EQUITY RESEARCH

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■ Biotechnology

QUICK TAKE: INDUSTRY UPDATE

FILGOTINIB'S FINCH 1 AND FINCH 3 PH III DATA DEMONSTRATE A COMPETITIVE PROFILE

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THE COWEN INSIGHT

GILD and partner GLPG released top-line data from the Phase III FINCH 1 and FINCH 3 trials of filgotinib in RA. Filgotinib demonstrated ACR20/50/70 efficacy on par with that of other JAK inhibitors, and safety appears best-in-class. We continue to believe filgotinib is a competitive JAK inhibitor and remain at Outperform on both GILD and GLPG.

FINCH 1 And FINCH 3 Establish A Competitive Profile For Filgotinib In RA

The News: After the market close last night, Gilead (GILD, Outperform, $63.69) and partner Galapagos (GLPG, Outperform, $96.13) announced results from filgotinib's Phase III FINCH 1 trial in patients with moderate to severe rheumatoid arthritis (RA) with an inadequate response to methotrexate (MTX) as well as results from the Phase III FINCH 3 trial of filgotinib in moderate to severe RA patients who were naïve to MTX therapy.

FINCH 1 was a double-blind, randomized, placebo- and active-controlled study in which n=1,759 patients were randomized 3:3:2:3 to receive either 100mg filgotinib, 200mg filgotinib, Humira, or placebo on a background of a stable dose of MTX. The primary endpoint was the proportion of patients who achieved an American College of Rheumatology 20 percent improvement score (ACR20) at week 12.

After 12 weeks of treatment, an ACR20 response was seen in 69.8% and 76.6% of patients receiving 100mg and 200mg of filgotinib, respectively, vs. 70.8% for those receiving Humira and 49.9% for those receiving placebo ($p<0.001$ for both doses). At week 12 ACR50 and ACR70 rates were also improved by filgotinib: ACR50 rates were 36.3% and 47.2% for 100mg filgotinib and 200mg filgotinib, respectively, vs. 35.1% for Humira and 19.8% for placebo ($p<0.001$ for both doses). ACR70 rates were 18.5% and 26.3% for 100mg filgotinib and 200mg filgotinib, respectively, vs. 14.2% for Humira and 6.7% for placebo ($p<0.001$ for both doses). At week 12 filgotinib also resulted in more patients having low disease activity [defined as DAS28(CRP)≤3.2] with 38.8% of 100mg filgotinib and 49.7% of 200mg filgotinib patients classified as low disease activity, compared to 43.4% of Humira-treated patients and 23.4% of placebo-treated patients. Filgotinib also increased the proportion of patients with clinical remission as defined by DAS28(CRP)<2.6, with 23.8% of 100mg filgotinib and 33.9% of 200mg filgotinib patients compared to 23.7% of Humira patients and 9.3% of placebo patients qualifying.

Filgotinib was safe and well-tolerated in FINCH 1, with similar rates of serious AEs in the 100mg filgotinib (5.0%), 200mg filgotinib (4.4%), Humira (4.3%), and placebo (4.2%) arms. The rate of serious infections (1.7%, 1.7%, 2.5%, and 0.8% for 100mg filgotinib, 200mg filgotinib, Humira, and placebo, respectively) and herpes zoster (0.4%, 0.4%, 0.6%, 0.4% for 100mg filgotinib, 200mg filgotinib, Humira, and placebo, respectively) were also similar across arms. There were three VTEs (two in the placebo arm and one in the 200mg filgotinib arm), four adjudicated MACEs (two in the placebo arm, one in the Humira arm, and one in the 100mg filgotinib arm), and five cases of malignancy (three in the placebo arm, one in the Humira arm, and one in the 100mg filgotinib arm). Five patients died during the trial (two in the placebo arm, two in the 200mg filgotinib arm, and one in the 100mg filgotinib arm).

Gilead and Galapagos also disclosed top-line data from **FINCH 3** in MTX-naïve patients with moderate to severe RA. FINCH 3 was a double-blind, randomized, active-controlled study in which n=1,252 patients were randomized 1:2:1:2 to receive either 100mg filgotinib + MTX, 200mg filgotinib + MTX, 200mg filgotinib monotherapy, or MTX monotherapy. The primary endpoint was the proportion of patients achieving ACR20 at week 24.

