

Wimal Kapadia

 +44-207-170-5153
 wimal.kapadia@berstein.com

 Rushee Jolly, Ph.D, CFA, ACA
 +44-207-170-0516
 rushee.jolly@berstein.com

European Specialty Pharma & Biotech

Galapagos NV

Rating

Market-Perform (Outperform *OLD*)

Target Price


155.00 EUR

Galapagos: Downgrade to Market-Perform - see you in 2H 2020?

GLPG is up 85% YTD and following the GILD deal, the Rinvoq (Upad) label and the stock close to our PT, we take a step back and wait until we approach stock moving catalysts in 2H20 where at current levels, the risk/reward will still be to the upside. Downgrade to M/P (for now).

Filgotinib risk/reward mixed. Our base assumptions are (i) GILD use a Priority Review Voucher and gain approval in 2Q20. (ii) Filgotinib gets a thrombosis warning on label similar to competition. (iii) Filgotinib to get both 100mg and 200mg doses filed (and approved) – likely to be the case but you cannot say with certainty. Whilst most investors we speak to tend to agree on all 3 – we are not sure all model filgotinib as conservatively. We agree that the upcoming p2 data in CLE and Sjogren's (deep dive - [link](#)) has a positive risk/reward but it is not stock moving. We think the safety nuances for filgo vs. peers will come out eventually but it will take time to educate physicians and until then you will have debate.

Toledo is unlikely to move the stock higher. We will see first data from the program in 1H20. The debate is if GLPG will move on p1 data - we are unconvinced by the magnitude.


2H20 gets very interesting again. We will get clarity soon on IPF futility timeline for the p3 and importantly, interim data will see the stock move given our view of "get the drug approved in IPF, it will be a blockbuster". The p2 PINTA data in 2H20 will support excitement in the franchise. Before the end of 2020 we will also get more from (i) MOR106 in AtD and (ii) GLPG1972 in OA – the latter has the potential to drive upside given the good economics.

Investment Implications

We admittedly should have downgraded GLPG at €15 higher. We do so now as investor queries have increased - should we buy with fresh money? Our view – No. The risk/reward on catalysts remains positive and if they were sooner, we would have maintained our rating. For holders we suggest maintaining or possibly trimming ahead of filgo approval. M/P PT €155.

EPS Adjusted	F18A	F19E	F20E	Financials	F18A	F19E	F20E	CAGR	Valuation Metrics	F18A	F19E	F20E
GLPG.NA (EUR)	(0.56)	0.33	2.54	Revenues (M)	318	446	725	51.1%	P/E Adjusted (x)	(263.8)	447.9	58.10
OLD		(0.81)	2.48	EBIT (M)	(358)	23	160	NA				
MSDLE15	107.28	108.60	119.12	Net Earnings (M)	(342)	20	171	NA				

Close Date	17-Oct-2019			
GLPG.NA Close Price (EUR)	147.70			
Target Price (EUR)	155.00			
Upside/(Downside)	5%			
52-Week Low	74.48			
52-Week High	171.20			
MSDLE15	1,611.52			
FYE	Dec			
Indicated Div Yield	NA			
Market Cap (EUR) (M)	9,151			
EV (EUR) (M)	8,028			
Performance	YTD	1M	6M	12M
Absolute (%)	83.3	2.9	45.2	65.3
MSDLE15 (%)	14.7	0.4	0.4	7.1
Relative (%)	68.6	2.5	44.8	58.2

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DETAILS

Having written a thesis review on the stock a few months ago we include much of the detail in this note once more for those interested including detailed thoughts on filgotinib, IPF, Toledo, MOR106 and GLPG1972. We upfront summarise our thinking and valuation, catalysts and scenarios.

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Summary and valuation, catalysts and scenarios

This is still a strong biotech – the next 9 months could just be a wobble period. If you are a long-term investor, GLPG is a name you should hold. They have a pipeline and a platform. There are 2 sides to the argument post the GILD deal. One is GLPG just got a little boring as future catalysts have now been diluted and a GILD take out is off the table. The other is one of excitement from acceleration of programmes—more catalysts will read out faster, but each is just less meaningful. We prefer the latter set-up – more shots on goal is a good thing particularly if the programs are very focused (IPF combination trials, acceleration of Toledo in 2020). If the filigo label does look negative (thrombo warning) and the IPF futility analysis is positive (could it be in 1H20?) than the 2 events could wash out.

- + **DCF suggests limited upside – the stock is close to fair value.** In terms of valuation, given a multiple based approach is of less value for a company in Galapagos' current position (no positive earnings until 2022), we use our SOTP DCF which suggests a value of €155 (Exhibit 1). For our DCF we assume a 0% terminal post 2030 (and WACC of 8.25%), reasonable given our assumption that filgotinib patents expire in 2033 and the rest of the pipeline will go beyond that period (GLPG1690 in 2034, GLPG1972 in 2035, MOR106 in 2037).

One could argue that this could be higher or lower and it's hard to disagree when thinking about the company in 10 years' time. In addition, we include €1B in value for the platform (inc. Toledo) which is more than offset by our assumptions on high R&D.

- + **R&D spend needs to be reflected.** Following on from our DCF, speaking to investors, our sense is that R&D spend ramp is not yet reflected in valuations and could explain why some of our peers continue to see value closer to €200. Alternatively, more pipeline contribution could also be part of the explanation. With GLPG suggesting a doubling in the R&D infrastructure post the GILD deal, we see an increase from €370M in 2019 to €500M in 2020 and to €700M peak in 2023 as realistic.

If we are wrong on this spend, then GLPG is worth more than our €155 valuation suggests but we do not have an issue with spending on R&D, that is what a biotech should do.

- + **Scenarios - A wide band skewed to the upside.** With respect to upside / downside cases, we flex filgotinib, IPF, CF and the 2 other early stage partnered products. We summarise these in Exhibit 2. Our bear case gets to a DCF valuation of €122 and our bull case €222. The risk/reward is still to the upside and this is without the possibility of filgotinib sales above and beyond our forecasts in not only the core modelled indications, but across the multiple additional indications in development. The range is not as wide as the past and maybe not what you need to invest in SMID-Cap biotech but that's perfectly fine with us.
- + **Catalysts –** Multiple read-outs over the next 18 months across all franchise but the main stock moving events in our mind come in 2H20 (Exhibit 3).

In short, this is not a situation to panic. If you are LT holder, you do not need to do anything. Our view remains that GLPG will be a good investment longer-term. This call is for those thinking to invest in the name fresh money. We suspect there could be a superior entry point next year and if we are wrong, we see no reason for the stock to run higher before 2H20.

EXHIBIT 1: DCF values Galapagos at €155/share

	US	OUS	Milestones	Total	% of Total	Probability
Filgotinib - I&I						
<i>Rheumatoid arthritis</i>	€ 12.3	€ 10.0		€ 22.3	14%	100%
<i>Ankylosing spondylitis</i>	€ 1.2	€ 0.9		€ 2.1	1%	80%
<i>Psoriatic arthritis</i>	€ 1.5	€ 1.8		€ 3.3	2%	80%
<i>Crohn's disease</i>	€ 4.8	€ 3.7		€ 8.6	6%	80%
<i>Ulcerative colitis</i>	€ 3.6	€ 2.4		€ 6.0	4%	90%
Milestone payments			€ 14.2	€ 14.2		
Filgotinib total	€ 23.5	€ 18.8	€ 14.2	€ 56.5	37%	
GLPG1690 - IPF (RoW & EU)	€ 4.1	€ 4.3	€ 1.3	€ 9.8	6%	30%
Triple combo - CF	€ 0.7	€ 0.4	€ 1.4	€ 2.4	2%	30%
MOR106 - AtD*	€ 0.4	€ 0.2	€ 1.6	€ 2.3	1%	30%
GLPG1972 - OA	€ 1.5	€ 0.2	€ 2.8	€ 4.4	3%	20%
Target discovery platform/technology				€ 18.6	12%	
Reimbursement revenue				€ 2.5	2%	
Services revenue				€ 1.2	1%	
Other income				€ 3.9	3%	
Total				€ 101.5	66%	
Terminal (0%)				€ 84.9	55%	
General & admin; sales & marketing				-€ 16.8	-11%	
Capex				-€ 4.8	-3%	
R&D				-€ 107.6	-70%	
Other Non-Op Items				€ 5.7	4%	
Total Other				-€ 123.6	-80%	
Net Debt				€ 91.2	59%	
TOTAL GROUP (SOTP)				€ 154.1	100%	
TOTAL GROUP (Group DCF)				€ 153.8		

Source: Company disclosure, Bernstein analysis and estimates

EXHIBIT 2: Galapagos scenario analysis suggests a positive risk/reward



	Base	Bear	Bull
Filgotinib base	100% success in RA, 80% in AS, 80% in PsA, 80%, CD, 90% in UC. Total sales of €2.4B	Total sales of €1.5B	100% success across all indications (€2.7B in 2030 sales)
Filgotinib upside	n/a	n/a	Filgotinib achieves peak sales of €4B in 2030
IPF	30% probability of €1.5B in 2030 revenues	Failure	100% probability of €1.5B in 2030 revenues
CF	30% probability of \$1.3B in 2030 revenues (assuming ABBV deal structure)	Failure	100% probability of \$1.3B in 2030 revenues (assuming ABBV deal structure)
MOR 106 in AD	30% probability of \$0.8B in 2030 revenues (14-22% royalty)	Failure	100% probability of \$0.8B in 2030 revenues (14-22% royalty)
GLPG1972 in OA	20% probability of \$1B in 2030 revenues (7% royalty on OUS sales)	Failure	100% probability of \$1B in 2030 revenues (7% royalty on OUS sales)
DCF	€ 154	€ 122	€ 222

Source: Company disclosure, Bernstein analysis and estimates. Note we do not account for changes in terminal value and only include value to 2030

EXHIBIT 3: Galapagos catalysts

Timing	Drug/Franchise	Comments
4Q19	Filgotinib	Topline data from P2 studies in Sjogren's Syndrome (NCT03100942, SC Oct-19) and cutaneous lupus (NCT03134222, SC Dec-19) by end of year
4Q19	Filgotinib	Initiation of two p3s in PsA in 4Q19 (NCT04115748 in biologic DMARD naïve patients, NCT04115839 in inadequate responders/intolerant to bDMARDs)
1H20	Toledo	Data from 1st Toledo compound (GLPG3312) to read out p1 (NCT03800472) in healthy volunteers in 1H20 (undisclosed target for use in inflammatory diseases) - will start a PoC in 1H20 in ulcerative colitis. Second compound (GLPG3970) entered the clinic in Sep (NCT04106297, SC Nov-20). Other data from Toledo from GLPG2534 and GLPG3121 in 1H20
1H 2020	MOR106 (Atopic dermatitis)	Data from MOR106 p2 i.v. studies - IGUANA (NCT03568071, SC Dec-19) and GECKO (NCT03864627, SC Jan-20, w/ corticosteroids). Subcutaneous p1 bridging study (NCT03689829) completes in Aug-19.
1H 2020	Filgotinib	Data from SELECTION1 p3 trial in ulcerative colitis - completed recruitment in 1Q19 (NCT02914522, SC Dec-19)
2H 2020	IPF	Data from PINTA P2 trial with GLPG1205 - currently expect recruitment to complete in 2019 (NCT03725852, SC May-20)
2H 2020	Systemic sclerosis (SSc)	Data from PoC p2 NOVESA trial with GLPG1690 in SSc (NCT03798366, SC Aug-20)
2H 2020	GLPG1972 (Osteoarthritis)	Data from ROCCELLA P2 trial in US of GLPG1972 - expect recruitment to complete in 2019 (NCT03595618, Dec-20)
2020	Filgotinib	Data from DIVERSITY1 p3 trial in Crohn's disease - delayed recruitment due to competition (NCT02914561, SC Dec-19)
2020	Filgotinib	Data from p2 study in lupus membranous nephropathy (LMN)
Late 2020/1H21	IPF	Data from ISABELA P3 trials with GLPG1690. Primary / study completion of both ISABELA 1 (NCT03711162) and ISABELA2 (NCT03733444) is listed as Dec-21, but recruitment faster than expected.
2020/21	Filgotinib	Data from CD sub-studies: small bowel CD (NCT03046056, SC Jul-20) and perianal fistulising CD (NCT03077412, SC Jan-21).
2022	Filgotinib	Data from p2 study in uveitis (NCT03207815, SC Jul-22)

Source: Company disclosure, clinicaltrials.gov, Bernstein analysis

#1 - Filgotinib risk/reward negative near-term

There is still plenty to debate (label, efficacy inferiority, 2 dose approval, CLE and Sjogren's). We briefly discuss each in turn with clinical data to support where needed.

We expect filgo to get a thrombosis warning. There is no doubt that post the FINCH data in totality, we think filgotinib can be considered best in class. We present the key safety data in Exhibits 4-8, but briefly comment that thrombosis is where Filgotinib really stands out:

- + With only 3 thrombosis events seen (2 from FINCH) we see a PE/DVT rate of 0.1/100PY across all key RA trials (we include retinal vein occlusion from FINCH 2 and confirmed there were no such events in FINCH 1 & 3). This compares vs. 0.4/100PY for upad. Using p3 data only, skews the difference even higher.
- + In other safety areas, Filgo fares well, including (i) Herpes zoster rate >2x lower vs. all peers, (ii) serious infection rates of 1.8/100PY, significantly below upad (2.7/100PY), (iii) MACE rate of 0.3/100PY vs. 1/100PY for upad. (iv) Death event rate of 0.3/100PY vs. 0.5/100PY for upad. There will certainly be some debate on the death that occurred in the 200mg + MTX arm and we will need to wait for details. However, given the death rate was similar across the FINCH trials vs. placebo/csDMARD (0.2%), we are not overly concerned and the 0.3/100PY event rate is in-line or below all JAK peers.

