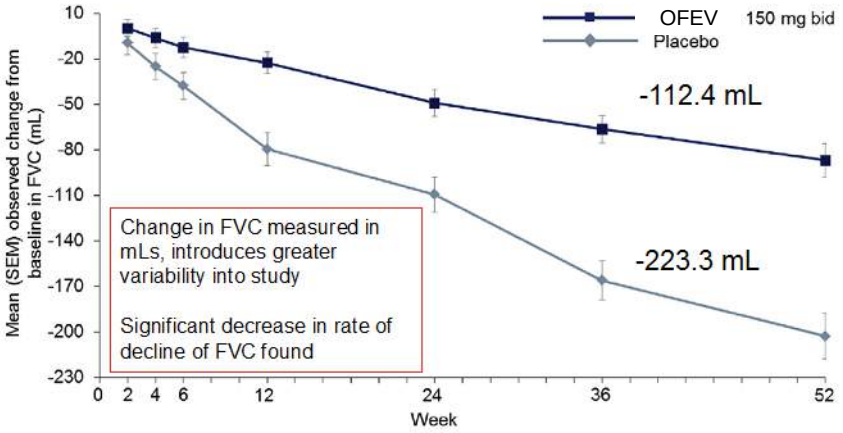


Absolute difference mL	36	104	123	148
Relative difference %	43.5	57.3	49.1	40.7
Rank ANCOVA p-value	<0.001	<0.001	<0.001	<0.001

Sources: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/208780Orig1s000SumR.pdf and Eur Respir J 2016 (47) DOI:10.1183/13993003.00026-2015.

Lessons From the OFEV Clinical Program—Clinically Meaningful Impact on Rate of Disease Progression

- **Approved based on pooled analysis of three Phase 3 studies**
- **Pooled analysis reflected outcomes from a total of 723 IPF patients treated with 150 mg BID OFEV vs. 508 patients on placebo**
- **Patients were >40yrs**
- **DlCO 35-79% and FVC >50% of predicted**
- **Pivotal, Randomized, Double-blind, placebo controlled**
- **52-weeks measured mean change in FVC in mL primary endpoint**



Sources: Adapted from https://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/022535Orig1s000SumR.pdf and Respiratory Medicine 2016 (113) DOI: 10.1016/j.rmed.2016.02.001 by H.C. Wainwright & Co.

Reduced Treatment Emergent Mortality Observed With Both OFEV and Esbriet

Patients, n(%)	Esbriet 2403 mg/d	Placebo	P-value
Treatment emergent Deaths	14 (2.2%)	32 (5.1%)	.007
SAE	128 (20.5%)	139 (22.3%)	.43

Patients, n (%)	OFEV 600 mg/d	Placebo	p-value
Treatment emergent deaths	25 (3.5%)	34 (6.7%)	0.027
SAE	217 (30%)	153 (30.1%)	1

Source: Adapted from Eur Respir J 2016 (47) DOI: 10.1183/13993003.00026-2015 and Respiratory Medicine 2016 (113) DOI:10.1016/j.rmed.2016.02.001 by H.C. Wainwright & Co.

Reduced all cause mortality (p= 0.04) evaluated based on deaths occurring between randomization and within 28 days of last dose of study drug. Outcomes assessed by blinded clinical investigators and involved 1,247 patients

Reduced treatment emergent mortality, p=0.027 measured as deaths occurring within 372 days of randomization and assessed by blinded adjudication committee involving 1,231 patients

Pamrevlumab Targets IPF

- **Pamrevlumab by Fibrinogen (FG-3019) is a human monoclonal antibody against connective tissue growth factor (CTGF) administered via IV.**
- **CTGF is regulated by many factors, including TGF-β, EGFR, and PDGF. All of which are targets of either OFEV or Esbriet, which bodes well for likely clinical efficacy, but limits opportunities for additive effects.**
- **In an open-label Phase 2 clinical trial of Pamrevlumab, without placebo, patients experienced low TEAE with normal levels of GI problems, unlike OFEV or Esbriet**

