

FINCH 1 & 3 Readout Expectations

FINCH Data Key Milestone – Limited Downside, Early MANTA Timeline Upside?

GLPG's FINCH 1 and 3 are set to read out (1Q19). We expect them to confirm filgotinib's highly competitive, best-in-class therapeutic profile in MTX-naïve and MTX-IR settings. The recent FINCH 2 readout ([note](#)) informs future filgo results relative to Upa, in our view. We believe filgo's consistent performance in historical trials leaves little to the imagination for FINCH 1 and 3; however, a hiccup (which we view as unlikely) could create downside for the shares. Potential downside risk is limited, in our view, as RA is *only the first indication for filgo* and the *one with the highest competitive hurdle*. IBD represents the next filgo opportunity, just as big as RA, but with greater need for an efficacious oral therapy. Also in IBD, filgo is ahead of Upa. *Reiterate Buy.*

- FINCH 1 & 3 Readout Expectations.** Our placebo-adjusted efficacy (ACR20/50/70/Remission) expectations for Filgo high-dose arms are 23/33/35/33% for FINCH 3 (wk 24) and 35/40/33/35% for FINCH 1 (wk 12) vs. Upa high-dose arms of 19/33/32/32% for Select-Early (wk24) and 30/37/30/33% for Select-Compare (wk 14); see [pp. 4-5](#) for analysis.
- FINCH Downside Scenario Unlikely, in Our View.** Subpar efficacy (to Upa) or unexpected safety would reduce filgo's market opportunity in RA. We estimate this could create downside in the shares to \$80, priming the company for potential takeover.
- MANTA Upside to Filgo NDA Submission Timeline?** We expect MANTA recruitment to accelerate, now up to 94 sites from 84 on last update ([p. 9](#)). *We see the potential for upside with filgotinib filing by mid-2019 that could set up for concurrent launch with Upa ([note](#)).* However, filgo filing by YE19 could hit the shares if MANTA trial becomes a bottleneck.
- '1690 (Autotaxin Inhibitor) P2a NOVESA Start in Systemic Sclerosis an Oppy Worth \$200mn Biobucks on Japan Collaboration Alone.** GLPG estimates 90K prevalence in US and EU and 40-60% 10-year mortality. Recent failures, including Roche's Tocilizumab P3, Bayer's Riociguat P2, and BMJ's Abatacept P2, have opened up the playing field. CRBP recently received a \$200mn biobucks collab deal from Kaken Pharma for SSc in Japan alone.
- Holy TOLEDO!: Blanket P2s on the Horizon – Another Filgo-Like Oppy?** Multiple Phase 2s are planned, pending positive P1 data. Target/moa are to be revealed shortly. Upcoming Catalysts: [p. 11](#).

Instinet, LLC, Equity Research

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Rating Remains	Buy
Target Price Remains	USD 140.00
Closing price 24 January 2019	USD 100.96
Potential upside	+38.7%

Research analysts

Americas Biotech

Christopher Marai, Ph.D. - ILLC
 Christopher.Marai@Instinet.com
 +1 212-310-5466

Allen Cha - ILLC
 allen.cha@instinet.com
 +1 212-310-5488

Jackson Harvey, Ph.D. - ILLC
 jackson.harvey@instinet.com
 +1 212 310 5453

Year-end: Dec	2017A		2018E			2019E		
EPS (€)	Actual	Prev.	Curr.	Cons.	Prev.	Curr.	Cons.	
1Q	-0.29A	-0.73A	-0.73A	N/A	0.00E	0.00E	-0.70E	
2Q	-0.72A	-0.42A	-0.42A	N/A	-0.87E	-0.87E	-0.90E	
3Q	-0.72A	0.28A	0.28A	N/A	-0.70E	-0.70E	-0.82E	
4Q	-0.59A	-0.54E	-0.54E	-0.39E	-0.85E	-0.85E	-0.91E	
Year	-2.34A	-1.42E	-1.42E	-1.96E	-2.44E	-2.44E	-2.94E	
Cash & Equivalents (€000)	1,151,211	1,320,690	1,320,690	1,150,676	1,219,636	1,219,636	983,492	

Source: Company data, FactSet, Instinet estimates

Key company data: See next page for company data and detailed price/index chart.

We anticipate FINCH 1 & 3 Readouts Will Validate Filgo’s \$6bn+ Market Oppy

We anticipate, this quarter 1Q19, the release of top-line results from pivotal trials FINCH 1 (MTX-IR) and FINCH 3 (MTX-Naive) evaluating filgotinib in moderate to severe rheumatoid arthritis (RA).