GLPG's previous expectations were for Filgo to get a black box warning for malignancies and infections, as is typical of the class, but avoid a warning for thrombotic events. Following the Upad label ([link](#)) which included a black box warning - "Thrombosis, including deep vein thrombosis, pulmonary embolism, and arterial thrombosis, have occurred in patients treated with Janus kinase inhibitors used to treat inflammatory conditions", our base assumption is that filgo receives a similar class effect label. More importantly, our commercial view would change very little if filgo did not receive the label (see comments below).

EXHIBIT 4: Filgotinib thrombo event rate analysis

Study name	Total enrolment	739	Treatment regimen	Estimated PYE	PE/DVT	PE + DVT	PE/DVT / 100 PYE	PE + DVT / 100 PYE
DARWIN-3 (p2) interim (wk 156)	739	MTX-inadequate		2,203	1	2	0.0	0.1
FINCH-1	1,759	MTX-inadequate	+MTX	441	1	1	0.2	0.2
FINCH-2	448	bDMARD-inadequate	+csDMARD	138	1	1	0.7	0.7
FINCH-3	1,252	MTX-naïve	+MTX / monotherapy	384	0	0	0.0	0.0
P2 + P3 trials	4,183			3,167	3	4	0.1	0.1
P3 only (FINCH 1-3)	3,459			964	2	2	0.2	0.2

Source: Company disclosure, Bernstein analysis and estimates. Filgotinib DARWIN LT follow-up ([link](#)), FINCH-1 ([link](#)), FINCH-2 ([link](#)) and FINCH-3 ([link](#))

EXHIBIT 5: Filgotinib vs. upadacitinib thrombo event rate analysis (p3 only, all doses - negative entries indicate Filgotinib superiority)

Patient profile	Treatment regimen	Filgotinib vs. Upadacitinib	PE/DVT per 100 PYE	PE + DVT per 100 PYE
MTX-inadequate	+MTX	FINCH-1 vs. SELECT-COMPARE	-0.4	-0.4
bDMARD-inadequate	+csDMARD	FINCH-2 vs. SELECT-BEYOND	-1.6	-2.1
MTX-naïve	+MTX / monotherapy	FINCH-3 vs. SELECT-MONO* & SELECT-EARLY	-0.5	-0.5

Source: Company disclosure, Bernstein analysis and estimates
 FINCH-1 ([link](#)), FINCH-2 ([link](#)) and FINCH-3 ([link](#)); SELECT-EARLY ([link](#)), SELECT-BEYOND ([link](#), [link](#)), SELECT-COMPARE ([link](#)), SELECT-MONOTHERAPY ([link](#)).
 * Note SELECT-MONO was in MTX-inadequate patients, not MTX naïve as per FINCH-3, but this remains the closest comparator. Also note that SELECT-MONO was only 14 weeks.

EXHIBIT 6: JAK-specific safety signals – RA (per 100 pt year exposure)

	Serious infection	Herpes Zoster	DVT/PE	DVT + PE
Filgotinib	1.8	1.5	0.1	0.1
Upadacitinib	2.7	3.4	0.4	0.4
Baricitinib	2.9	3.3	0.5	0.6
Tofacitinib	2.5	3.6	n/a	0.2
Adalimumab	4.7	1.7	n/a	n/a

Source: Tofacitinib LT safety update ([link](#)); baricitinib long term safety update ([link](#)) and CV safety update ([link](#)); upadacitinib BALANCE-1 ([link](#)) and BALANCE-2 ([link](#)), BALANCE LTE ([link](#)), SELECT-EARLY ([link](#)), SELECT-NEXT ([link](#)), SELECT-BEYOND ([link](#), [link](#)), SELECT-COMPARE ([link](#)), SELECT-MONOTHERAPY ([link](#)); filgotinib DARWIN LT follow-up ([link](#)), FINCH-1 ([link](#)), FINCH-2 ([link](#)) and FINCH-3 ([link](#)); adalimumab LT safety ([link](#)); company disclosure, Bernstein analysis and estimates

Note: where patient years of drug exposure have not been provided, these are estimated (# patients on drug x study duration). Filgotinib DARWIN LT follow-up data excludes patient groups with <10 patients and patients on doses <200mg/day

EXHIBIT 7: JAK-specific safety signals – RA p3 only (per 100 pt year exposure)

	Serious infection	Herpes Zoster	DVT/PE	DVT + PE
Filgotinib: p3 only	3.0	1.2	0.2	0.2
Upadacitinib: p3 only	4.1	4.1	0.8	0.9

Source: Upadacitinib SELECT-EARLY ([link](#)), SELECT-NEXT ([link](#)), SELECT-BEYOND ([link](#), [link](#)), SELECT-COMPARE ([link](#)), SELECT-MONOTHERAPY ([link](#)); FINCH-1 ([link](#)), FINCH-2 ([link](#)) and FINCH-3 ([link](#)); company disclosure, Bernstein analysis and estimates

Note: where patient years of drug exposure have not been provided, these have been estimated (# patients on drug x study duration)

EXHIBIT 8: Safety data summary: RA clinical studies (incidence rate per 100 patient years)

	Tofacitinib		Baricitinib		Upadacitinib		Filgotinib	
	Events	IR (/100PY)	739	IR (/100PY)	Events	IR (/100PY)	Events	IR (/100PY)
Patients	7,061		2,203		3,230		2,827	
Patient years (est)	22,875		7,860		2,203		3,167	
Deaths	59	0.3	5	0.4	10	0.5	9	0.3
Serious infections	576	2.5	27	2.9	59	2.7	56	1.8
Pneumonia	124	0.5			2	0.1	3*	0.1
Herpes zoster	782	3.6	34	3.3	74	3.4	46	1.5
Opportunistic infections	90	0.4			20	0.9	0	0.0
Tuberculosis	38	0.2	11	0.1	0	0.0	0	0.0
Malignancies (ex NMSC)	117	0.6	11	0.8	20	0.9	12	0.4
GI perforations	28	0.1	3	0.0	5	0.2	0	0.0
MACE	85	0.4	3	0.5	22	1.0	8	0.3
DVT/PE		0.0	42	0.5	8	0.4	3	0.1
DVT + PE	55	0.2	49	0.6	9	0.4	4	0.1
DVT	27	0.1	30	0.4	3	0.1	3	0.1
PE	28	0.1	19	0.2	6	0.3	1	0.0

Source: Tofacitinib long term safety update ([link](#)); baricitinib long term safety update ([link](#)) and cardiovascular safety update ([link](#)); upadacitinib BALANCE-1 ([link](#)) and BALANCE-2 ([link](#)), BALANCE LTE ([link](#)), SELECT-EARLY ([link](#)), SELECT-NEXT ([link](#)), SELECT-BEYOND ([link](#), [link](#)), SELECT-COMPARE ([link](#)), SELECT-MONOTHERAPY ([link](#)); Filgotinib DARWIN LT follow-up ([link](#)), FINCH-1 ([link](#)), FINCH-2 ([link](#)) and FINCH-3 ([link](#)); Bernstein analysis and estimates

Note: where patient years of drug exposure have not been provided, these have been estimated (# patients on drug x study duration). Filgotinib DARWIN long-term follow-up data excludes patient groups with <10 patients and patients on doses <200mg/day

* DARWIN data only

Grey shading = Data not provided in FINCH-1, FINCH-3 and Darwin updates on 28 March 2019. These figures are therefore based on FINCH-2 and Darwin 132-week data (1024 pts, 2180 patient years)

We do not see efficacy as a debate – at least not one that will drive prescribing. We present the key efficacy endpoints from FINCH 1-3 in Exhibits 6-9 and a summary of the ACR 20 efficacy vs the competition in RA in Exhibit 13. Efficacy had never been a focus for investors, but after the FINCH 1 & 3 data came out, question marks were initially raised as (i) In FINCH 1, superiority vs. Humira was not achieved across most efficacy metrics. Whilst this was not a concern in itself, upadacitinib was able to achieve superiority (the Humira arm in FINCH 1 looked exceptionally strong vs. historical data). (ii) In FINCH 3, the mono arm was not convincing vs. MTX (unusually high).

Firstly, when comparing vs. upadacitinib using updated data post EULAR-19 (Exhibits 14-16), you could argue filgotinib is inferior using placebo adjusted rates, but on an absolute basis, filgotinib actually looks a little better. In addition, comparing Humira adjusted outcomes, yes Filgo is a little worse off, but the differences are not significant. Also worth remembering that upad will not have a Humira superiority claim on label. Secondly, and more broadly, in FINCH-2 (biological DMARD-inadequate patients), on ACR20 (primary), filgo appears to trump the competition, with Kezvara and upad coming closest.

In short, we do not consider efficacy a debate for Filgotinib. Yes, looking across the data sets and metrics, you could make an argument that upad is superior on efficacy, but there is very little in it and more importantly we do not see this impacting prescribing of the drug. We expect physicians to view the efficacy vs. upad as comparable.

EXHIBIT 9: FINCH-1 efficacy data (MTX-inadequate pts, +MTX)

	Week 12				Week 24			
	Placebo + MTX (n=475)	Humira + MTX (n=325)	100mg + MTX (n=480)	200mg + MTX (n=475)	Placebo + MTX (n=475)	Humira + MTX (n=325)	100mg + MTX (n=480)	200mg + MTX (n=475)
<i>Proportion of patients achieving:</i>								
ACR20	49.9%	70.8%	69.8%***	76.6%***	59.2%	74.5%	77.7%	78.1%
ACR50	19.8%	35.1%	36.3%***	47.2%***	33.3%	52.6%	52.7%	57.9%
ACR70	6.7%	14.2%	18.5%***	26.3%***	14.9%	29.5%	29.4%	36.2%
DAS28(CRP)≤ 3.2 (low disease activity)	23.4%	43.4%	38.8%***	49.7%***^	33.7%	50.5%	53.1%	60.6%
DAS28(CRP)< 2.6 (clinical remission)	9.3%	23.7%	23.8%***^	33.9%***^^	16.2%	35.7%	35.2%	48.4%

Source: EULAR 2019 presentation, Bernstein analysis

* p<0.05 versus placebo, ** p<0.01 versus placebo, *** p<0.001 versus placebo, ^ non-inferior to adalimumab, ^^ superior to adalimumab

EXHIBIT 10: FINCH-2 efficacy data (bDMARD-inadequate pts)

	Week 12			Week 24		
	Placebo (n=148)	100mg (n=153)	200mg (n=147)	Placebo (n=148)	100mg (n=153)	200mg (n=147)
<i>Proportion of patients achieving:</i>						
ACR20	31.1%	57.5%***	66.0%***	34.5%	54.9%***	69.4%***
ACR50	14.9%	32.0%***	42.9%***	18.9%	35.3%**	45.6%***
ACR70	6.8%	14.4%*	21.8%***	8.1%	20.3%**	32.0%***
DAS28(CRP)≤ 3.2 (low disease activity)	15.5%	37.3%***	40.8%***	20.9%	37.9%**	48.3%***
DAS28(CRP)< 2.6 (clinical remission)	8.1%	25.5%***	22.4%***	12.2%	26.1%**	30.6%***

Source: ACR 2018 ([link](#)), Bernstein analysis

* p<0.05 versus placebo, ** p<0.01 versus placebo, *** p<0.001 versus placebo.

EXHIBIT 11: FINCH-3 efficacy data (MTX-naïve pts, +MTX arm)

	Week 12			Week 24		
	MTX (n=416)	100mg + MTX (n=207)	200mg + MTX (n=416)	MTX (n=416)	100mg + MTX (n=207)	200mg + MTX (n=416)
<i>Proportion of patients achieving:</i>						
ACR20		**	***	71.4%	80.2%*	81.0%***
ACR50		***	***	45.7%	57.0%**	61.5%***
ACR70		***	***	26.0%	40.1%***	43.8%***
DAS28(CRP)≤ 3.2 (low disease activity)	28.6%	50.2%***	55.8%***	46.2%	62.8%***	68.8%***
DAS28(CRP)< 2.6 (clinical remission)	17.1%	31.9%***	39.7%***	29.1%	42.5%***	54.1%***

Source: EULAR 2019 presentation, Bernstein analysis

* p<0.05 versus placebo, ** p<0.01 versus placebo, *** p<0.001 versus placebo

Note that as at 12 weeks, the ACR20, 50 and 90 significance but not percentages of patients were specified in the detailed 2019 EULAR presentation

EXHIBIT 12: **FINCH-3 efficacy data (MTX-naïve pts, +monotherapy arm)**

	Week 12		Week 24	
	MTX (n=416)	200mg once daily (n=210)	MTX (n=416)	200mg once daily (n=210)
<i>Proportion of patients achieving:</i>				
ACR20		**	71.4%	78.1%
ACR50		***	45.7%	58.1%**
ACR70		***	26.0%	40.0%***
DAS28(CRP) ≤ 3.2 (low disease activity)	28.6%	48.1%***	46.2%	60.0%***
DAS28(CRP) < 2.6 (clinical remission)	17.1%	29.5%***	29.1%	42.4%***

Source: EULAR 2019 presentation, Bernstein analysis

* p<0.05 versus placebo, ** p<0.01 versus placebo, *** p<0.001 versus placebo

Note that as at 12 weeks, the ACR20, 50 and 90 significance but not percentages of patients were specified in the detailed 2019 EULAR presentation