	FG-3019 15 mg/kg	FG-3019 30 mg/kg
Change from baseline FVC mLs (SE)	-150 (40)	−130 (60)

- **No placebo was used so the significance of these results is unclear**

- **Another Phase 2, placebo controlled clinical trial, PRAISE, measured qHRCT estimated FVC**

Change from baseline, LS Mean (SD) of qHRCT	W24 mLs (SD)	W48 mLs (SD)
FG-3019	25.1 (17.63)	75.7 (24.55)
Placebo	100.4 (19.2)	159.1 (31.06)
p-value	.009	.038

- **Pamrevlumab is likely to perform as well as Esbriet or OFEV, does not have the AEs, but does require injection**

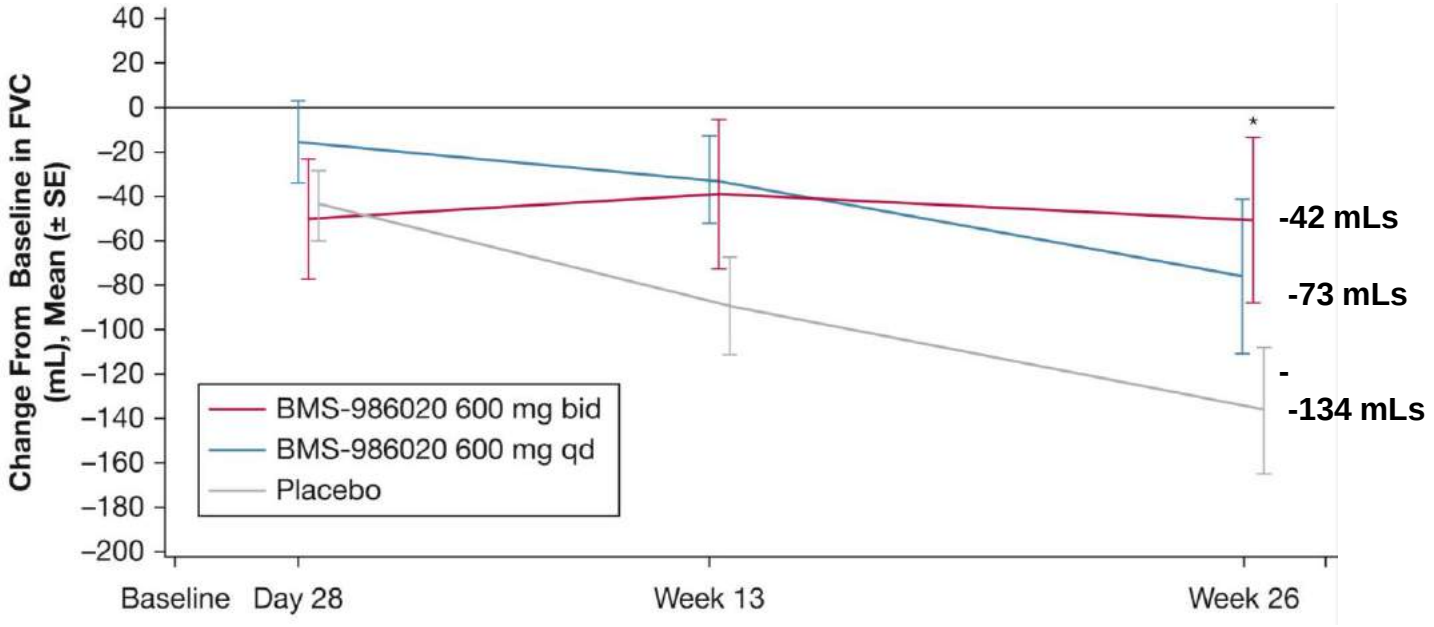
Source: Eur Respir J. 2016 (47;5), American Thoracic Society 2018 International Conference, Matrix Biol. (2018) 68–69, 44–66.