After 24 weeks of treatment, an ACR20 response was seen in 80.2% and 81.0% of patients receiving 100mg filgotinib + MTX and 200mg of filgotinib + MTX, respectively, and 78.1% of patients receiving 200mg filgotinib monotherapy, vs. 71.4% for those receiving MTX alone ($p<0.05$ and $p<0.001$ for 100mg filgotinib + MTX and 200mg filgotinib + MTX, respectively).

Please see pages 4 to 8 of this report for important disclosures.

At week 24 ACR50 and ACR70 rates were also improved by filgotinib: ACR50 rates were 57.0% and 61.5% for 100mg filgotinib + MTX and 200mg filgotinib + MTX, respectively, and 58.1% for 200mg filgotinib monotherapy vs. 45.7% for MTX alone ($p<0.01$ and $p<0.001$ for 100mg filgotinib + MTX and 200mg filgotinib + MTX, respectively). ACR70 rates were 40.1% and 43.8% for 100mg filgotinib + MTX and 200mg filgotinib + MTX, respectively, and 40.0% for 200mg filgotinib monotherapy, vs. 26.0% for MTX alone ($p<0.001$ for both 100mg filgotinib + MTX and 200mg filgotinib + MTX). Filgotinib also increased the proportion of patients with clinical remission at week 24 as defined by DAS28(CRP)<2.6, with 42.5% and 54.1% of 100mg filgotinib + MTX and 200mg filgotinib + MTX patients, respectively, and 42.4% of 200mg filgotinib monotherapy patients qualifying, compared to 29.1% of patients treated with MTX alone.

Filgotinib was also safe and well-tolerated in FINCH 3, with similar rates of serious AEs in the filgotinib 100mg + MTX (2.4%), filgotinib 200mg + MTX (4.1%), 200mg filgotinib monotherapy (4.8%), and MTX (2.9%) arms of the trial. The rate of serious infections (1.0%, 1.0%, 1.4%, and 1.0% for 100mg filgotinib + MTX, 200mg filgotinib + MTX, 200mg filgotinib monotherapy, and MTX, respectively) and herpes zoster (0.5% in each arm) were also similar across arms. There was one case of VTE in the MTX arm, five adjudicated MACEs (two in the MTX arm, two in the 200mg filgotinib + MTX arm, and one in the 200mg filgotinib monotherapy arm), and one case of malignancy in the MTX arm. One patient in the 200mg filgotinib + MTX arm died during the trial. More detailed results from both trials will be shared at an upcoming medical conference.

Next Steps: We Anticipate Filings In The EU And Japan During 2019, With Timelines In The U.S. Dependent Upon Discussions With FDA. Filgotinib's Phase III program tested both the 100mg and 200mg doses of filgotinib in the Phase III program, and the partners will make a decision about which to file for approval based on the associated benefit:risk. GILD/GLPG will interact with regulatory authorities in the EU, Japan, and U.S. following receipt of the FINCH data to determine the respective paths to approval. Though neither GILD nor GLPG has formally committed to timelines in any geographic location, GLPG's financial guidance suggests management anticipates an EU product launch in 2020. Investors debate whether the MANTA study of filgotinib monitoring testicular safety could remain rate-limiting to any regulatory filings (especially to the FDA, who requested MANTA). Both GILD and GLPG have suggested that they will make the case to the regulators (particularly the FDA) that the FINCH safety database is adequate though management will have clarity only after the regulatory discussions have concluded. Clinicaltrials.gov lists the primary completion date for the MANTA trial as January 2021, though GILD has said it is working to accelerate its timeline, through expanded recruitment.

Our Take: Efficacy Appears Competitive, Low Rate Of DVTs Could Be Differentiating. We think that the results from FINCH 1 and FINCH 3 suggest that filgotinib has a profile competitive with other JAK inhibitors in the treatment of rheumatoid arthritis. Filgotinib's efficacy appears to be at least as strong as the other JAK inhibitors. In FINCH 1 200mg filgotinib led to an ACR20/50/70 rate of 77%/47%/26% at 12 weeks in RA patients who had an inadequate response to MTX (IR-MTX). These data compare well with the results produced by Xeljanz, Olumiant, and upadacitinib in their Phase III programs. For example, 5mg Xeljanz produced an ACR20/50/70 rate of 61%/34%/12% at 3 months in the Phase III ORAL-STANDARD trial in IR-MTX patients. In the RA-BEAM trial in IR-MTX patients, 4mg Olumiant (note: only 2mg dose approved in the U.S.) produced an ACR20/50/70 rate of 70%/45%/19% at 12 weeks. In upadacitinib's Phase III SELECT-COMPARE trial in IR-MTX patients, 15mg upadacitinib produced an ACR20/50/70 rate of 71%/45%/25% at 12 weeks.