EXHIBIT 13: **Efficacy benchmarking in RA, JAK inhibitors vs approved drugs, ACR20 data**

MOA	RA Agents	Company	Conventional DMARD-Inadequate				TNFi-Inadequate		
			Monotherapy		+DMARD		+DMARD		
			Wk 12-16	Wk 24-30	Wk 12-16	Wk 24-30	Wk 12-16	Wk 24-30	
anti-TNFα	Humira	AbbVie	19%	46%	61%	63%		TNF inhibitors are traditional 1L drugs, especially Humira, Enbrel and Remicade	
	Enbrel	Amgen	23%	11%	33%	27%			
	Remicade 3 mg/kg q8w	J&J				20%			
	Cimzia	UCB	9%	46%		14%			
	Simponi 50 mg	J&J			33%	28%	18%		16%
	Simponi Aria	J&J			25%	32%	35%		31%
anti-CTLA-4	Orencia	BMS	Similar retention as Orencia + MTX		37%	40%	18%	20%	Other MOAs have often shown efficacy in the TNFi-inadequate setting
anti-CD20	Rituxan	Biogen & Genentech					18%	51%	
anti-IL6R	Actemra SC	Genentech	IV is superior to MTX at Wk 24 (70% vs. 53%)			32%	IV is Superior to Placebo at Wk 24 (30% vs. 10%)		
	Kevzara	Regeneron & Sanofi	Superior to Humira Mono (71% vs. 58%) at Wk 24		35%	33%	38%	34%	
anti-IL6	olokizumab (P2b)	UCB/R-Pharm	No planned trials				30%	55%	
anti-IL1R	Kineret	Sobi			24%	22%			
anti-JAK1/3	Xeljanz 5 mg bid	Pfizer	Inferior to Xel+MTX and Humira+MTX		27%	25%	24%		JAK inhibitors, where newer agents have promising mono data
anti-JAK1/2	Olumiant 4 mg qd	Eli Lilly & Incyte	40%	62%	40%	70%	27%	27%	
anti-JAK1	filgotinib 200 mg (P3)	Gilead & Galapagos	71%	78%	50%	59%	31%	35%	
	upadacitinib 30 mg	AbbVie	41%	71%	36%	66%	28%	56%	

Legend	
Control	15%
Target	60%

Source: Company disclosure, medical literature, USPI, ClinicalTrials.gov, Bernstein analysis

Note that FINCH-3 data has been used for cDMARD inadequate monotherapy comparison purposes here, although whilst the data used from FINCH-3 is mono, patient background is actually MTX-naïve.

EXHIBIT 14: Filgotinib (200mg) vs. Upadacitinib (15mg) efficacy in RA (positive entries indicate Filgotinib superiority)

Patient profile	Treatment regimen	Filgotinib vs. Upadacitinib	ACR20	ACR50	ACR70	DAS28(CRP) ≤ 3.2 (low disease activity)	DAS28(CRP) < 2.6 (clinical remission)
MTX-inadequate	+MTX	FINCH-1 vs. SELECT-COMPARE	11%	4%	2%	6%	8%
bDMARD-inadequate	+csDMARD	FINCH-2 vs. SELECT-BEYOND**	8%	3%	10%	-4%	-2%
MTX-naïve	+MTX arm	FINCH-3 vs. SELECT-EARLY	2%	1%	-1%	9%	6%
	monotherapy arm	FINCH-3 vs. SELECT-MONO*	n/a	n/a	n/a	n/a	n/a

Source: Company disclosure, Bernstein analysis and estimates.

FINCH-1 ([link](#)), FINCH-2 ([link](#)) and FINCH-3 ([link](#)); SELECT-EARLY ([link](#)), SELECT-BEYOND ([link](#), [link](#)), SELECT-COMPARE ([link](#)), SELECT-MONOTHERAPY ([link](#)).

Note that data is 24 weeks unless stated.

* Note that there is no true comparator from the upad trials for the mono arm in FINCH-3. The closest comparator, SELECT-MONO was in MTX-inadequate patients, not MTX naïve as per FINCH-3, and we currently only have 24wk FINCH-3 data vs 14 wk from SELECT-MONO.

EXHIBIT 15: Placebo or MTX adjusted efficacy of Filgotinib (200mg) vs. Upadacitinib (15mg) in RA (positive entries indicate Filgotinib superiority)

Patient profile	Treatment regimen	Filgotinib vs. Upadacitinib	Adjusted vs	ACR20	ACR50	ACR70	DAS28(CRP) ≤ 3.2 (low disease activity)	DAS28(CRP) < 2.6 (clinical remission)
MTX-inadequate	+MTX	FINCH-1 vs. SELECT-COMPARE	Placebo + MTX	-13%	-8%	-4%	-10%	1%
bDMARD-inadequate	+csDMARD	FINCH-2 vs. SELECT-BEYOND**	Placebo	2%	-4%	8%	-11%	-4%
MTX-naïve	+MTX arm	FINCH-3 vs. SELECT-EARLY	MTX	-11%	-11%	-8%	-5%	-5%
	monotherapy arm	FINCH-3 vs. SELECT-MONO*	n/a	n/a	n/a	n/a	n/a	n/a

Source: Company disclosure, Bernstein analysis and estimates.

FINCH-1 ([link](#)), FINCH-2 ([link](#)) and FINCH-3 ([link](#)); SELECT-EARLY ([link](#)), SELECT-BEYOND ([link](#), [link](#)), SELECT-COMPARE ([link](#)), SELECT-MONOTHERAPY ([link](#)).

Note that data is 24 weeks unless stated.

* Note that there is no true comparator from the upad trials for the mono arm in FINCH-3. The closest comparator, SELECT-MONO was in MTX-inadequate patients, not MTX naïve as per FINCH-3, and we currently only have 24wk FINCH-3 data vs 14 wk from SELECT-MONO.

** SELECT BEYOND placebo patients switched to Upa post week 12, therefore 12-week placebo data is used here from SELECT BEYOND trial vs 24 week FINCH-2 data

EXHIBIT 16: Humira adjusted efficacy of Filgotinib (200mg) vs. Upadacitinib (15mg) in RA (positive entries indicate FINCH-1 %'s are higher)

	FINCH-1		Filgo adjusted	SELECT-COMPARE			FINCH-3 vs SELECT COMPARE		
	Filgo + MTX (n=475)	Humira + MTX (n=325)		Upad + MTX (n=651)	Humira + MTX (n=327)	Upad adjusted	Filgo / Upad	Humira	Adjusted
ACR20	78.1%	74.5%	3.6%	67.4%	57.2%	10.2%	11%	17%	-7%
ACR50	57.9%	52.6%	5.3%	53.9%	41.9%	12.0%	4%	11%	-7%
ACR70	36.2%	29.5%	6.7%	34.7%	22.9%	11.8%	2%	7%	-5%
DAS28(CRP) ≤ 3.2 (low disease activity)	60.6%	50.5%	10.1%	54.7%	38.5%	16.2%	6%	12%	-6%
DAS28(CRP) < 2.6 (clinical remission)	48.4%	35.7%	12.7%	40.9%	26.9%	14.0%	8%	9%	-1%

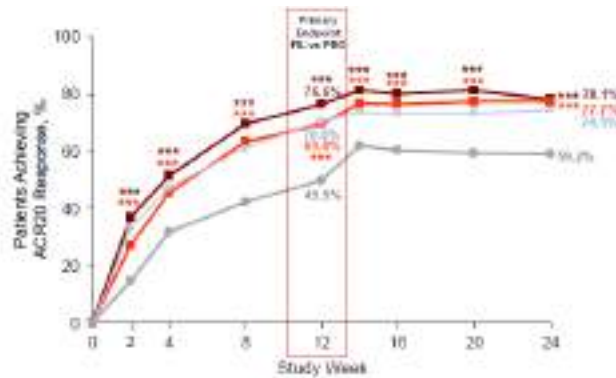
Source: Company disclosure, Bernstein analysis and estimates.

FINCH-1 ([link](#)), SELECT-COMPARE ([link](#)) at 24 and 26 weeks, respectively.

Both filgo doses should be approved. The FINCH 1-3 trials assessed both the 100mg and 200mg doses. In terms of efficacy, and looking to FINCH-1 and FINCH-3, we can see a dose-response curve (more apparent in the more stringent ACR70), highlighting that whilst the magnitude is not significant, higher doses are more efficacious (Exhibits 17-20), something that other JAKs have not achieved and hence the lack of multiple doses. Importantly, and what drives our confidence in approvals for both doses, is that from a safety perspective, there was no real differences between the two doses (Exhibit 21). *In short*, with a

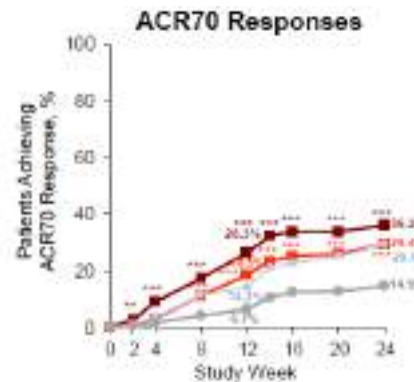
fraction more efficacy for no apparent detrimental effect, we would expect both doses to be approved, allowing for flexibility of incremental dosing (start most patients on 100mg and go from there).

EXHIBIT 17: **FINCH 1 – ACR20 dose response**



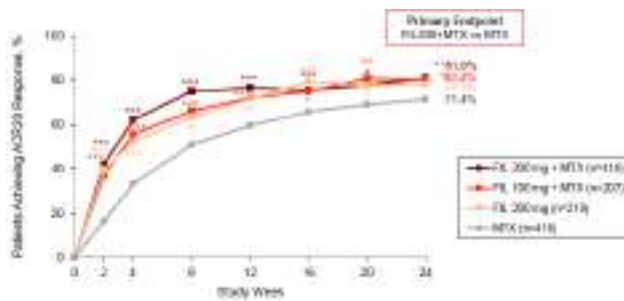
Source: EULAR 2019 presentation. Note: Maroon – Filgo 200mg, red – Filgo 100mg, light grey – ADA, dark grey – pbo

EXHIBIT 18: **FINCH 1 – ACR70 dose response**



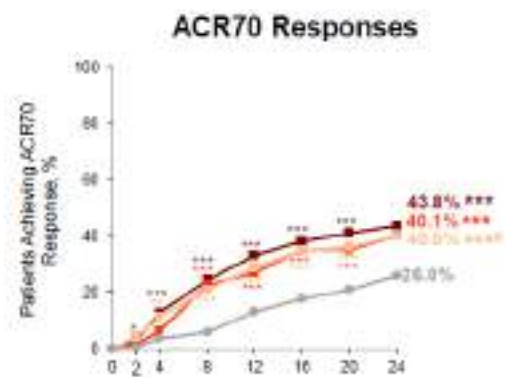
Source: EULAR 2019 presentation. Note: Maroon – Filgo 200mg, red – Filgo 100mg, light grey – ADA, dark grey – pbo

EXHIBIT 19: **FINCH 3 – ACR20 dose response**



Source: EULAR 2019 presentation. Note: Maroon – Filgo 200mg, red – Filgo 100mg, light grey – ADA, dark grey – pbo

EXHIBIT 20: **FINCH 3 – ACR70 dose response**



Source: EULAR 2019 presentation. Note: Maroon – Filgo 200mg, red – Filgo 100mg, light grey – ADA, dark grey – pbo

EXHIBIT 21: **Comparative safety summary of 100mg and 200mg doses across FINCH trials**

	FINCH-1		FINCH-2		FINCH-3	
	100mg n = 480	200mg n = 475	100mg n = 153	200mg n = 147	100mg + MTX n = 207	200mg + MTX n = 416
Any TEAE	(59.6%)	(60.4%)	(63.4%)	(69.4%)	(69.6%)	(65.9%)
TEAE leading to drug discontinuation	(1.7%)	(2.9%)	(3.9%)	(3.4%)		
TEAE leading to study discontinuation	(1.0%)	(1.7%)			(1.4%)	(1.9%)
Serious TEAE	(5.0%)	(4.4%)	(5.2%)	(4.1%)	(2.4%)	(4.1%)
Serious infections	(1.7%)	(1.7%)	(2.0%)	(0.7%)	(1.0%)	(1.0%)
Herpes zoster	(0.4%)	(0.4%)	(1.3%)	(1.4%)	(0.5%)	(0.5%)
Adjudicated MACEs	(0.2%)	(0.0%)	(0.7%)	(0.0%)	(0.0%)	(0.5%)
Thrombotic events	(0.0%)	(0.2%)	(0.0%)	(0.7%)	(0.0%)	(0.0%)
Malignancies excluding NMSC	(0.2%)	(0.0%)	(0.0%)	(0.0%)	(0.0%)	(0.0%)
Deaths	(0.2%)	(0.4%)	(0.0%)	(0.0%)	(0.0%)	(0.2%)

Source: FINCH-1 (EULAR 2019 presentation), FINCH-2 ([link](#)), FINCH-3 (EULAR 2019 presentation), Bernstein analysis

Positive risk/reward in to Cutaneous Lupus and Sjögren's data. Later this year, we will see proof-of-concept p2 data from two lesser discussed opportunities for Filgotinib - Cutaneous Lupus Erythematosus (CLE) and Sjögren's Syndrome (SS; see our [deep dive](#)). In brief:

- + CLE is a skin condition that is distinct from, but overlaps with, SLE (the more widely debated lupus indication). With treatment based on reducing symptoms, no approved therapies, little in the way of competition and ~230K US patients, CLE represents a sizeable opportunity (~\$0.5B with just a 10% share). Whilst scientific basis for JAKs in CLE exists, clinical data is thin on the ground and the PoC trial is small (15-20 Filgo patients). Another concern - CLE (like SLE) appears to be a drug developers graveyard. We are intrigued by the opportunity, but cautious for now.
- + SS is a chronic, inflammatory autoimmune (AI) disease that results in sicca syndrome (dryness of skin, eyes, mouth) and, often, systemic effects (neurological, malignancies etc). Treatment is focussed on symptomatic relief and with no approved therapies despite being the 2nd largest autoimmune disease after RA (~4M US patients), SS is a worthy target (~\$1B). Whilst the biological rationale for JAKs is sound, (i) the disease is complex / heterogenous (concomitant AI), (ii) limited clinical data and (iii) the pipeline appears full with others (a little) ahead. SS is a sizeable and largely ignored indication and so feels like a worthwhile pursuit but similarly to CLE, we need more data.