IPF Correlates Point to LPA as a Novel Target
Enter GLPG1690

- **PDGF secreted at four times the normal amount from IPF patient's alveolar macrophages**
- **Enhanced expression of FGF-2, FGFR-1, and FGFR-2 have been noted in IPF patients, and these are upregulated by TGF-β**
- **Serum levels of VEGF correlate well with IPF disease progression**
- **Lysophosphatidic acid (LPA) has been found in bronchoalveolar lavage fluid and exhaled breath condensate of IPF subjects. LPA acts as a signaling molecule through LPAR which couple to G-proteins**

Source: UpToDate, Inc. 2019 and Front. Med. 2018 https://doi.org/10.3389/fmed.2018.00180

LPA Target Clinically Validated in 26-Week Trial Using a Different Drug



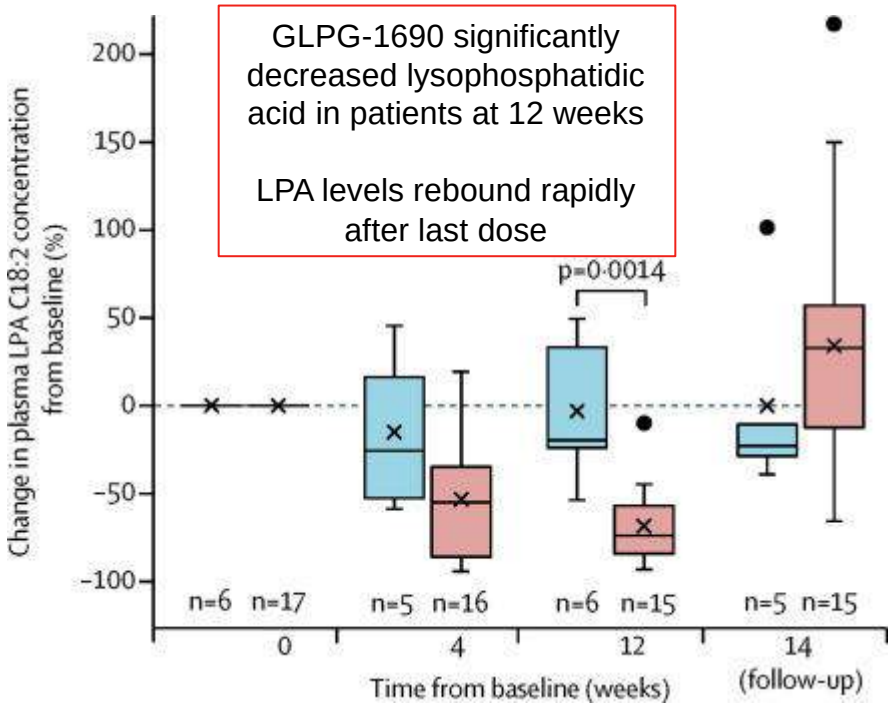
Source: Chest 2018 (154;5) DOI: 10.1016/j.chest.2018.08.1058

- **Bristol Myers Squibb's (BMY; not rated) small molecule BMS-986020 was tested in Randomized, Double-Blind, Placebo-Controlled, Phase 2 Trial in IPF patients over 26 weeks measuring safety and efficacy.**
- **Study stopped due to off-target cholecystitis, which BMS reports is not a class effect of LPA antagonists, and are developing new anti-LPA drugs**
- **Stat-sig reduced FVC decline in 600 mg bid dose compared with placebo at 26 weeks and plateauing of FVC**

GLPG1690 Engaged the Intended Target and Reduced LPA Levels in a Small 12-Week Study

Phase 2a FLORA study

- **Treated a total of 17 IPF patients treated with 600 mg QD GLPG1690 and compared to five patients on placebo**
- **Patients were >40yrs**
- **DiCO >30% and FVC >50% of predicted**
- **Pivotal, Randomized, Double-blind, placebo controlled**
- **12-weeks measured mean change in FVC in mL primary endpoint**



Source: Adapted from The Lancet Respiratory Medicine 2018 (6;8) DOI: 10.1016/S2213-2600(18)30181-4 by H.C. Wainwright & Co.

