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Biotechnology

Galapagos N.V.

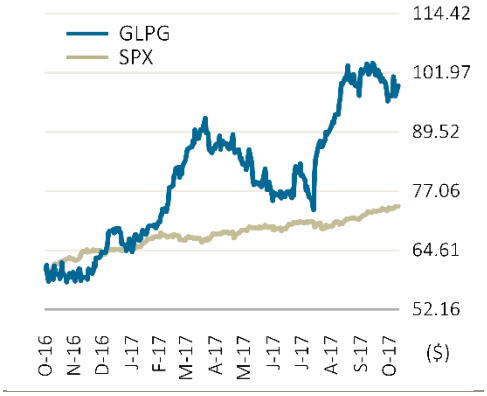
Key Insights from ACR for Filgotinib - Safety Profile Continues to Be Key to Unlocking JAK1 Utilization

We attended the American College of Rheumatology (ACR) Conference in San Diego this week, and also hosted a dinner with key members of the Galapagos management team. Our meetings and conversations at ACR continue to support our thesis that 1) next generation JAK1 inhibitors have a significant opportunity to take share within Rheumatoid Arthritis, and 2) filgotinib continues to have a potential best-in-class profile. We reiterate our Buy rating on GLPG and $118PT.

- **Perception of JAK 'class-effect' safety profiles is a storied history that we think filgotinib can change:** A key question asked of the DARWIN 3 presenter at the keynote discussion was whether filgotinib, as the 4th JAK inhibitor in late stage studies, presents an actively different safety profile relative to the 'JAK class'. Going back to the approval of tofacitinib in 2012, the safety concerns were mostly focused on rates of opportunistic infections versus cardiovascular implications. Given that filgotinib is currently registering both low rates of infection and cardiovascular events relative to tofa, upadacitinib, baricitinib, and the IL and anti-TNF classes, we do think there is an opportunity to differentiate if current event rates hold as the datasets expand.
- **Methotrexate (MTX) independence could also be a key aspect to disrupting current utilization of biologics:** We found the presentation of the tofa+MTX combo and tofa mono therapy versus adalimumab + MTX as foreshadowing the disruption of the MTX combo since tofa+MTX proved superior to the anti-TNF combo and tofacitinib mono therapy generally looked non-inferior. Given that we think filgotinib could prove more effective than tofa, the relative MTX comparison could become clinically impactful.
- **Selectivity of JAK1 continues to be supportive as the mechanistic differentiator of filgotinib:** Filgotinib is a less potent drug relative to upadacitinib and baricitinib, but that lack of potency has not affected efficacy as reported to date, and importantly, the selectivity of the drug is defining a mechanistic differentiation against the other next-gen JAK inhibitors that engage JAK2. A third-party analysis by McInnes et al. helped to validate the selectivity thesis of filgotinib.
- **Valuation:** Our $118PT values GLPG at ~4x EV/ 2022E Sales.

GLPG	**$99.24**
12 month target	$118.00
BUY	
52 week range	$57.96 - $104.02
Market Cap (m)	$5,048

Price Performance



Source: IDC

Estimates

	1Q16 A	2Q16 A	3Q16 A	4Q16 A	FY16 A	1Q17 A	2Q17 E	3Q17 E	4Q17 E	FY17 E	FY18 E
Sales	15	34	16	87	152	40	0	0	0	0	0
EBITDA (Adj.)	0	0	0	0	0	(7)	(21)	(29)	(25)	(82)	(107)
Diluted EPS (Adj.)	0.00	0.00	0.00	0.00	0.00	(0.28)	(0.71)	(0.78)	(0.56)	(2.34)	(2.34)

Source: BTIG Estimates and Company Documents ($ in millions, except per share amount)

Key Insights from ACR for Filgotinib - Safety Profile Continues to Be Key to Unlocking JAK1 Utilization

Perception of JAK 'class-effect' safety profiles is a storied history that we think filgotinib can change: A key question asked of the DARWIN 3 presenter at the keynote discussion was whether filgotinib, as the 4th JAK inhibitor in late stage studies, presents an actively different safety profile relative to the 'JAK class'. This discussion point is interesting, as the 'class effect' of safety is a more recent phenomenon that we think is based upon the safety concerns regarding DVT/ PE experienced with baricitinib, versus a long-standing issue dating back to tofacitinib. Going back to the approval of tofacitinib in 2012, the safety concerns were mostly focused on rates of opportunistic infections versus cardiovascular implications.