In short, if successful, these additional indications could be significant opportunities to differentiate the drug vs the other JAKs, improve coverage and bolster sales but we cannot get bullish just yet purely given the lack of data and risky nature of development in these diseases. With no approved therapies for either opportunity and investors unlikely to give much credit for these indications, risk/reward is to the upside. However, these are very early read-outs and GILD/GLPG would need to run additional p2 trials before progressing to pivotal – in short, unlikely to move the stock today.

Could the product be on the US market in 2Q20? Given GILD have a priority review voucher, we would not be overly surprised if it was used for filgotinib, further cutting the window for ABBV's upad to gain traction in the market. Our base assumption remains 4Q20 approval and leave a possible 2Q20 approval as upside. We note that GLPG will likely need to compensate GILD if they are to use the voucher (company did not confirm).

The sales wobble is small regardless of outcomes on efficacy, safety and doses approved. We take a conservative approach for filgotinib driven by what we believe to be a tough commercial environment with or without a superior safety label (and multiple doses) - (i) ABBV will use Humira for favourable upad coverage (payors only need 1 JAK at preferred level) and can point to data on the label (not a claim) for superiority vs. Humira which filgotinib cannot, (ii) pricing deterioration across all classes and (iii) future generic Xeljanz (2022/23). These all limit the share gain for filgotinib (30% in RA). We forecast peak sales of \$3B in 2030 (€2.4B risk-adj; Exhibit 22) with major contribution from the GI indications where we expect filgo to do well. Ultimately a potentially faster approval, whilst positive, will not change the fact that we will not know what the Filgotinib label will look like in 2020 or the tough dynamics of the market. As our recent formulary analysis highlighted, coverage was strong across new classes but this has come at a cost - price ([link](#)). As the market becomes further saturated, we expect this trend to continue. In short, you don't buy GLPG for filgotinib alone.

EXHIBIT 22: **Filgotinib market model**

	US		EU	
	2025E	2030E	2025E	2030E
Patient model				
RA				
% Patients with DMARD failure treated with JAKs	21%	26%	14%	17%
Filgotinib % share of these patients	34.0%	31.0%	32.0%	28.0%
Filgotinib sales (\$M)	\$715	\$732	\$314	\$312
Patients treated (000's)	22.6	28.9	33.0	39.4
AS				
% Patients with DMARD failure treated with JAKs	2%	5%	3%	5%
Filgotinib % share of these patients	70.0%	50.0%	50.0%	55.0%
Filgotinib sales (\$M)	\$84	\$120	\$27	\$46
Patients treated (000's)	2.7	4.7	2.9	5.8
PsA				
% Patients with DMARD failure treated with JAKs	7%	11%	6%	11%
Filgotinib % share of these patients	26.0%	38.0%	36.0%	32.0%
Filgotinib sales (\$M)	\$87	\$182	\$76	\$115
Patients treated (000's)	2.7	7.2	8.0	14.6
Crohns				
% Patients with DMARD failure treated with JAKs	16%	20%	10%	15%
Filgotinib % share of these patients	54.0%	59.0%	50.0%	50.0%
Filgotinib sales (\$M)	\$320	\$387	\$123	\$167
Patients treated (000's)	10.1	15.3	12.9	21.1
UC				
% Patients with DMARD failure treated with JAKs	10%	20%	9%	15%
Filgotinib % share of these patients	34.0%	30.0%	35.0%	31.0%
Filgotinib sales (\$M)	\$226	\$353	\$76	\$108
Patients treated (000's)	7.1	13.9	8.0	13.6
Total				
Total Filgotinib sales (\$M)	\$1,433	\$1,774	\$617	\$748
Total Filgotinib sales (€M)	€ 1,305	€ 1,616	€ 562	€ 681
Cost per patient per year (€K)	€ 28.8	€ 23.0	€ 8.7	€ 7.2
Total Filgotinib patients treated (000's)	45.3	70.1	64.7	94.4
Prescription model				
JAKs share of volume	15%	22%	18%	25%
Filgotinib JAKs share	31.2%	26.1%	16.1%	14.1%
Filgotinib total share	4.7%	5.8%	2.9%	3.6%
Filgotinib volume (TRx in US, Unit in EU)	561	842	773	1,213
Filgotinib \$ per TRx/ € per Unit	\$2,600	\$2,080	€ 714	€ 593
Total Filgotinib sales (\$M)	\$1,459	\$1,751	\$606	\$790
Total Filgotinib sales (€M)	€ 1,329	€ 1,595	€ 552	€ 719

Source: IQVIA, Company disclosures, Bernstein analysis and estimates

#2 - IPF in 2020 remains the game changer

Galapagos have a broad IPF portfolio of assets with differing mechanisms and we could see updates for both key trials in 2020 (i) p3 futility update for GLPG 1690 which will see no interim data but will confirm a go/no-go from the agency on trial progression. If the probability that the primary will not be met is small enough, the trial will continue. This is enough to be a major catalyst in our view. (ii) p2 data for GLPG 1205 in 2H20 could support the debate particularly on the combination approach in IPF. We dig deeper on the former first.

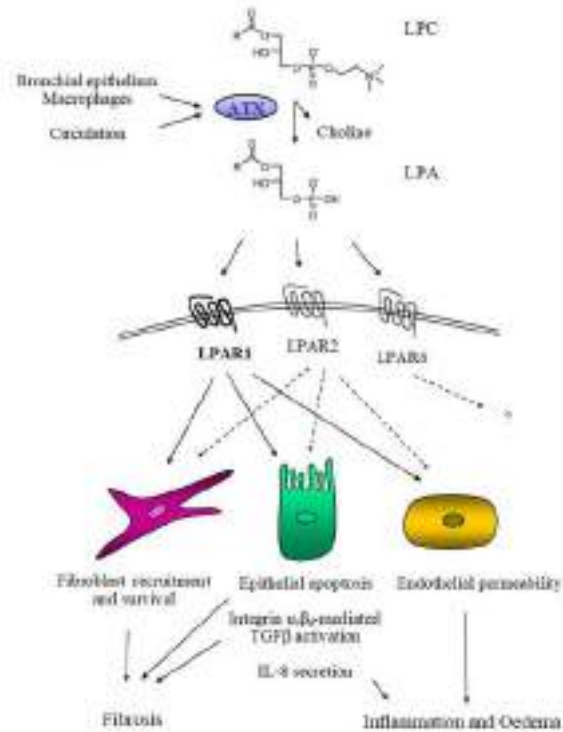
GLPG1690 is a selective autotaxin (ATX) inhibitor. IPF is a severe, progressive lung disease marked by a highly variable clinical course which makes a confident diagnosis challenging to achieve. The track record of products in IPF is pretty poor and the only curative therapy for IPF remains lung transplantation. Drug treatment changed in 2014 with the approval of 2 drugs for the treatment of IPF (Esbriet and Ofev). However, tolerability is an issue, with substantial discontinuation rates for both medicines.

In IPF, ATX levels rise in the bronchoalveolar fluid, and increased ATX activity has been detected in a range of inflammatory and fibroproliferative diseases in the lung, kidney and skin. ATX is the enzyme responsible for generating lysophosphatidic acid (LPA), with LPA being formed locally in areas with increased ATX levels and acting locally via its receptors.

In the lung, LPA signalling via LPAR1, and possibly via LPAR2, activates G-protein-mediated signal transduction cascades (Exhibit 23). Apoptosis is triggered in epithelial cells, which in modelled pulmonary fibrosis is the initiating pathogenic event. Epithelial cells are also induced to secrete IL-8, which is both proinflammatory and stimulates permeability of endothelial cells,

thus promoting pulmonary oedema. LPA has several effects on fibroblasts: it is a chemotactic factor that promotes fibroblast recruitment, while also being a stimulator of fibroblast activation (via TGF beta) and promotor of fibroblast survival.

EXHIBIT 23: **Schematic: role of autotaxin in pulmonary fibrosis**

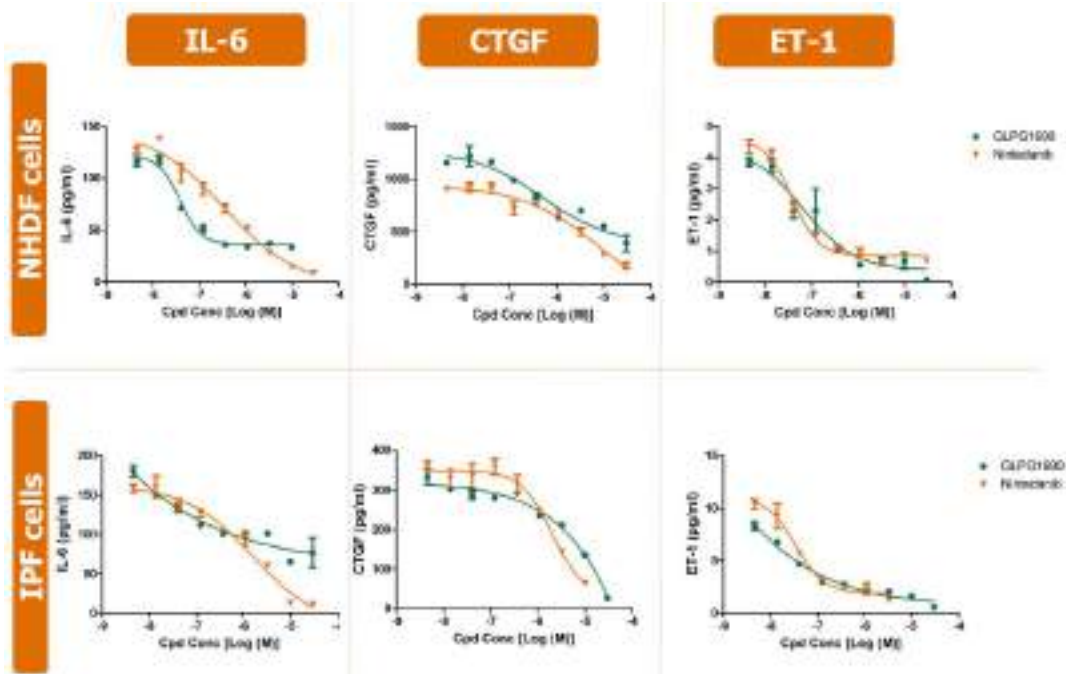


Source: Ninou et al (2018) Front. Med. ([link](#))

It should be noted that LPA signals through at least six receptors (including LPAR1 and LPAR2) which are expressed differentially across a wide range of tissues and with overlapping specificities. While GLPG1690 targets autotaxin (thereby reducing LPA production more generally, and reducing the effects of LPA through any of its receptors), LPAR1 is also being considered as a potential target for IPF treatment (e.g., BMS-986020 is an LPA receptor antagonist being developed by BMS that has completed p2 trials for IPF, although the data highlighted elevated liver enzymes and no active trials are on-going - [link](#)). The choice to target autotaxin might lead to unintended consequences; for example, LPAR2 is thought to protect against excessive innate immune responses to tissue injury, so targeting ATX might reduce this protective effect. However early clinical trials (discussed below) do not seem to suggest that GLPG1690 has unacceptably high rates of adverse events.

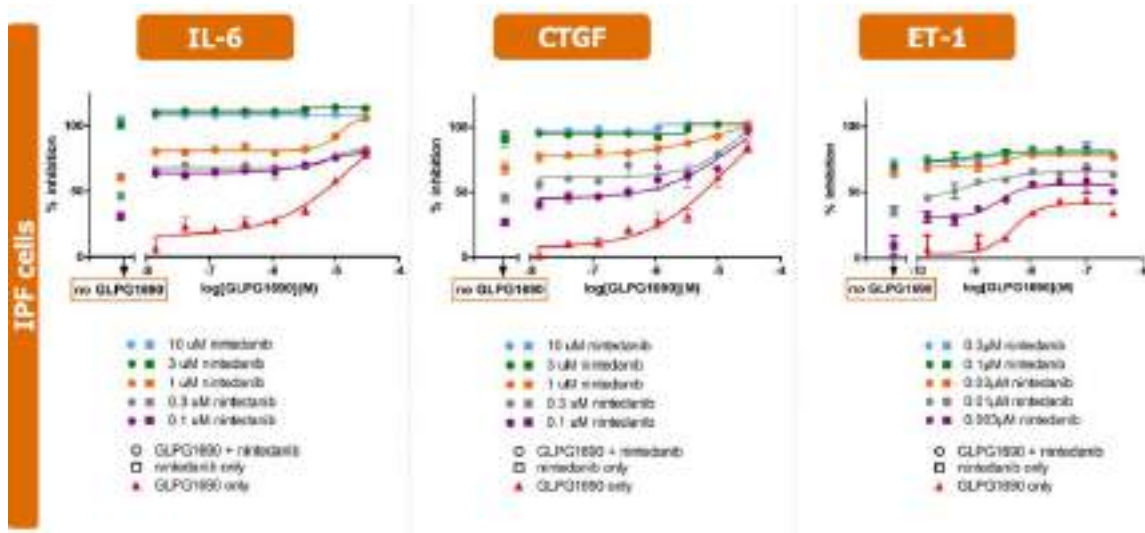
Earlier clinical and pre-clinical data was supportive for further testing. A couple of quick points that supported progress into p2. (i) Pre-clinical data demonstrates dose-dependent reductions of several TGF-beta induced pro-fibrotic mediators like ET-1, IL-6 and CTGF (Exhibit 24). When combined with Ofev, the added inhibitory effect can be seen (Exhibit 25). (ii) p1 study demonstrated dose dependant reductions in plasma LPA18:2, a biomarker for autotaxin inhibition (Exhibit 26) with *in vivo* IC₅₀ for reduction LPA18:2, in line with *ex vivo* IC₅₀ (Exhibit 27; good correlation between PK and PD for LPA reduction).