Functional Respiratory Imaging Identifies GLPG1690 Improvement in Phase 2a

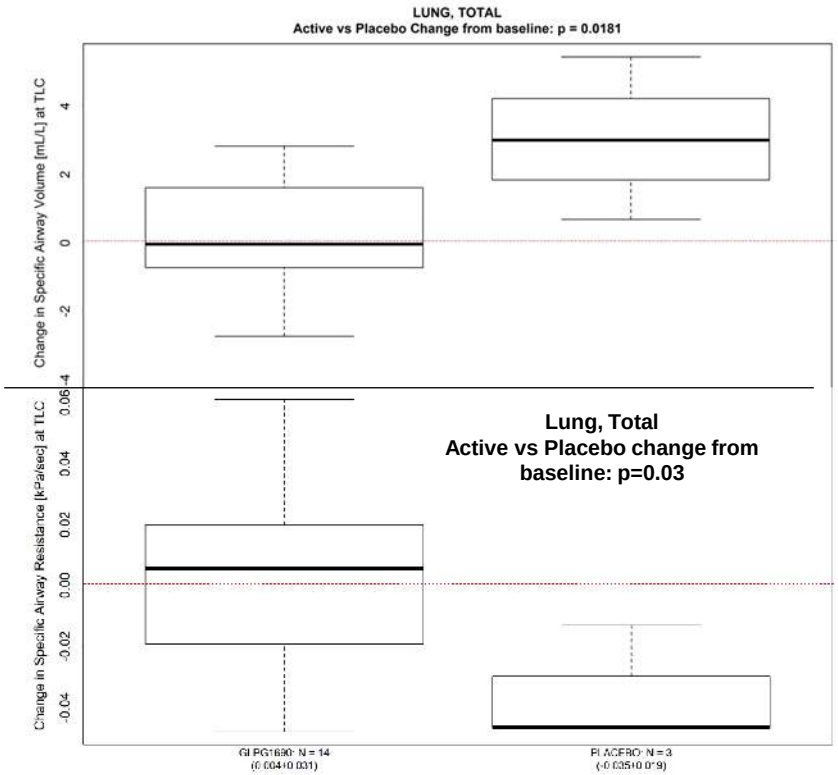
FRI could be better at describing IPF progression qualitatively and quantitatively than FVC

- Lobe volumes and airway volumes could already be severely affected by IPF even when FVC is normal
- Endpoints describing changes in regional anatomical structure and function have the potential to be more sensitive than FVC, resulting in smaller and shorter clinical trials