Filgotinib datasets still need to expand but maintain a best-in-class safety profile to date: Given that filgotinib is currently registering both low rates of infection and cardiovascular events relative to tofacitinib, upadacitinib, baricitinib and the IL and anti-TNF classes, we do think there is an opportunity to differentiate if current event rates hold as the datasets expand. The drug now has >1700 patient years of experience, which is significant, but still below the 4000 - 5000 patient level that will be evaluable with a full battery of RA clinical studies. While broader study populations could likely increase the currently low rates of herpes zoster infections with filgotinib (regional effect), we find the totality of event rates for DVT/ PE, 1 in DARWIN studies, to be very encouraging relative to the 31 cases reported with baricitinib and the 2 new cases of PE reported with upadacitinib within the SELECT-BEYOND study.

Methotrexate (MTX) independence could also be a key aspect to disrupting current utilization of biologics: Despite aging safety and efficacy profiles, anti-TNF biologics continue to the be the dominant class of drugs in RA used after MTX front line. We appreciate the long-standing treatment experience of the anti-TNF class relative to the newer IL-6 class and the value proposition of tofacitinib, but we think that over time filgotinib and other next-gen JAK1 inhibitors could disrupt the current landscape. We found the presentation of tofacitinib combo MTX and mono therapy versus adalimumab + MTX (NCT02187055, ORAL STRATEGY) as foreshadowing this disruption, since tofacitinib + MTX proved superior to the anti-TNF combo and tofacitinib mono therapy generally looked non-inferior (Figure 1). Given that we think filgotinib could prove more effective than tofacitinib, the relative MTX comparison could become clinically impactful as it is increasingly viewed that effectiveness of the anti-TNF class is dependent on co-administration of MTX, for delaying immunogenicity, which has been observed between ranges of ~20 - 40%. We acknowledge that such studies are unlikely to be run near-term, as they would most likely occur post filgotinib's approval for RA (potentially 2020).

Figure 1. Proportion of patients reporting improvement ≥ minimal clinically important difference (%)

	Tofacitinib 5 mg BID monotherapy (N = 384)	Tofacitinib 5 mg BID + MTX (N = 376)	ADA 40 mg Q2W + MTX (N=386)
Month 6	73	78	77
Month 12	77	78	76

Source: 1906 - Tofacitinib with and without Methotrexate Versus Adalimumab with Methotrexate for the Treatment of Rheumatoid Arthritis: Patient-Reported Outcomes from a Phase 3b/4 Randomized Trial, ACR 2017

Selectivity of JAK1 continues to be supportive as the mechanistic differentiator of filgotinib: Filgotinib is a less potent drug relative to upadacitinib and baricitinib, but that lack of potency has not affected efficacy as reported to date, and importantly the selectivity of the drug is defining a mechanistic differentiation against the other next-gen JAK inhibitors that engage JAK2. Importantly, a third-party analysis by McInnes et al. at helped to validate the selectivity thesis of filgotinib, whereby it was noted "Filgo did not appear to modulate GM-CSF signalling (JAK2/2), while %SI and T>IC were similar between bari and upadacitinib (ABT)" (Figure 2).