EXHIBIT 24: Effect of Ofev and GLPG1690 on TGF-beta induced IL-6, CTGF and ET-1



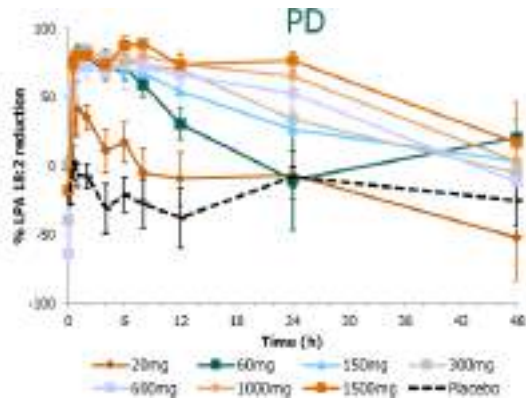
Source: Galapagos

EXHIBIT 25: Combined effects of GLPG1690 and nintedanib



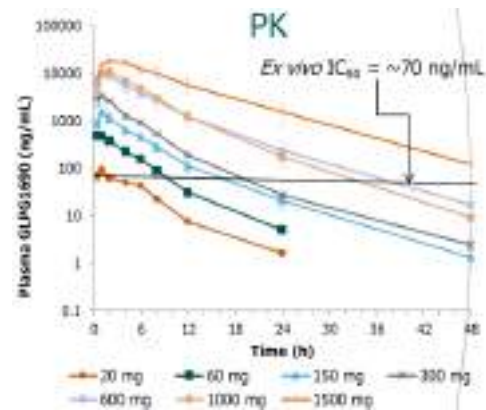
Source: Galapagos

EXHIBIT 26: Dose-dependent reduction of LPA18:2 in plasma from healthy volunteers by GLPG1690



Source: Galapagos

EXHIBIT 27: 60 mg dose is first dose with plasma concentrations durable above the ex vivo LPA18:2 IC50



Source: Galapagos

Phase 2a FLORA efficacy results were encouraging (link), we just wish it were a little bigger. The 12-week study involved 23 IPF patients (centrally confirmed) who had not been receiving Ofev or Esbriet 4 weeks prior to entering the study and no exacerbations of IPF 6 weeks prior to entering the study (17 patient on 600mg GLPG1690 daily, 6 placebo). The baseline duration of IPF was higher in the drug group (1.9 years vs. 1 year) but baseline FVC was similar, albeit better in drug arm (2.8L vs. 2.7L, 75.3% of predicted normal vs. 69.7%). We asked physicians if this could possibly have skewed the data set and ultimately the answer was mixed (year 1 vs. year 2 is not a big deal but day 1 vs. year 3 would be).

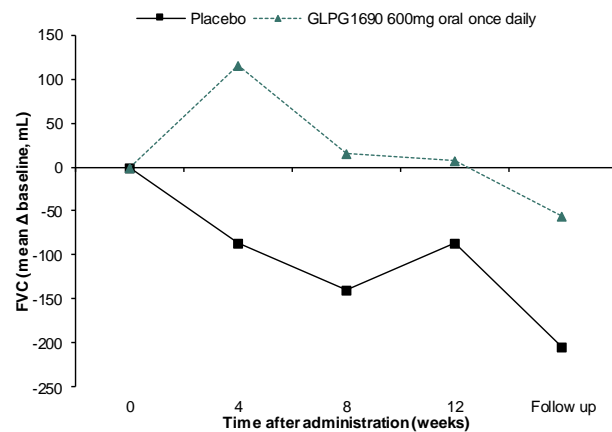
The mean time to C_{max} was 4.0 hours for GLPG1690 and while no formal analysis was done of the GLPG1690 trough, visual inspection showed week 1 sample concentrations consistent with previous studies where trough concentrations were established 4 days after the first dose. The FLORA study also examined reductions in plasma LPA 18:2, which supported the findings from earlier studies (Exhibit 29), with PK and PD data similar to healthy volunteers and target engagement demonstrated through plasma LPA 18:2 reduction.

Importantly, proof of concept was met. FVC increased 8mL with treatment at 12 weeks vs. a decrease of 87mL with placebo (Exhibit 28, observed-case analysis; comparable results for LOCF where FVC increased 25mL vs. a 70mL decrease with placebo). Functional respiratory imaging (FRI) confirmed disease stabilization. Mean change from specific airway volume was significantly lower in the treatment group (0.079mL/L vs. 3.038mL for placebo, p=0.0137).

There were no significant differences in quality of life as assessed by self-reported St George's Respiratory Questionnaire (SGRQ). A mean reduction of 5-8 points was taken to be a clinically important improvement (based on previous estimates of the minimum important difference in IPF). The mean changes from baseline to 12 weeks were: -5.45 in the symptom domain (vs. +2.90 for placebo), -2.32 in the activity domain (vs. +4.14 for placebo) and +3.22 in the impact domain (vs. -3.90 for placebo).

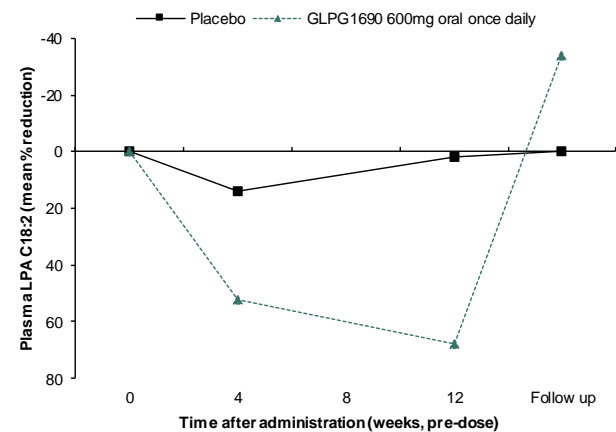
In short, a stabilisation of FVC at 12 weeks is a very good outcome, albeit from a very short, small population study.

EXHIBIT 28: **Stabilised FVC**



Note: Week 8 timepoint p<0.05; data is observed-case analysis
 Source: Maher et al, The Lancet Respiratory Medicine 2018 ([link](#)), Bernstein analysis

EXHIBIT 29: **Sustained reduction in plasma LPA**



Source: Maher et al, The Lancet Respiratory Medicine 2018 ([link](#)), Bernstein analysis

Safety profile also encouraging. TEAEs were reported in 4 (67%) and 11 (65%) of patients in the placebo and treatment groups respectively, with most AE being mild to moderate in severity (Exhibit 30). Two patients had AEs deemed related to treatment, although it is not disclosed what these events were. Of the serious events, two affected patients were in the placebo group, and one affected patient in the treatment group had cholangiocarcinoma (bile duct cancer) symptoms that were noted 1 day after the first dose of treatment but which had also occurred during screening. No patients died or had acute IPF exacerbations. The most common types of adverse events are shown in Exhibit 31. The most common type of adverse event was infections and infestations, but these occurred in a similar proportion of patients in the treatment (41%) and placebo (50%) groups.

EXHIBIT 30: **Treatment emergent adverse events (number of patients, percent)**

	FLORA	
	GLPG1690 (n=17)	Placebo (n=6)
Any adverse event	11 (65)	4 (67)
Mild	4 (24)	0
Moderate	6 (35)	3 (50)
Severe	1(6)	1 (17)
Serious events	1 (6)	2 (33)
Events resulting in death	0	0
Events related to treatment	2 (12)	0
Events leading to discontinuation of study drug:		
Temporary discontinuation	2 (12)	0
Permanent discontinuation	1 (6)	1 (17)

Source: Maher et al, The Lancet Respiratory Medicine 2018 ([link](#)), Bernstein analysis

EXHIBIT 31: **Most frequent adverse events**

	FLORA			
	GLPG1690 (n=17)		Placebo (n=6)	
	Patients (%)	# events	Patients (%)	# events
Infections and infestations	7 (41)	10	3 (50)	8
Respiratory, thoracic, and mediastinal disorders	4 (24)	8	2 (33)	4
Gastrointestinal disorders	2 (12)	2	2 (33)	2
Musculoskeletal and connective tissue disorders	1 (6)	1	2 (33)	6
Cardiac disorders	0	0	1 (17)	2
Renal and urinary disorders	0	0	1 (17)	3
Vascular disorders	0	0	1 (17)	1
General disorders and investigations	2 (12)	2	1 (17)	1
Investigations	2 (12)	2	1 (17)	1

Source: Maher et al, The Lancet Respiratory Medicine 2018 ([link](#)), Bernstein analysis

The product compares well vs. approved products. As we have previously stated, cross trials comparisons in IPF are a challenge. Even more so given the fact that the GLPG1690 study (i) was over a shorter period of only 12 weeks vs. +52-weeks for Esbriet/Ofev, (ii) only recruited 17 drug treated patients vs. hundreds for Esbriet/Ofev, (iii) recruited a slightly different patient population, (iv) had different endpoints (Exhibit 32).

We have to take 17 patient data with a pinch of salt but looking at the 12-week data for both Esbriet and Ofev, (i) neither were able to demonstrate any form of improvement in FVC, which GLPG1690 did, (ii) both have inferior tolerability profiles, particularly GI, and (iii) both have inferior dosing schedules.

EXHIBIT 32: Comparisons of FLORA study to Esbriet/Ofev studies

	GLPG1690	Esbriet (pirfenidone)		Ofev (nintedanib)	
Study names	FLORA (P2)	CAPACITY-1 and 2	ASCEND	TOMORROW	INPULSIS-1 and 2
Phase	P2	P3	P3	P2	P3
Total patients	23	1,247		1,231	
Drug-treated patients	17	623		723	
Study duration	12 weeks	72 weeks	52 weeks	52 weeks	52 weeks
Primary endpoint(s)	Safety (adverse events), tolerability, PK & PD	Change in % predicted FVC	Absolute change in % predicted FVC	Rate of decline in FVC	Rate of decline in FVC
Summary of other endpoints	Changes in pulmonary function (spirometry), biomarkers, HRCT images, QoL measures	Absolute change in % predicted FVC, progression-free survival, 6MWT, SpO ₂ , DLCO, dyspnea score, worsening of IPF	n/a	Absolute/relative changes in FVC% predicted and FVC, survival, SpO ₂ , PaCO ₂ , DLCO, dyspnea, 6MWT, FEV1/FVC, SGRQ scores, lung capacity measures, exacerbations, time to progression	As per TOMORROW, plus time to death or transplant and additional questionnaires (e.g., SOBQ, CASA-Q, PGI-C, EQ-5D)
Patient population:					
IPF diagnosis confirmation	Centrally confirmed	'Confident' local diagnosis	Centrally confirmed	Centrally confirmed	Centrally confirmed
IPF diagnosis duration	n/a	n/a	6-48 months	<5 years	<5 years
Patient age	≥40 years	Between 40 and 80	Between 40 and 80	>40 years	>40 years
% FVC	≥50%	≥50%	Between 50% and 90% inclusive	>50%	≥50%
% carbon monoxide diffusing capacity (% DLCO)	≥30%	Between 35% and 90% inclusive	Between 30% and 90% inclusive	Between 30% and 79% inclusive	Between 30% and 79% inclusive
FEV1/FVC ratio	≥0.7	n/a	≥0.8	n/a	≥0.7

Source: Company disclosure, Bernstein analysis and estimates

Phase 3 trials on-going. The programme consists of two identical trials: ISABELA 1 ([NCT03711162](#)) and ISABELA 2 ([NCT03733444](#)) with a total of 1,500 IPF patients. These patients remain on their current standard of care (which may include Esbriet or Ofev) and randomised to one of two doses or placebo. The primary endpoint will be the change in FVC (in mL) at 52 weeks. The studies will also look at hospitalisations, mortality, quality of life, and safety/tolerability. All patients to be treated until last patient passes the 52-week milestone – meaning that for a subset of patients the study will collect longer term data. We will likely need to wait until late 2020 (at best) to see any outcome from the study but as mentioned earlier, a futility analysis will provide some context as to how the trial is progressing (at 1 year for 25% of patients powered to demonstrate a 80mL FVC change). If this is positive, sentiment could turn increasingly positive.

The general consensus view from physicians is that Galapagos have an ambitious plan as it will highlight if there is any additional benefit when combined with existing treatment options. With a very heterogenous patient pool, sub-population analysis may not read well. Regardless, demonstrate benefit and the product will be used either alone or in combination with Esbriet or Ofev.