FRI correlations with FVC describe IPF in high resolution

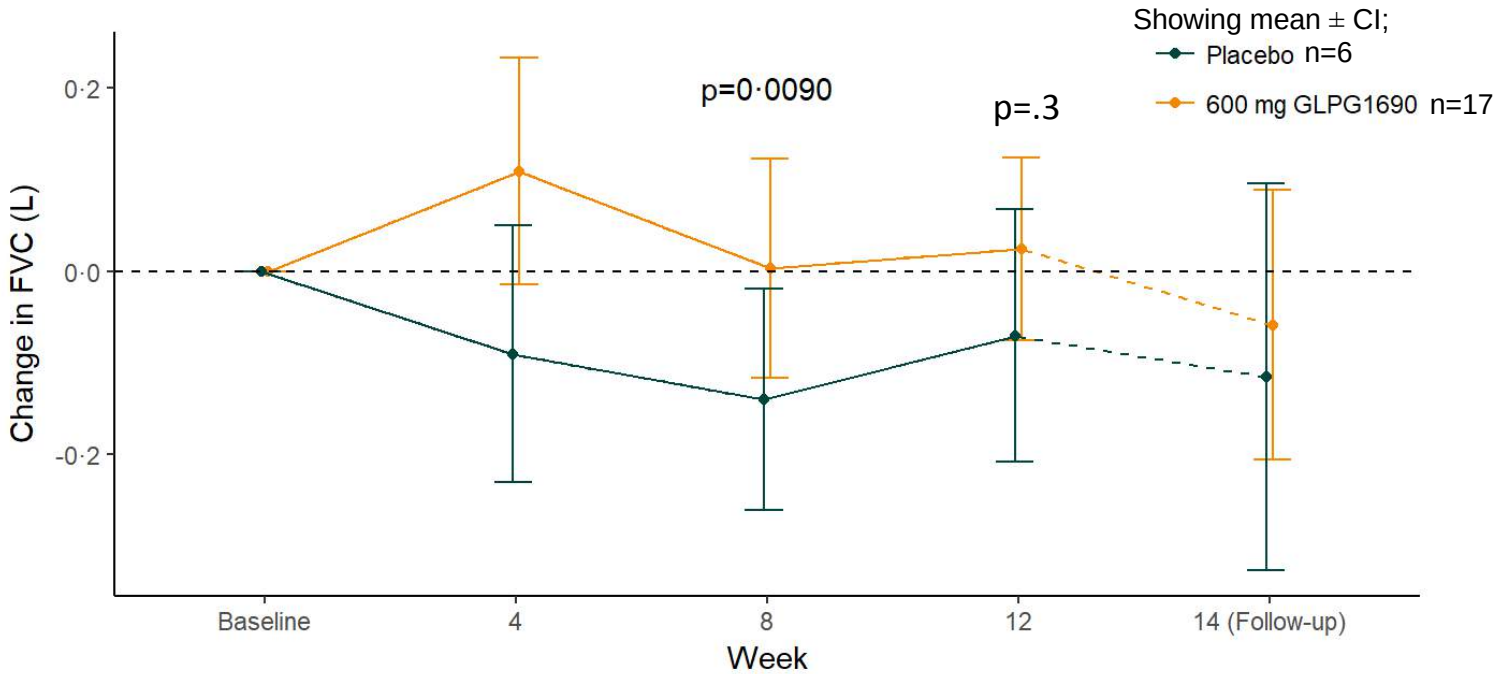
- FRI-determined specific airway volume negatively correlate with FVC (R^2=.18, p<.001)
- FRI-determined lobe volume positively correlated with FVC (R^2=.61, p<.001)
- FRI-determined fibrotic tissue negatively correlates with FVC (R^2=.38, p<.001)

FRI detects a significant change in airway volume in GLPG1690 treated group at W12 when FVC did not



Source: Am J Respir Crit Care Med (199;1) DOI: 10.1164/rccm.201803-0444PP and Respiratory Research 2018 (19:213) DOI:10.1186/s12931-018-0918-5