- Detailed results will likely be presented at EULAR 2019 Madrid Congress (June 12-15), with abstract submission deadline for late breakers April 5-15.
 - Abstracts will be posted approximately one month before the Congress (May 12-15).

Our Expectations

Below, we detail our expectations for filgotinib in earlier lines of RA treatment (Figs. 1-6), a lucrative tx line that will allow broad frontline utilization. We anticipate this data will further support filgo’s best-in-class therapeutic profile, warranting chronic dosing across multiple settings. We anticipate

- efficacy at least as good as (likely greater than) Upadacitinib based on trial design (Figs. 2-3), and
- safety to be best-in-class (among JAK inhibitors) and better than that of stronger biologics (e.g., TNF α , IL-6); note Adalimumab comparator in FINCH 1.

Fig. 1: FINCH Program Overview

	Trial Name	Patient Characteristics	Enrolled	Length of trial	Primary endpoint
1Q19	FINCH 1	Mtx inadequate responders	1759	52 wks	ACR20 at 12wk
	FINCH 2	IR-bDMARDs	449	24-wks	ACR20 at 12wk
1Q19	FINCH 3	Mtx naive	1252	52 wks	ACR20 at 24wk

Source: Company data, clinicaltrials.gov, Instinet research

Fig. 2: Pivotal P3 JAK inhibitor Trials in MTX-Naive and MTX-IR RA Population

Company	Filgotinib GLPG/GILD	Upadacitinib ABBV	Tofacitinib PFE	Baricitinib INCY/LLY	Our Comments
MTX-Naive RA	FINCH 3 <ul style="list-style-type: none"> • Early RA and MTX-naive. • \pm MTX Vs. MTX 	SELECT-EARLY <ul style="list-style-type: none"> • Limited to no Tx with MTX • Prior exposure to non-MTX csDMARD accepted with washout • Mono Tx vs. MTX 	ORAL Start <ul style="list-style-type: none"> • <3 yr duration • Mono Tx vs. MTX 	RA-BEGIN <ul style="list-style-type: none"> • Limited to no Tx with MTX • \pm MTX Vs. MTX 	<ul style="list-style-type: none"> • FINCH 3 broadly targets early and late MTX naive pts. • SELECT-EARLY has a more stringent criteria but may leave some efficacy on the table as mono tx (See Fig. 2)
MTX-IR RA	FINCH 1 <ul style="list-style-type: none"> • MTX-IR • + MTX vs. Humira vs. placebo • Radiographic Endpt 	SELECT-COMPARE <ul style="list-style-type: none"> • MTX-IR • Mono Tx vs. Humira vs. placebo • Radiographic Endpt SELECT-MONOTHERAPY <ul style="list-style-type: none"> • MTX-IR • Mono Tx vs. MTX 	ORAL Scan <ul style="list-style-type: none"> • MTX-IR • +MTX vs. placebo • Radiographic Endpt ORAL Standard <ul style="list-style-type: none"> • MTX-IR • + MTX • vs. Humira vs. placebo ORAL Strategy <ul style="list-style-type: none"> • MTX-IR • Mono Tx vs. + MTX vs. Humira + MTX 	RA-BEAM <ul style="list-style-type: none"> • MTX-IR • Min. 10yrs and highly active disease • +MTX vs. placebo • Radiographic Endpt 	<ul style="list-style-type: none"> • FINCH 1’s +MTX design may offer additional efficacy vs. Upa’s SELECT-MONOTHERAPY, which only tested Upa mono tx – which may offer competitive advantage but likely leave efficacy on the table. • SELECT-COMPARE used only Upa 15mg (lower dose)

Source: Company data, clinicaltrials.gov, Instinet research

FINCH 3 vs. SELECT-EARLY

MTX-Naïve

Aside from small nuances (noted in Figs. 2-3), we look to Upa's SELECT-EARLY as filgo's FINCH 3 comparator by baseline patient characteristics.

We set our expectations for the monotherapy arms for apples-to-apples comparison.