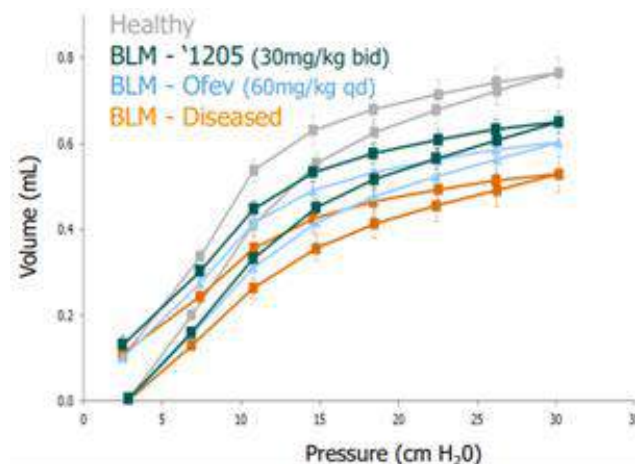
Galapagos has other candidates in IPF but only one to discuss for now. Galapagos do have several other molecules in their pipeline for IPF (GLPG2384, GLPG3499) but only GLPG1205 is currently in the clinic.

GLPG1205 is a GPR84 inhibitor. G-protein coupled receptor 84 is a fatty acid receptor that is highly expressed on bone marrow cells, splenic T and B cells and circulating granulocytes, monocytes and macrophages, although in the latter cell types its expression depends on upregulation in response to inflammatory conditions. GPR84 is also expressed in many organs, including the lung. The role of GPR84 is not yet well characterised, however it is known to be upregulated by lipopolysaccharide and by Staphylococcus enterotoxin B, and to enhance the induction of IL-12 (which supports Th1 helper T cell responses) and IL-8 (a chemokine expressed by macrophages, epithelial cells, endothelial cells and airway smooth muscle cells). IL-8 is known to play a role in IPF: serum levels of IL-8 are elevated in patients with IPF and correlates with disease activity ([link](#)) and mediates fibrogenic mesenchymal progenitor cells (MPCs) in IPF ([link](#)).

GPR84 has typically been associated with metabolic and inflammatory disorders but studies in mouse models of fibrosis have shown that GPR84 also plays a role in fibrotic disease in a range of tissues. For example, *Gpr84* knockout mice have reduced kidney fibrosis in an adenine-induced nephropathy model, and treatment with PBI-4050 (known to be both an agonist of GPR40 and an inhibitor of GPR84) reduces lung fibrosis in a bleomycin mouse model ([link](#)).

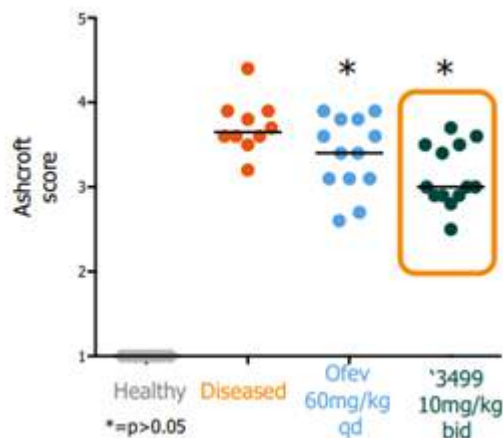
Pre-clinical studies of GLPG1205 have been promising. In a bleomycin mouse model GLPG1205 seems to provide better improvement of respiratory capacity vs Ofev (Exhibit 33). Human trials of this candidate in ulcerative colitis demonstrated tolerability but no effect. The PINTA p2 trial ([NCT03725852](https://clinicaltrials.gov/ct2/show/study/NCT03725852)) is on-going, is expected to complete recruitment before year-end and will report headline data in 2H20. The trial is testing 100mg once daily oral (2 capsules) for 26 weeks in 60 IPF patients. Galapagos seem excited by GLPG1205, suggesting it is a very potent and effective molecule.

EXHIBIT 33: GLPG1205 - Inspiratory capacity



Source: Galapagos

EXHIBIT 34: GLPG3499 - Signs and symptoms score



Source: Galapagos

If they work, they will sell. Whilst the addressable population is large (~125k patients in the US), diagnosis and thus treatment rates are low (our estimates suggest less than 20% in the US). Physicians suggest if their patients are diagnosed with the disease, they would typically use one of the 2 approved products. Importantly, Galapagos have designed the ISABELA p3 trials to include arms on top of SoC. Important, given KOLs suggest use on top of existing products is the most likely outcome for pipeline assets. Our base assumption is that 30% of Esbriet/Ofev patients will also receive GLPG1690, equivalent to 13.5k patients in 2030 in the US, below the number of patients being treated today for the disease. We must also acknowledge the competitor pipeline in IPF. Promedior and Fibrogen have the products most debated but with such an array of targets and such early stage data, it is too hard to call who offers the biggest threat. Regardless, there is enough unmet need (even on top of existing treatment) that success for one may not limit success for others. We did consider the impact of combination therapy and the incremental cost of treatment, but physicians were quick to point to PAH, where triplet therapy now sets the bar at over \$250k and reimbursement continues to be strong.

With Galapagos owning full rights for the IPF portfolio, our peak sales estimates of €1.5B in 2030 (very realistic for an efficacious product, 2 existing products already +\$1B 5 years in, detailed model in Exhibit 35) can be a big contributor to GLPG value (see our valuation analysis below). We would not call IPF a graveyard for drug development (we have better examples e.g. SLE) but given some patients may go periods of months with no worsening of disease, it will always be challenging to say with certainty that GLPG1690 will demonstrate superiority (hence our 30% probability of success). The initial data suggests the product should do well and given the complementarity to existing treatment, we would expect to see an additive benefit for patients. The way we see it, get an approval (late 2021/early 2022 launch) and the drug will sell.

EXHIBIT 35: **GLPG1690 IPF US market model**

	2015	2016	2017	2018	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
US market																
TRx																
Esbriet	51,045	69,438	72,041	77,055	87,666	95,556	107,023	118,795	133,051	145,025	156,627	167,591	177,647	186,529	193,990	201,750
Ofev	32,805	58,829	71,767	82,338	87,666	95,556	107,023	118,795	133,051	145,025	156,627	167,591	177,647	186,529	193,990	201,750
Total baseline	83,850	128,267	143,808	159,393	175,332	191,112	214,046	237,591	266,102	290,051	313,255	335,183	355,294	373,058	387,981	403,500
% growth		53%	12%	11%	10.0%	9.0%	12.0%	11.0%	12.0%	9.0%	8.0%	7.0%	6.0%	5.0%	4.0%	4.0%
GLPG1690	0	0	0	0	0	0	10,702	26,135	42,576	60,911	75,181	87,147	95,929	104,456	112,514	121,050
Others	0	0	0	0	0	0	17,124	42,766	69,186	89,916	109,639	127,369	145,670	164,146	182,351	201,750
Total add-on	0	0	0	0	0	0	27,826	68,901	111,763	150,826	184,820	214,517	241,600	268,602	294,865	322,800
% share of baseline TRx																
Esbriet	61%	54%	50%	48%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%
Ofev	39.1%	45.9%	49.9%	51.7%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%
Add-on % share of baseline TRx																
GLPG1690	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	5.0%	11.0%	16.00%	21.0%	24.00%	26.0%	27.0%	28.0%	29.0%	30.0%
Others	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	8.0%	18.0%	26.00%	31.0%	35.00%	38.0%	41.0%	44.0%	47.0%	50.0%
Total add-on	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	13.0%	29.0%	42.0%	52.0%	59.0%	64.0%	68.0%	72.0%	76.0%	80.0%
Sales (\$m)																
Esbriet	395	562	630	701	814	905	1,013	1,125	1,260	1,373	1,483	1,111	1,060	1,113	1,157	1,203
Ofev	293	512	663	798	866	963	1,079	1,197	1,341	1,462	1,579	1,182	1,128	1,184	1,232	1,281
Total baseline	687	1,075	1,293	1,499	1,680	1,868	2,092	2,322	2,601	2,835	3,062	2,293	2,188	2,297	2,389	2,484
GLPG1690	0	0	0	0	0	0	105	255	416	595	735	852	938	1,021	1,100	1,183
Other	0	0	0	0	0	0	167	418	676	879	1,072	1,245	1,424	1,604	1,782	1,972
Total add-on	0	0	0	0	0	0	272	673	1,092	1,474	1,806	2,097	2,361	2,625	2,882	3,155
Total IPF	687	1,075	1,293	1,499	1,680	1,868	2,364	2,995	3,693	4,309	4,868	4,390	4,549	4,922	5,271	5,639
Realised price per TRx																
Esbriet	7,731	8,100	8,741	9,100	9,282	9,467	9,467	9,467	9,467	9,467	9,467	6,627	5,964	5,964	5,964	5,964
Ofev	8,917	8,711	9,239	9,688	9,882	10,080	10,080	10,080	10,080	10,080	10,080	7,056	6,350	6,350	6,350	6,350
GLPG1690					9,582	9,773	9,773	9,773	9,773	9,773	9,773	9,773	9,773	9,773	9,773	9,773
Other					9,582	9,773	9,773	9,773	9,773	9,773	9,773	9,773	9,773	9,773	9,773	9,773
Growth in realised price per TRx																
Esbriet		5%	8%	4%	2.0%	2.0%	0.0%	0.0%	0.0%	0.0%	0.0%	-30.0%	-10.0%	0.0%	0.0%	0.0%
Ofev		-2%	6%	5%	2.0%	2.0%	0.0%	0.0%	0.0%	0.0%	0.0%	-30.0%	-10.0%	0.0%	0.0%	0.0%
GLPG1690					2.0%	2.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Other					2.0%	2.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Addressable population																
US Population ('000s)	321,040	323,406	325,719	328,123	330,540	332,965	335,387	337,799	340,189	342,552	344,877	347,154	349,378	351,545	353,651	355,695
IPF prevalence (# per 100,000)	36.5	37.0	37.5	38.0	38.5	39.0	39.5	40.0	40.5	41.0	41.0	41.0	41.0	41.0	41.0	41.0
# US patients with IPF ('000)	117,180	119,660	122,145	124,687	127,258	129,856	132,478	135,120	137,777	140,446	141,400	142,333	143,245	144,133	144,997	145,835
Implied patients treated (assumes 9 TRx per year)																
Baseline																
Esbriet	5,672	7,715	8,005	8,562	9,741	10,617	11,891	13,199	14,783	16,114	17,403	18,621	19,739	20,725	21,554	22,417
Ofev	3,645	6,537	7,974	9,149	9,741	10,617	11,891	13,199	14,783	16,114	17,403	18,621	19,739	20,725	21,554	22,417
Baseline total	9,317	14,252	15,979	17,710	19,481	21,235	23,783	26,399	29,567	32,228	34,806	37,243	39,477	41,451	43,109	44,833
% of patients treated with baseline ther:	8%	12%	13%	14%	15%	16%	18%	20%	21%	23%	25%	26%	28%	29%	30%	31%
Add-on																
GLPG1690	0	0	0	0	0	0	1,189	2,904	4,731	6,768	8,353	9,683	10,659	11,606	12,502	13,450
Others	0	0	0	0	0	0	1,903	4,752	7,687	9,991	12,182	14,152	16,186	18,238	20,261	22,417
Add-on total	0	0	0	0	0	0	3,092	7,656	12,418	16,758	20,536	23,835	26,844	29,845	32,763	35,867
% of patients treated with add-on therap:	0%	0%	0%	0%	0%	0%	2%	6%	9%	12%	15%	17%	19%	21%	23%	25%
GLPG revenue																
GLPG sales (\$m)				0	0	0	105	255	416	595	735	852	938	1,021	1,100	1,183
FX (EUR/USD)				0.85	0.90	0.91	0.91	0.91	0.91	0.91	0.91	0.91	0.91	0.91	0.91	0.91
GLPG US sales (€m)	0	0	0	0	95	233	379	542	669	776	854	930	1,002	1,078	1,155	1,231

Source: IQVIA, World Bank, UN World Population Prospects 2017, British Lung Foundation, Nalysnyk et al (2012) Eur Respir Rev ([link](#)), Company disclosure, Bernstein analysis and estimates

#3 - Toledo p1 in 1H20 - but will it drive value?

The Toledo program has been much hyped by Galapagos, but there is little in the way of actual concrete information. The 1st compound (GLPG3312) entered the clinic with p1 (safety, tolerability, PK/PD) readout in healthy volunteers due in 2H19 ([NCT03800472](#), SC Jul-19) and will move to a PoC in ulcerative colitis (UC) in 2H19. The second compound (GLPG3970) is due to enter the clinic this year. Whilst UC is the first indication, we know that Toledo could be broadly applicable in inflammation, although we do not know anything about the target. We note that GLPG filed a patent (WIPO Patent WO/2019/105886A1; [link](#)) that was published last month that *may* allow us to infer a little more.

The patent refers to a class of compounds that inhibit salt-inducible kinases (SIK kinases) that could be used for the prophylaxis and/or treatment of inflammatory, autoinflammatory, autoimmune, proliferative, fibrotic and cartilage/bone related diseases associated with hypersecretion of TNFα, interferons, IL-6, IL-12 and/or IL-23. More specifically, the patent gives examples of SLE, CLE, lupus nephritis, dermatomyositis, Sjogren's, psoriasis, RA, PsA, MS, trisomy 21, UC and/or CD as hypersecretory diseases, but plenty of other disease examples are given. Quite some list, with significant overlap with Filgo.