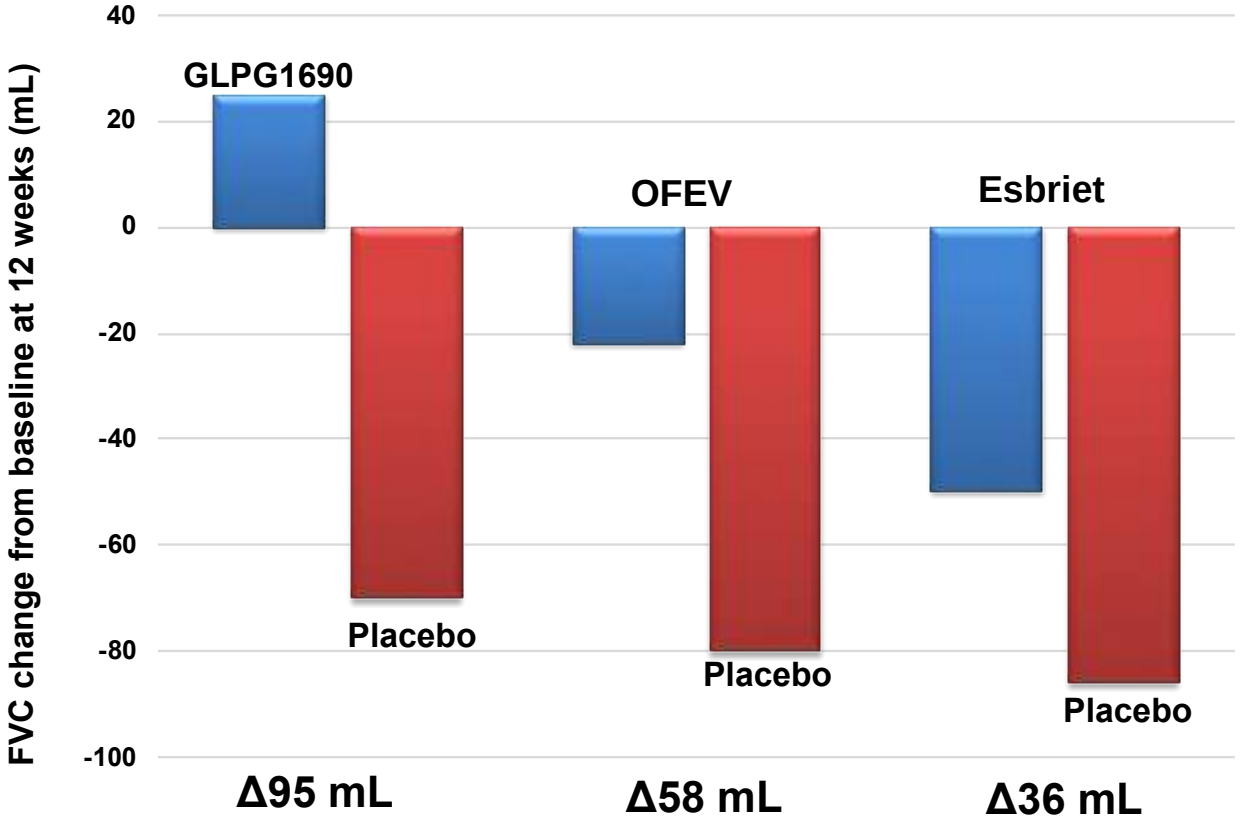
FVC Trends Favor GLPG1690, but Study Size and Duration Limit Interpretation



Source: The Lancet Respiratory Medicine 2018 (6;8) https://doi.org/10.1016/S2213-2600(18)30181-4 .

- **Trends in FVC over 12-weeks observation favor patients treated with GLPG1690**
- **However, no significant difference detected in FVC at 12 weeks using paired t-test**

FVC Increase in the 23 Patients on GLPG1690 Is Larger Than effects Observed With OFEV and Esbriet at Week 12



If the FVC data are reconfirmed in the ISABELA 1 & 2 studies GLPG1690 the outcome would be clinically and commercially very significant

Source: H.C. Wainwright & Co.

GLPG1690 Appears More Tolerable Than OFEV and Esbriet

Comparison of fold-increase over placebo for adverse events that occurred at >10% frequency in patients

	GLPG1690	OFEV	Esbriet
Bronchitis	n/a	0.95	1
Cough	0.71	0.87	1
Diarrhoea	0.18	3.44	1
Dyspepsia	0.71	n/a	3
Dyspnoea	n/a	0.66	1
Acid reflux	n/a	n/a	2
Nasopharyngitis	0.71	0.83	1
Nausea	n/a	3.42	2
Infections	0.82	0.83	1
Vomiting	n/a	3.93	2
n/a indicates incidences were less than 10% in placebo and treatment arms			

Source: BMJ Open Resp Res 2019, H.C. Wainwright & Co. estimates.