Fig. 3: Key Differences in FINCH 3 (Filgo) vs. SELECT-EARLY (Upa)

FINCH 3 Enrollment Criteria

Criteria

Key Inclusion Criteria:

- Have a diagnosis of RA (2010 ACR/EULAR criteria) and are ACR functional class I-III
- Have ≥ 6 swollen joints (from a swollen joint count based on 66 joints (SJC66)) and ≥ 6 tender joints (from a tender joint count based on 68 joints (TJC68)) at both screening and Day 1.
- Limited or no prior treatment with MTX

Key Exclusion Criteria:

- Previous treatment with any janus kinase (JAK) inhibitor
- Previous therapy for longer than 3 months with conventional synthetic disease modifying antirheumatic drugs (csDMARDs) other than MTX or hydroxychloroquine
- Use of any licensed or investigational biologic disease-modifying antirheumatic drugs (bDMARDs)

NOTE: Other protocol defined Inclusion/Exclusion criteria may apply.

We note FINCH 3 targets a more broad early and late stage MTX naive pts – more “real world” entry criteria

SELECT-EARLY tests only mono tx vs. FINCH 3's ± MTX design - We compare only monotherapy arms

SELECT EARLY Enrollment Criteria

Criteria

Inclusion Criteria:

- Duration of symptoms consistent with RA for ≥ 6 weeks who also fulfill the 2010 ACR/EULAR classification criteria for RA.
- Naïve to Methotrexate (MTX) or, if already on MTX, have received no more than 3 weekly MTX doses with requirement to complete a 4-week MTX washout before the first dose of study drug.
- Subjects with prior exposure to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) other than MTX may be enrolled if completed the washout period.
- Subject meets the following minimum disease activity criteria: greater than or equal to 6 swollen joints (based on 66 joint counts) and greater than or equal to 6 tender joints (based on 68 joint counts) at Screening and Baseline Visits.
- Greater than or equal to 1 bone erosion on x-ray (by local reading) OR in the absence of documented bone erosion, both positive rheumatoid factor and positive anti-cyclic citrullinated peptide autoantibodies are required at Screening.

Exclusion Criteria:

- Intolerant to Methotrexate (MTX)
- Prior exposure to any Janus kinase (JAK) inhibitor (including but not limited to tofacitinib, baricitinib, and filgotinib).
- Prior exposure to any biologic disease-modifying anti-rheumatic drugs (bDMARDs)
- History of any arthritis with onset prior to age 17 years or current diagnosis, inflammatory joint disease other than RA (including but not limited to gout, systemic lupus erythematosus, psoriatic arthritis, axial spondyloarthritis including ankylosing spondylitis and non-radiographic axial SpA, reactive arthritis, overlap connective tissue diseases, scleroderma, polymyositis, dermatomyositis, fibromyalgia [currently with active symptoms]). Current diagnosis of secondary Sjogren's Syndrome is permitted.

Source: clinicaltrials.gov, Instinet research

FINCH 1 vs. SELECT-MONOTHERAPY

MTX IR

FINCH 1's filgo + MTX design will likely yield greater efficacy than Upa's SELECT-MONOTHERAPY (Upa comparator trial), which evaluated only Upa monotherapy vs. MTX (possibly leaving some efficacy on the table).

We compare Wk 12 from FINCH 1 and Wk 14 from SELECT-MONOTHERAPY, as it had a cross-over design where placebo switched over to 2 doses of Upa post Wk-14.