SIKs are multifunctional proteins, widely expressed that are particular involved in cellular energy homeostasis with three isoforms (SIK1-3). SIKs have been noted to control the localisation and phosphorylation of a number of two key classes of transcriptional regulatory factors - histone deacetylases (HDACs) and cAMP-regulated transcriptional coactivators (CRTC)s, which amongst other activities, also controls macrophage phenotype. One recent paper noted that small molecule SIK inhibition could mimic cAMP-induced signals in IBD, osteoporosis and skin pigmentation ([link](#)), another noted their impact on pancreatic β-cells suggesting a role in diabetes and obesity ([link](#)) and another noted a role in oncology ([link](#)). Clearly, there is wide ranging potential from this target (if indeed this is Toledo!) and we shall dig a little deeper into this in due course. From our initial search, we were unable to find any other SIK inhibitors in the clinic, despite a few in the lab. Despite GLPG's excitement, we will need more to ascribe any value for the program (you could argue we do via the platform, see DCF).

#4 - MOR106 data in Atopic Dermatitis in 1H20 - the economics don't help

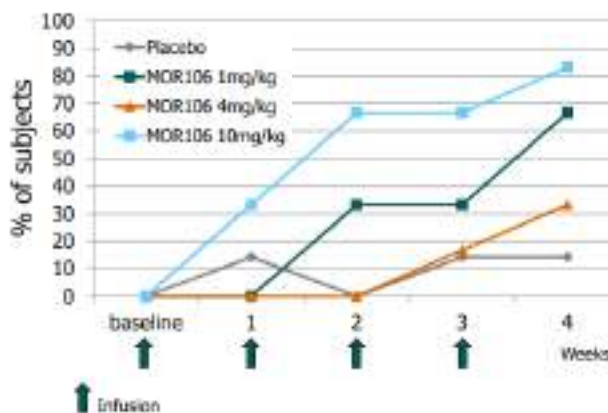
Investors had given little consideration for the product thus far. The economics are less favourable than other pipeline assets but MOR106 must still be a consideration as a potential catalyst. We provide a summary below.

MOR106 in AtD was jointly developed with Morphosys. MOR106 is a selective inhibitor of IL-17C, one of six members of the IL-17 family (IL-17A to IL-17F). The IL-17 market is already crowded, but the current therapies have different IL-17 targets: Cosentyz and Taltz both inhibit IL-17A, while Siliq inhibits IL-17A, IL-17F and IL-17E (also known as IL-25). MOR106 is the first publicly disclosed human monoclonal antibody with IL-17C as the target.

The role of IL-17C is not well characterised but is believed to induce the production of proinflammatory cytokines and also has a function in mucosal immunity and autoimmune responses. In experimental autoimmune encephalomyelitis, a model of T-cell-mediated autoimmune disease, mice lacking IL-17C were less likely to exhibit EAE symptoms and had much milder disease. Importantly, IL-17C is produced by keratinocytes where it acts locally to amplify inflammatory mediators, and IL-17C expression is increased in atopic dermatitis skin.

Early data is encouraging. Starting with the pre-clinical data, using two mouse models of atopic dermatitis, MOR106 neutralisation of IL-17C reduced skin inflammation ([link](#)). A phase 1b study in 25 patients tested three dosing regimens (1mg/kg, 4mg/kg and 10mg/kg) versus placebo over a 4-wk period of weekly IV infusions. Drug exposure was approximately dose proportional and the drug was well tolerated with only mild or moderate adverse events (Exhibit 37), although one patient did develop anti-drug antibodies. Skin efficacy was promising, with a fast onset of response which was maintained after stopping treatment for at least two months of follow up. Up to 83% of patients receiving the high dose achieved EASI 50 or better by week 4 (Exhibit 36) ([link](#)). Somewhat comparable to Dupixent p2 data.

EXHIBIT 36: MOR106 P1 study: % patients with 50% EASI improvement



Source: Galapagos, Bernstein analysis

EXHIBIT 37: MOR106 P1 study: safety data

	Placebo (n=7)	1mg/kg (n=6)	4mg/kg (n=6)	10mg/kg (n=6)
Number (%)				
TEAE	2 (28.6)	5 (83.3)	5 (83.3)	3 (50.0)
Serious	0	0	0	0
Death	0	0	0	0
Worst TEAE intensity				
Mild	0	2 (33.3)	2 (33.3)	1 (16.7)
Moderate	2 (28.6)	3 (50.0)	3 (50.0)	2 (33.3)
Severe	0	0	0	0
Treatment related	0	2 (33.3)	1 (16.7)	1 (16.7)
Permanently stopped	1 (14.3)	1 (16.7)	0	0

Source: Galapagos, Bernstein analysis

Phase 2 data should be expected in 1H20. The Phase 2 IGUANA study will recruit 240 patients with moderate to severe atopic dermatitis ([NCT03568071](#)). Five dosing regimens will be tested over a 12-week period with the primary outcome focused on

EASI score. As a reference, Dupixent demonstrated EASI-75 scores in ~50% of patients across the SOLO-1 and 2 studies (vs. 12-15% for placebo) both with the weekly and biweekly dosing and 35-40% of patients achieving clearing or near clearing of skin lesions. With trial completion expected in Dec-19, we do not have to wait long for an update. Most importantly, the global licensing deal by Novartis for the asset, whilst limiting the economics for Galapagos, has led to an acceleration and expansion in the program with the p2 GECKO trial with steroids also initiated ([NCT03864627](#), SC Jan-20) which uses the subq version of the product whilst the subq p1 bridging study is also on-going ([NCT03689829](#)). *In short*, this is a real asset and Novartis will be expanding in to new indications in the near future.

We forecast revenues of €0.8B by 2030 at 30% probability. This is the tricky part. Whilst prevalence rates are incredibly high (~7% in adults, ~13% in children), this will not be the population from which to consider market potential. MOR106 is being assessed concomitantly with topical corticosteroids in moderate to severe AtD. Amongst children, the split of mild, moderate and severe disease is 67%, 26% and 7% and in adults the disease is marginally more severe (60%, 29% and 11%; [link](#), [link](#)). From discussions with KOLS, moderate AtD is relatively well controlled with topical corticosteroids and so the severe pool is the more relevant target, despite being smaller with ~2.7M US patients (2M adults) vs ~7.6M US patients (~5.3M adults) in the moderate pool. Treatment rates with biologics are low currently and we estimate biologics (i.e. Dupixent) treated ~18k patients (~1% of severe adult pool) in 2018. Naturally, with Dupixent the first AtD biologic only approved in 2017, this will increase, but a ~5% penetration for biologics in the severe pool and limited penetration in moderate adult and paediatric patients implies a total biologic eligible pool of ~150k patient is reasonable.

Coming to market share, it's important to mention that Dupixent is a well-tolerated and highly effective AtD drug and so it sets the bar pretty high here. Additionally, AtD is one of the most competitive fields we have looked at in some time with a plethora of approaches in the mid-late stage pipeline including JAKs, cytokines (IL-13, IL17, IL23, IL-31, several IL-33s) and a whole heap of other approaches (NK-1R, OX40, histamine, cannabidiol, CD40, SLO, LXR). Yes, JAKs have a safety record that might hinder them and the IL data as mixed (some good, some ok), but it is clear that MOR106 will face competition. On this basis, and until we see detailed data, we think a 15% market share is as good as it gets and at ~\$25k per patient implies US sales of ~\$560M, with OUS sales potentially adding ~\$200M further. Given Dupixent consensus sits at >\$6B, this is not particularly a stretch. Our caution is driven by lack of additional data and what looks like a competitive pipeline.

Our forecasts account for the 50% of milestone payments (up to €850M) and low-teen to low-twenties royalties, with MorphoSys taking the other half. We assume milestones are split between sales (\$200M/€175M, of which GLPG could take half) with regulatory/development milestones accounting for the remainder (~€670M). We assume GLPG receives €220M in regulatory/development milestones between now and approval. The remaining €230M will come from additional indications, possibly psoriasis (although this is already quite crowded), but inflammatory diseases of the joints, CNS and cardiovascular system are also potential options ([link](#)). We don't model other approvals within our 2030-time horizon and thus do not give credit for additional milestones.

#5 - GLPG1972 in Osteoarthritis in 2H20 - fast recruitment but not much to go on

Osteoarthritis is a degenerative disease leading to joint destruction and loss of cartilage. Symptoms include pain, swelling, and reduced motion in affected joints. Osteophytes (bone spurs) may develop at the joint edges, and fragments of bone or cartilage may detach and float in the joint space – causing more pain and damage. The knee, hip and small joints of the hands are most commonly affected. Osteoarthritis is the most common form of arthritis, affecting ~12% of the global population. Diagnosis typically involves ruling out other forms of arthritis. Osteoarthritis may be indicated in a patient over the age of 50 and for whom the pain gets worse with increased use of the joints. Osteoarthritis typically manifests with joint stiffness in the morning that lasts less than 30 minutes (or not at all), while RA will typically have prolonged joint stiffness in the morning.

Currently available therapies treat the symptoms but are not disease modifying. For mild disease, therapy is focused on exercise, weight loss, supportive foot wear or other devices intended to minimise joint strain. Severe symptoms are treated with systemic painkillers (e.g., paracetamol, NSAIDs, cox-2 inhibitors, opioids) or topical painkillers (e.g., NSAIDs, capsaicin cream). Steroids may be injected into the joints to provide short-term relief. Platelet rich plasma, extracted from the patient's own blood for intraarticular injection, is a newer therapy that may enhance healing. In extreme cases, joint reconstruction, replacement or fusion surgery may be necessary.

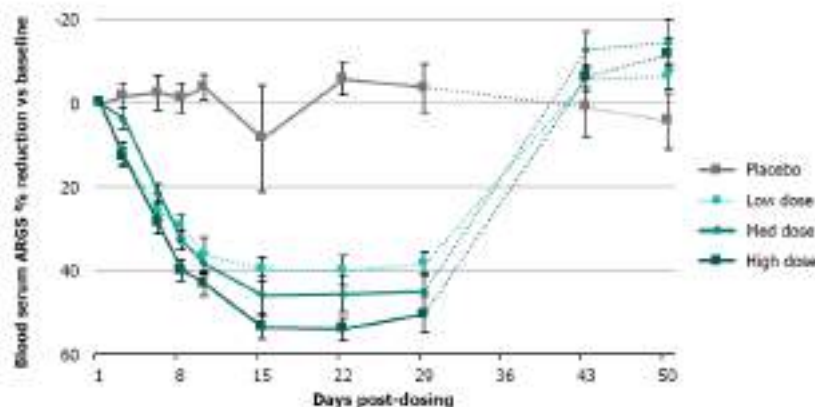
The pipeline is not exactly full. Drugs are either focused on enhanced pain management or ultimately attempting to be disease modifying.

- + *Enhanced pain management.* (i) Tanezumab (Pfizer/Lilly), a nerve growth factor inhibitor that delivered positive p3 top-line results in July 2018 with improvement to pain, physical function, and overall patient assessment of their OA and longer-term data in 2Q19 ([link](#)). It remains unclear on next steps for the product. (ii) Fasinumab (Regeneron/Teva), also an inhibitor of NGF, which similarly reported positive p3 results in August 2018. The market does seem overly excited by either.
- + *Potential disease modifying action.* (i) Invossa (TissueGene/Kolon), is a mixture of non-transduced allogeneic (i.e., donor) human chondrocytes and allogeneic human chondrocytes expressing transforming growth factor beta 1 (TGF- β 1). Invossa is already approved in Korea on the basis of symptom relief only (not disease modifying activity), but TissueGene/Kolon expects to get FDA approval as a DMOAD (disease modifying osteoarthritis drug) by collecting evidence of disease modifying activity in the Korean market in a post-marketing study of 3,000 participants. On symptom relief alone Invossa's results are impressive: 84-88% symptom reduction lasting up to two years. (ii) JointStem (Nature Cell/Biostar) is an autologous adipose-derived mesenchymal stem cell technology currently undergoing phase 2 testing in the US and Korea. It recently suffered a set-back when it failed to get conditional approval from the Korean regulators who considered that their submitted study data included too few patients, demonstrated lack of efficacy in more than half of patients, demonstrated that stem cell therapy was not as effective as platelet-rich plasma therapy, and had an insufficient wash out period to exclude the possibility of corticosteroids contributing to the results. (iii) SM04690 (Samumed), a small molecule Wnt pathway inhibitor and potentially a disease modifying therapy, reported positive p2 results in terms of structural progression and patient reported pain/function.

GLPG1972 has an interesting MoA but data is limited. The product is an inhibitor of ADAMTS-5 (A Disintegrin and Metalloproteinase with Thrombospondin motifs). ADAMTS-5 is a secreted, extracellular enzyme which plays a role in extracellular matrix remodelling. In joints, it plays a role (along with ADAMTS-4) in breaking down aggrecan in cartilage, which leaves the collagen matrix exposed and subject to degradation. Although both ADAMTS-4 and 5 are present in cartilage, ADAMTS-5 is 1000-fold more potent *in vitro*. ADAMTS-5 expression is induced by IL-1, TNF- α , IL-6, S100A8 and S100A9 – all known to be upregulated in inflammatory diseases ([link](#)). Data in several mouse models suggests a role for ADAMTS-5 in osteoarthritis: mice lacking ADAMTS-5 are protected from surgery induced osteoarthritis and antigen-induced arthritis models, and exhibit blockade of fibrosis and accumulation of aggrecan in the joints.

P1b studies support the notion of GLPG1972 as a DMOAD demonstrating significant reductions in circulating levels of ARGS neopeptide, a biomarker for cartilage breakdown (Exhibit 38).

EXHIBIT 38: GLPG treatment reduces biomarker for cartilage breakdown (p1b)



Source: Galapagos

Phase 2 study recruiting very fast, data expected in 2H20. The large p2 ROCCELLA trial in 852 patients with knee osteoarthritis completed recruitment in 9 months (vs. the 14 expected; [NCT03595618](#)), with the goal to demonstrate disease modifying efficacy, not just pain relief. The primary outcome measure will measure cartilage reduction (via quantitative MRI) after 52 weeks of treatment.