- **GI symptoms are less frequent with GLPG1690 compared with OFEV and Esbriet**
- **GI adverse events are a primary reason for poor patient compliance with current IPF medications**
- **AEs led to drug discontinuation in 20.9% and 26.3% of Esbriet-treated and OFEV-treated patients with IPF, respectively**

ISABELA Phase 3 program and Comparison to Other IPF Phase 3's

- Galapagos intends to test GLPG1690 in 1,500 IPF patients over 52 weeks in a global program consisting of two identically designed trials, ISABELA 1 (NCT03711162) and ISABELA 2
- All patients would continue the assigned treatment until the last patient in each of the studies has completed 52 weeks of treatment
- Implies some patients would be followed for substantially more than 52 weeks, allowing for a broader assessment of treatment-related adverse events (NCT03733444)
- Patients would be randomized to receive either 200 mg or 600 mg GLPG1690 or a placebo, in addition to their IPF standard of care treatment
- Doses selected are expected to allow plasma concentrations >80% inhibitory concentration of LPA to be attained for ≥60% of the dosing interval.
- Rate of decline of forced vital capacity (FVC) in mL over 52 weeks is the primary endpoint
- Disease progression defined as the composite endpoint of first occurrence of ≥10% absolute decline in percent predicted forced vital capacity (%FVC) or all-cause mortality is a key secondary endpoint
- Interim study with 42 patients per condition after 52-weeks

Study	Age	Characteristics	Study Weeks	Treatment groups	N
GLPG1690 Phase 2a	>40	FVC>50% DlCO>30%	12	Placebo GLP 600 mg/day	5 15
GLPG1690 Phase 3 (ISABELA)	>40	FVC>45% DlCO>30%	52	Placebo + (Esb/OFEV/None) GLPG1690 600 mg mg/day + (Esb/OFEV/None) GLPG1690 200 mg/day + (Esb/OFEV/None)	1:1:1
OFEV	>40	FVC>50% DlCO>35-79%	52	Placebo OFEV 150 mg bid	723 508
Esbriet	40-80	FVC>50% DlCO>35%	52	Placebo Esbriet 2403 mg bid	624 623

Historical Drop	Placebo	OFEV	Esbriet
	223 mLs	**112 mLs**	**132 mLs**

Source: BMJ Open Resp Res 2019, H.C. Wainwright & Co.

Statistical Analysis of ISABELA trials

- The proportion of subjects who have an absolute decline ≥10% in %FVC at least once during the study, or who die, will be analysed using logistic regression analysis using data up to week 52
- FVC and %FVC will be analysed by subgroups (eg, baseline characteristics, background treatment and stratum)
- Time-to-event data (including hospitalisations and mortality) will be presented as Kaplan-Meier estimates
- In addition, a Cox proportional hazards model with terms for age, sex, height and stratum may be used to estimate and test hazard ratios for each dose compared with placebo
- A Bonferroni approach will be applied to the alpha level with a focus on the higher dose. Using this approach, the GLPG1690 600 mg and 200 mg doses will be tested versus placebo at a 0.04 and 0.01 level, respectively
- A sample size of 250 per group will have 80% power to show a significant effect, assuming GLPG1690 600 mg has an effect ≥80 mL in the overall population

	0 significant %	1 significant %	2 significant %	Powering %
G600-80 mLs G200-80 mLs	6.8	23.4	69.9	93.2
G600-80 mLs G200-60 mLs	10.1	46.9	43.0	89.9
G600-80 mLs G200-20 mLs	11.5	84.4	4.1	88.5
G600-80 mLs G200-0 mLs	11.2	88.0	0.7	88.8
G600-90 mLs G200-60 mLs	5.1	51.1	43.8	94.9
G600-90 mLs G200-60 mLs	95.2	4.5	0.3	4.8