Figure 2. pSTAT Inhibition and Time Above IC50 for Baricitinib, Upadacitinib, Filgotinib and Tofacitinib

	CD4+ T cells				NK cells				Monocytes			
Stimulation/ pSTAT	Bari 4 mg	ABT 15 mg 30 mg	Filgo 100 mg 200 mg	Tofa 5 mg 10 mg	Bari 4 mg	ABT 15 mg 30 mg	Filgo 100 mg 200 mg	Tofa 5 mg 10 mg	Bari 4 mg	ABT 15 mg 30 mg	Filgo 100 mg 200 mg	Tofa 5 mg 10 mg
STAT Inhibition (%)												
IL-15/pSTAT5	36	43* 54***	8*** 15***	72*** 85***	24	27 37*	6** 12*	62*** 79***	NI			
IL-21/pSTAT3	27	41*** 51***	6*** 13***	61*** 76***	27	38* 48***	7*** 14**	61*** 76***	NI			
GM-CSF/pSTAT5	NI			NA	NI			NA	41	47 57**	5*** 9***	NA
IL-6/pSTAT3	29	23 32	12** 18*	39** 54***	NI				32	28 37	10*** 16**	46*** 61***
IL-10/pSTAT3	27	22 28	11* 17	39* 53**	23	15* 21	9** 16	34** 48***	14	18 26**	3* 6	25*** 40***
IFN-γ/pSTAT1	NI				NI				37	33 43	4*** 9***	43** 61***
Time Above IC_{50} (h)												
IL-15/pSTAT5	5.5	9.6** 12.7***	0.3** 3.6	21.2*** 24***	1	5.7* 7.7***	0 2.4	17*** 23***	NI			
IL-21/pSTAT3	0.7	8.9*** 11.5***	0 2.8	17*** 23.6***	1.2	8.0*** 10.4***	0 2.9	17.5*** 23.9***	NI			
GM-CSF/pSTAT5	NI			NA	NI			NA	8.5	10.5 14*	0** 1.1**	NA
IL-6/pSTAT3	1.9	3.8 5.9*	0.5 3.3	7.3* 14.8***	NI				3.6	5.4 7.4*	0.3 3.6	10.8* 18.2***
IL-10/pSTAT3	1.2	1.9 4.2	0 2.4	7.6* 15.1***	0.4	0.3 3.0	0 3.3*	4.2* 11.8***	0	2.6 4.8**	0 0.3	0.8 7.8***
IFN-γ/pSTAT1	NI				NI				6	6.8 9.0*	0*** 1.1**	9.4** 16.8***

[a]JAKis were administered once daily (Bari, ABT, Filgo) or twice daily (Tofa). *p<.01, **p<.001, ***p<.0001 compared to Bari. GM-CSF=granulocyte macrophage colony stimulating factor; IC_{50}=half maximum inhibitory concentration; IFN=interferon; IL=interleukin; NA=not assayed; NI=no induction; NK=natural killer; pSTAT=phosphorylated signal transducer and activator of transcription.

Source: *2870 - Ex Vivo Comparison of Baricitinib, Upadacitinib, Filgotinib, and Tofacitinib for Cytokine Signaling in Human Leukocyte Subpopulations, ACR 2017*