It can be debated whether GLPG1972 would be the "first" DMOAD to market but the product is dosed orally, an advantage over competitors in the clinic (IV) and the product would face fewer logistical challenges than Invossa (requires that live cells must

then survive transport and storage, typically using cryopreservation, and requires a laboratory technician at the clinical centre to reconstitute the cells for injection into the patient). In a battle for patient share, convenience should be a huge advantage, and we expect Invossa would need vastly superior efficacy to become standard of care.

Big potential but little probability for now - €1B at 20% probability. First off, much like MOR106, the headline population of OA is large (120m total in US/EU and growing) and DMOADs are likely to be used only in the most severe population. That being said, pain prescriptions for OA patients alone are suggested to be \$4B a year and we must also consider the costs of joint replacements. Under the agreement for GLPG1972, Servier has ex-US rights and responsibility for further clinical development, registration and commercialisation. Galapagos retains US commercialisation rights and is also eligible for milestone payments (up to €290M), as well as royalties ex-US (single digit – we assume 7%). In short, if it works, this will be big for the company and is heavily risk-adjusted by most.

Financial forecasts

EXHIBIT 39: Galapagos revenue detail

€ million	FY 2016	FY 2017	FY 2018	FY 2019E	FY 2020E	FY 2021E	FY 2022E	FY 2023E	FY 2024E	FY 2025E
Revenue Summary										
EUR/USD as of 04/10/2019	0.90	0.89	0.85	0.90	0.91	0.91	0.91	0.91	0.91	0.91
Summary of candidate revenue streams										
Filgotinib										
Gilead sales ex-co-promotion regions (\$ M)	0	0	0	0	32	299	728	1,136	1,586	1,929
Gilead sales in co-promotion regions (\$ M)				0	5	41	106	168	218	261
Galapagos royalty (€ M)	0	0	0	0	6	55	141	230	337	425
Benelux (€ M)	0	0	0	0	0	3	8	13	17	20
Reimbursement of profits from co-promotion regions (€ M)				0	1	12	31	49	63	75
Upfront license fee recognition	26	62	85	279	355	355	355	355	355	355
Share subscription agreement	4	9	12	15	0	0	0	0	0	0
Milestone payments	55	9	28	64	246	118	185	89	241	182
Total filgotinib revenue	84	81	124	357	609	543	720	736	1,014	1,058
Idiopathic pulmonary fibrosis										
Revenue EU sales (€ M)	0	0	0	0	0	11	26	40	56	67
Galapagos royalty on ex-EU sales (€ M)	0	0	0	0	0	6	16	26	36	45
GILD milestone				0	0	88	0	0	0	0
Total IPF revenue	0	0	0	0	0	17	41	66	92	112
Cystic fibrosis										
AbbVie reported sales (\$ M)	0	0	0	0	0	0	49	93	154	209
China/S Korea sales (€ M)										
Galapagos share of Benelux sales (€ M)										
Galapagos royalty (€ M)	0	0	0	0	0	0	2	4	7	10
Upfront license fee recognition	0	0	52	2	0	0	0	0	0	0
Milestone payments	27	34	37	24	3	4	5	9	9	14
Total CF revenue	27	34	89	26	3	4	7	13	17	24
Atopic dermatitis										
Novartis reported sales (\$ M)	0	0	0	0	0	0	0	10	52	94
Galapagos royalty (€ M)	0	0	0	0	0	0	0	1	3	6
Upfront license fee recognition	0	0	48	0	0	0	0	0	0	0
Milestone payments	0	0	0	3	3	0	15	45	9	9
Total AtD revenue	0	0	48	3	3	0	15	46	12	15
Osteoarthritis										
US sales (\$M)	0	0	0	0	0	0	10	30	60	84
Servier reported sales - OUS (\$ M)	0	0	0	0	0	0	4	12	18	27
Galapagos royalty on US sales (€ M)	0	0	0	0	0	0	2	5	11	15
Galapagos royalty OUS (€ M)	0	0	0	0	0	0	0	1	1	2
Upfront license fee recognition	0	0	0	0	0	0	0	0	0	0
Milestone payments	0	0	9	0	49	36	46	20	0	12
Total OA revenue	0	0	9	0	49	36	33	26	12	29
Summary by revenue type										
Product revenue	0	0	0	0	0	14	34	53	73	87
Profit share on co-promotion regions				0	1	12	31	49	63	75
R&D revenue	122	118	279	405	682	682	787	805	1,031	1,096
Recognition of upfront payments / license fees	26	62	196	295	355	355	355	355	355	355
Milestone payments	82	43	73	91	301	246	251	163	260	217
Reimbursement income	10	3	9	19	20	20	20	20	20	20
Royalties	0	0	0	0	6	61	161	267	397	504
Services revenue	8	9	10	10	10	10	10	10	10	10
Other income	22	29	29	32	32	32	32	32	32	32
Intersegment elimination	0	0	0	0	0	0	0	0	0	0
Total revenue	152	156	318	446	725	750	893	948	1,209	1,300

Source: Company disclosure, Bernstein analysis and estimates

EXHIBIT 40: Income Statement

Income Statement €M	Annual FY 2015	Annual FY 2016	Annual FY 2017	Annual FY 2018	Annual FY 2019E	Annual FY 2020E	Annual FY 2021E	Annual FY 2022E	Annual FY 2023E	Annual FY 2024E	Annual FY 2025E
Revenue	61	152	156	318	446	725	750	893	948	1,209	1,300
Research and development expenses	-130	-140	-219	-323	-371	-500	-600	-650	-700	-700	-700
General and administrative expenses	-19	-22	-24	-36	-41	-45	-45	-45	-40	-40	-40
Sales and marketing expenses	-1	-2	-3	-4	-11	-20	-30	-50	-60	-70	-80
Operating Profit	-89	-11	-90	-358	23	160	75	148	148	399	480
Net financials	0	8	-26	16	-2	17	16	15	14	14	14
Profit Before Tax	-120	54	-116	-342	21	177	91	163	163	412	494
Income tax	1	-0	-0	-0	20	-7	-3	-6	-6	-15	-19
Net Income	-118	54	-116	-342	20	171	88	157	156	397	475
Basic EPS	-3.32	1.18	-2.34	-0.56	0.34	2.72	1.38	2.45	2.43	6.12	7.27
Diluted EPS	-3.32	1.14	-2.34	-0.56	0.33	2.54	1.29	2.29	2.27	5.71	6.79
Margin analysis (%)											
R&D (of revenue)	-214%	-92%	-140%	-102%	-87%	-69%	-80%	-73%	-74%	-58%	-54%
G&A (of revenue)	-32%	-14%	-16%	-11%	-10%	-6%	-6%	-5%	-4%	-3%	-3%
Operating margin	-148%	-8%	-58%	-113%	5%	22%	10%	17%	16%	33%	37%
Tax rate (of EBT)	-1%	0%	0%	0%	-7%	-4%	-4%	-4%	-4%	-4%	-4%

Source: Company disclosure, Bernstein analysis and estimates

EXHIBIT 41: Balance Sheet

Balance Sheet €M	Annual FY 2015	Annual FY 2016	Annual FY 2017	Annual FY 2018	Annual FY 2019E	Annual FY 2020E	Annual FY 2021E	Annual FY 2022E	Annual FY 2023E	Annual FY 2024E	Annual FY 2025E
Assets											
Non-Current Assets											
Intangible assets	2	1	2	4	8	10	11	12	12	12	12
PPE	14	15	17	23	52	53	55	59	62	64	66
Receivables and others	53	60	69	84	91	91	91	91	91	91	91
Total Non-Current Assets	68	76	89	111	151	153	157	162	165	167	169
Current Assets											
Receivables	13	20	40	30	88	99	102	120	126	160	172
Marketable securities and financial assets	6	7	6	8	7	7	7	7	7	7	7
Cash and cash equivalents	340	973	1,151	1,291	5,459	5,341	5,103	4,910	4,728	4,750	4,875
Others	7	7	0	0	0	0	0	0	0	0	0
Total Current Assets	374	1,007	1,198	1,329	5,553	5,447	5,212	5,037	4,861	4,918	5,053
Total Assets	443	1,083	1,286	1,439	5,704	5,601	5,369	5,199	5,026	5,085	5,223
Liabilities											
Non-Current Liabilities											
Deferred income	0	215	97	0	-14	-13	-11	-10	-8	-7	-5
Other non-current liabilities and provisions	5	4	5	5	26	26	26	26	26	26	26
Total Non-Current Liabilities	5	221	103	5	12	13	15	16	18	19	21
Current Liabilities											
Deferred income	40	71	123	150	3,391	3,034	2,677	2,321	1,964	1,607	1,250
Corporate tax payable	3	1	1	1	1	1	1	1	1	1	1
All other current liabilities and provisions	30	32	48	69	42	107	127	139	149	151	153
Total Current Liabilities	72	104	172	220	3,434	3,142	2,805	2,461	2,114	1,759	1,404
Total Liabilities	78	325	274	225	3,445	3,155	2,820	2,477	2,132	1,778	1,425
Total Equity	365	759	1,012	1,214	2,259	2,448	2,553	2,728	2,903	3,318	3,811
Total Equity and Liabilities	443	1,083	1,286	1,439	5,704	5,603	5,373	5,205	5,034	5,096	5,235

Source: Company disclosure, Bernstein analysis and estimates

EXHIBIT 42: Cash Flow Statement

Statement of Cashflows €M	Annual FY 2015	Annual FY 2016	Annual FY 2017	Annual FY 2018	Annual FY 2019E	Annual FY 2020E	Annual FY 2021E	Annual FY 2022E	Annual FY 2023E	Annual FY 2024E	Annual FY 2025E
CFO											
EBIT	-120	54	-116	-29	21	177	91	163	163	412	494
Adjustments for non-cash items	0	0	0	0	0	16	17	18	19	20	21
Change in working capital	0	0	0	0	3,127	-302	-338	-361	-351	-388	-365
Reversal of financial items	-0	-8	26	-4	0	-17	-16	-15	-14	-14	-14
Financial items paid / received	1	1	1	3	-1	17	16	15	14	14	14
Taxes paid	-0	-2	-0	-0	-1	-7	-3	-6	-6	-15	-19
CFO	-115	239	-147	-142	3,177	-115	-233	-186	-176	28	131
CFI											
Purchase and sale of PPE	-6	-4	-5	-10	-11	-13	-15	-17	-17	-17	-17
Purchase and sale of intangibles	-1	-0	-2	-3	-6	-6	-6	-6	-6	-6	-6
Purchase and sale of marketable securities	0	-3	0	-2	-0	0	0	0	0	0	0
CFI	-4	-7	-1	-16	-17	-19	-21	-23	-23	-23	-23
CFF											
Dividends paid											
Capital contributions & treasury purchases	271	392	348	280	0	0	0	0	0	0	0
Warrants exercised	0	4	5	8	18	18	18	18	18	18	18
CFF	271	396	353	288	16	16	16	16	16	16	16
Net Cash Flow For The Period	152	628	206	129	3,177	-118	-238	-193	-182	22	124
Exchange rate adjustments	0	5	-28	10	2	0	0	0	0	0	0
Cash and cash equivalents at beginning	188	340	973	1,151	1,291	4,469	4,351	4,114	3,921	3,739	3,761
Cash and Cash Equivalents At End	340	973	1,151	1,291	4,469	4,351	4,114	3,921	3,739	3,761	3,885

Source: Company disclosure, Bernstein analysis and estimates

DISCLOSURE APPENDIX

TICKER TABLE

Ticker	Rating	Oct 17, 2019 Closing Price	Target Price	TTM Rel. Perf.	EPS Adjusted			P/E Adjusted		
					2018A	2019E	2020E	2018A	2019E	2020E
GLPG.NA	M	EUR 147.70	155.00	58.2%	EUR (0.56)	0.33	2.54	(263.75)	447.9	58.10
OLD	O					(0.81)	2.48			
MSDLE15		1,611.52			107.28	108.60	119.12	15.02	14.84	13.53

O - Outperform, M - Market-Perform, U - Underperform, N - Not Rated

VALUATION METHODOLOGY

Galapagos NV

We set our price target using a DCF SOTP approach

RISKS

Galapagos NV

Downside risks

- + Filgotinib safety profile is undifferentiated vs. JAK peers
- + Later stage IPF pipeline fails to deliver
- + Toledo and the remainder of the pipeline fails to deliver

Upside risks

- + Filgotinib safety profile is differentiated vs. JAK peers
- + Later stage IPF pipeline delivers
- + Toledo value increases ahead of data

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12-Month Rating History as of 10/16/2019

Ticker	Rating Changes
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GLPG.NA	O (IC) 09/11/18
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Rating Guide: O - Outperform, M - Market-Perform, U - Underperform, N - Not Rated

Rating Actions: IC - Initiated Coverage, DC - Dropped Coverage, RC - Rating Change

GLPG.NA / Galapagos NV (EUR)

Date	Rating	Target
11-Sep-2018	O(IC)	100.00
18-Sep-2018	O	122.00
03-Jan-2019	O	115.00
22-Feb-2019	O	110.00
12-Apr-2019	O	115.00
26-Apr-2019	O	120.00
15-Jul-2019	O	150.00
29-Jul-2019	O	155.00

O - Outperform
M - Market-Perform
U - Underperform
N - Not Rated
IC - Initiated Coverage



Source: Bernstein - As of 16-Oct-2019

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