Fig. 4: Summary of FINCH Data expectations

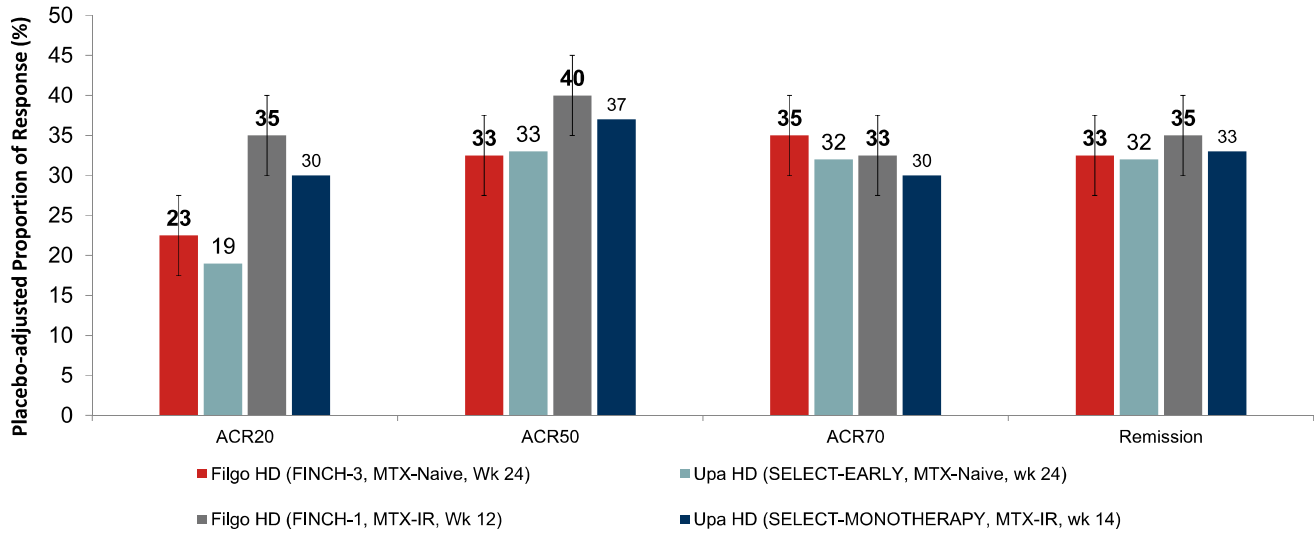
Vs. comparable UPA P3 trials

Phase 3 Early-line RA Trials	ACR20 (%)	ACR50 (%)	ACR70 (%)	Remission (%)
Filgo HD (FINCH-3, MTX-Naive, Wk 24)	23	33	35	33
Upa HD (SELECT-EARLY, MTX-Naive, wk 24)	19	33	32	32
Filgo HD (FINCH-1, MTX-IR, Wk 12)	35	40	33	35
Upa HD (SELECT-MONOTHERAPY, MTX-IR, wk 14)	30	37	30	33

Source: Company data, Instinet estimates

Fig. 5: Our Expectations of Top-Line Efficacy Measures from Filgo HD Arms vs. Upa HD

Filgo arm in FINCH-3 represents the monotherapy arm for comparison to Upa mono tx high-dose in SELECT-EARLY; FINCH 1 filgo high-dose arm is on top of MTX (wk 12) vs. Upa high-dose mono tx in SELECT-MONOTHERAPY (wk 14)



Source: Company data, Instinet estimates

Safety Expectations – Mounting Exposures but Consistent Profile

- We expect safety results to continue to reflect filgo’s best-in-class tolerability profile, warranting the ideal chronic therapy following remission.
 - Low Infection risks in 0-2% range.
 - Serious AEs in low- to mid-single-digit %.
 - PE/DVT’s below 1%, lower than background rate and Upa.
- Though safety may be weighted higher in RA (where competition is fierce), we believe any negative read-throughs impact filgo’s pipeline indications to lesser degree due to higher unmet need.
- Any single-digit incidences of DVT/PE or deaths are likely noise, considering the large trial population of ~n=3000.

Fig. 6: FINCH 2 Safety Summary

We anticipate FINCH 1 and 3 to be roughly similar to FINCH 2 safety profile

Drug (Name of Pivotal Trial)	Upadacitinib (P3 SELECT-BEYOND)					Filgotinib (P3 FINCH 2)		
	Weeks 0-12			Weeks 12-24*		Week 24		
	Assessment Period	Low Dose	High Dose	Low Dose	High Dose	PBO	Low Dose	High Dose
Trial Arm								
n	169	164	165	228	223	148	153	147
Serious AE	0 (0.0%)	8 (4.9%)	12 (7.3%)	10 (4.4%)	10 (4.5%)	5 (3.4%)	8 (5.2%)	6 (4.1%)
PE/DVT	0 (0.0%)	1 (0.6%)	1 (0.6%)	3 (1.3%)	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Deaths	0 (0.0%)	0 (0.0%)	1 (0.6%)	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%) [^]
Herpes Zoster	1 (0.6%)	1 (0.6%)	4 (2.4%)	2 (0.9%)	3 (1.3%)	0 (0.0%)	2 (1.3%)	2 (1.4%)
Serious Infections	0 (0.0%)	1 (0.6%)	4 (2.4%)	3 (1.3%)	3 (1.3%)	2 (1.4%)	3 (2.0%)	1 (0.7%)
Opportunistic Infections	0 (0.0%)	1 (0.6%)	2 (1.2%)	0 (0.0%)	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Malignancy	1 (0.6%)	1 (0.6%)	2 (1.2%)	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MACE	0 (0.0%)	1 (0.6%)	1 (0.6%)	0 (0.0%)	1 (0.4%)	1 (0.7%)	1 (0.7%)	0 (0.0%)

* Week 12-24 Includes PBO switches to Upa 15 or Upa 30mg

[^] 1 case of retinal vein occlusion, non-serious

Source: Company data, Instinet estimates