Income Statement

Galapagos, Inc. Income Statement		Mar-17	Jun-17	Sep-17	Dec-17		Mar-18	Jun-18	Sep-18	Dec-18						
EUR € mm	2016E	1Q17E	2Q17	3Q17	4Q17E	2017E	1Q18E	2Q18E	3Q18E	4Q18E	2018E	2019E	2020E	2021E	2022E	2023E
Total Revenue	**152**	**40**	**33**	**33**	**39**	**145**	**39**	**39**	**39**	**39**	**154**	**154**	**194**	**457**	**886**	**1663**
Product Revenues		0	0	0	0	0	0	0	0	0	0	0	40	303	732	1509
Reimbursement Revenues	130	34	27	27	33	120	33	33	33	33	130	130	130	130	130	130
Other Income	22	6	6	6	6	24	6	6	6	6	24	24	24	24	24	24
Cost of Goods Sold	0.00	0	0	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-2	-15	-37	-75
Gross Profit	**152**	**40**	**33**	**33**	**39**	**145**	**39**	**39**	**39**	**39**	**154**	**154**	**192**	**442**	**849**	**1588**
Gross Margin %							100%	100%	100%	100%	100%	100%	99%	97%	96%	95%
Operating Expenses	**-163**	**-51**	**-55**	**-63**	**-65**	**-234**	**-65**	**-66**	**-66**	**-67**	**-264**	**-269**	**-536**	**-815**	**-723**	**-1009**
Research and Development	-140	-45	-48	-56	-57	-207	-58	-58	-58	-58	-232	-232	-410	-485	-512	-679
Research and Development % of Sales	1	1.127	145%	169%	149%	144%	151%	151%	151%	151%	151%	151%	1025%	160%	70%	45%
General and administrative expenses	-22	-6	-6	-6	-7	-24	-6	-6	-6	-7	-25	-26	-26	-27	-28	-28
G & A % of Sales	22%	0.141	19%	18%	17%	17%	15%	17%	16%	17%	16%	17%	14%	6%	3%	2%
Sales and marketing expenses	-2	-1	-1	-1	-1	-3	-2	-2	-2	-2	-7	-11	-100	-303	-183	-302
Sales and marketing % of Sales	2%	0.014	2%	2%	3%	2%	4%	4%	5%	5%	4%	7%	250%	100%	25%	20%
Operating Profit	**-11**	**-11**	**-22**	**-30**	**-26**	**-89**	**-27**	**-28**	**-27**	**-28**	**-110**	**-115**	**-344**	**-373**	**126**	**579**
Operating Profit Margin %	-8%	-28%	-65%	-89%	-69%	-61%	-70%	-72%	-71%	-73%	-71%	-74%	-178%	-82%	14%	35%
Fair value re-measurement of Share Sub Agreement	57	0	0	0												
Other financial income	10	1	1	1												
Other financial expenses	-2	-3	-15	-8		-27					0.00	0.00	0.00	0.00	0.00	0.00
Pretax Income	**54**	**-14**	**-36**	**-37**	-26	-112	-27	-28	-27	-28	-110	-115	-344	-373	126	579
Income Tax Provision	0	0	0	0												
Tax Rate	1%	0%	0%	0%												
Net Income	**54**	**-14**	**-36**	**-37**	-26	-112	-27	-28	-27	-28	-110	-115	-344	-373	126	579
Basic Shares Outstanding	45.06	46.26	48.04	45.53	47.05	46.72	47.05	47.05	47.05	47.05	47.05	47.05	47.05	47.05	47.05	47.05
Diluted Shares Outstanding	46.43	48.33	49.99	47.05	47.05	48.11	47.05	47.05	47.05	47.05	47.05	47.05	47.05	47.05	47.05	47.05
Basic EPS		-0.29	-0.74	-0.80	-0.56	-2.40	-0.57	-0.59	-0.58	-0.60	-2.34	-2.43	-7.32	-7.93	2.69	12.30
Diluted EPS		-0.28	-0.71	-0.78	-0.56	-2.34	-0.57	-0.59	-0.58	-0.60	-2.34	-2.43	-7.32	-7.93	2.69	12.30
Diluted EPS Growth % YoY																
Non-Gaap Adjustments																
GAAP EPS																
Share Price		$83.46	$76.52	$101.75	$102.77	$102.77	$103.80	$104.83	$105.88	$106.94	$106.94	$111.28	$115.80	$120.50	$125.40	$130.49

Source: Company Reports, Bloomberg, BTIG Research Estimates, November 2017

BTIG Covered Companies Mentioned in this Report

GALAPAGOS N.V. (GLPG, Buy, $118.00 PT; Current Price: $99.24; Analyst: Dane.Leone)

Appendix: Analyst Certification and Other Important Disclosures

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I, Dane Leone, CFA, hereby certify that the views about the companies and securities discussed in this report are accurately expressed and that I have not received and will not receive direct or indirect compensation in exchange for expressing specific recommendations or views in this report.

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Galapagos N.V. (GLPG, Buy, $118.00 PT)

Valuation: Our $118PT values GLPG at ~4.x EV/ 2022E Sales.

Risks: Our Buy rating and $118 price target may prove inaccurate due to a number of risks related to Galapagos (GLPG) being an unprofitable early stage company with limited clinical data across the Cystic Fibrosis, Rheumatoid Arthritis, and Inflammatory Bowel Disease Portfolios.

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