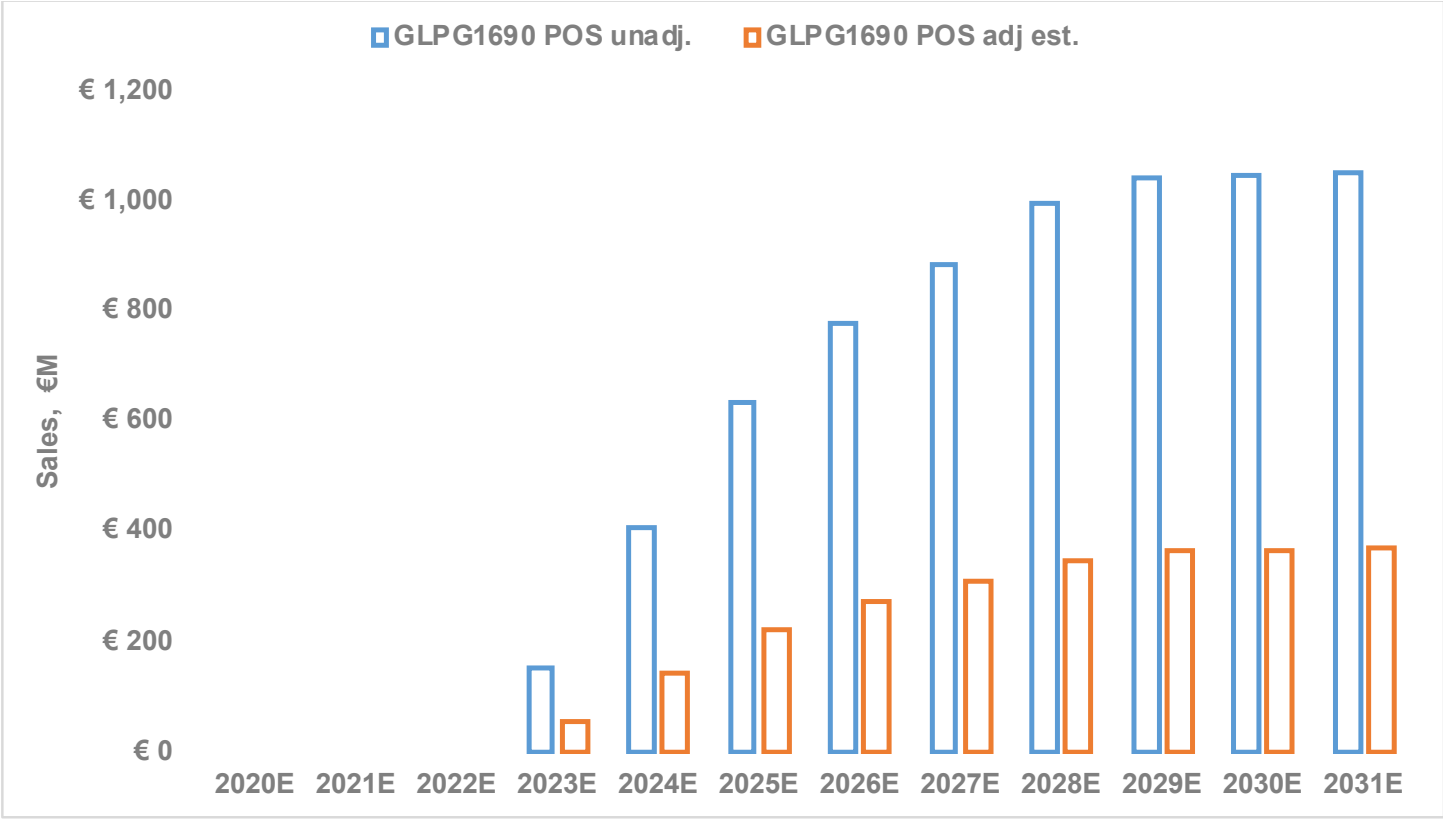
G600 and G200 are the two doses and the mLs denotes the treatment differences of the treatment groups with placebo. Assuming a standard deviation on W52 decline in FVC of 275 mL, the probability that zero, one or two of the treatment comparisons with placebo will be statistically significant and the power for each scenario are provided in the table

Source: BMJ Open Resp Res 2019.

Why we Think ’1690 is Valuable

- **‘1690 inhibits ATX and drops LPA *in vivo***
- **12-week average FVC increase, not decrease, in 17 patients is unprecedented**
- **FRI shows stabilization of IPF upon ‘1690 dosing**
- **‘1690 has low GI and Nausea AEs**
- **LPA target validated in IPF from BMS study as well**
- **Huge unmet need with best drugs having 25% attrition due to AEs**

GLPG1690 POS-Adjusted and Unadjusted Estimates



Source: H.C. Wainwright & Co. estimates.