Our consultants have indicated that while branded drugs are not used ahead of MTX, demonstration of front-line monotherapy efficacy is important for the adoption of new RA agents in later lines of therapy. In this regard, filgotinib's FINCH 3 efficacy data in MTX-naïve patients are encouraging. In FINCH 3, 200mg filgotinib monotherapy led to an ACR20/50/70 rate of 78%/58%/40% at 24 weeks in MTX-naïve RA patients. These results are comparable to those produced by other JAK inhibitors in this population. In the Phase III ORAL-START trial, 5mg Xeljanz monotherapy led to an ACR20/50/70 rate of 71%/47%/26% at 6 months. In the Phase III RA-BEGIN trial, 4mg Olumiant monotherapy led to an ACR20/50/70 rate of 77%/60%/42% at week 24. Similarly, in the Phase III SELECT-

EARLY trial, 15mg upadacitinib monotherapy led to ACR20/50/70 rates of 79%/60%/44% at week 24.

One potential weakness in the efficacy data for filgotinib is the lack of a demonstration of superiority to Humira. Though efficacy measures were generally directionally superior for filgotinib vs. Humira in FINCH 1, most failed to reach the level of statistical significance. Clinical remission rates for 100mg filgotinib (23.8%) and 200mg filgotinib (33.9%) were nominally non-inferior and superior, respectively, to Humira at 23.7% ($p<0.01$ for both), but only when the comparison was not adjusted for multiple testing. However, the rate of low disease activity in the 200mg filgotinib arm (49.7%) was able to show non-inferiority ($p<0.001$) to Humira (43.4%) with an adjustment for multiplicity. These data stand in contrast to upadacitinib, which demonstrated superiority to Humira in IR-MTX patients on ACR20/50/70, rate of low disease activity, and rate of clinical remission at week 12 in the Phase III SELECT-COMPARE trial.

In terms of safety, it appears possible that filgotinib may have a best-in-class profile. A full evaluation is not possible without the release of the detailed data. However, as there was no imbalance in serious AEs, serious infections, herpes zoster, malignancy, MACE, or death, the top-line results suggest that filgotinib's safety profile is very good. Furthermore, given the observed imbalance in DVTs in one of Olumiant's randomized Phase III trials and an imbalance in PEs in a long-term RA safety study of Xeljanz, VTE risk has become more of a concern for physicians and investors. In aggregated 24 week data from FINCH 1, 2, and 3 only one case of VTE has been observed (in the 200mg filgotinib cohort in FINCH 1) out of a total of n=2,088 patients treated with filgotinib vs. 3 cases out of a total of n=1,039 patients treated with MTX in these trials. For comparison, there were six cases of PE among 498 RA patients who received upacitinib in the Phase III SELECT-BEYOND trial.

A more complete analysis of the competitive position of filgotinib will come once the full results from the Phase III program are available. We would be especially curious to see detailed patient characteristics given ACR response rates in the Humira arm in FINCH 1 and the MTX arms in both FINCH 1 and FINCH 3 are higher than in RA trials for other JAK inhibitors. Nonetheless, with the early data implying that filgotinib is at least as effective and possibly safer than other JAKs, the results increase our confidence that filgotinib is both approvable and a competitive JAK inhibitor.

VALUATION METHODOLOGY AND RISKS

Valuation Methodology

Biotechnology:

In calculating our 12-month target price, we employ one or more valuation methodologies, which include a discounted earnings analysis, discounted cash flow analysis, net present value analysis and/or a comparable company analysis. These analyses may or may not require the use of objective measures such as price-to-earnings or price-to-sales multiples as well as subjective measures such as discount rates.

We make investment recommendations on early stage (pre-commercial) biotechnology companies based upon an assessment of their technology, the probability of pipeline success, and the potential market opportunity in the event of success. However, because these companies lack traditional financial metrics, we do not believe there are any good methodologies for assigning a specific target price to such stocks.

Investment Risks

Biotechnology:

There are multiple risks that are inherent with an investment in the biotechnology sector. Beyond systemic risk, there is also clinical, regulatory, and commercial risk. Additionally, biotechnology companies require significant amounts of capital in order to develop their clinical programs. The capital-raising environment is always changing and there is risk that necessary capital to complete development may not be readily available.

ADDENDUM

Stocks Mentioned In Important Disclosures

Ticker	Company Name
GLPG	Galapagos NV (ADR)
GILD	Gilead Sciences

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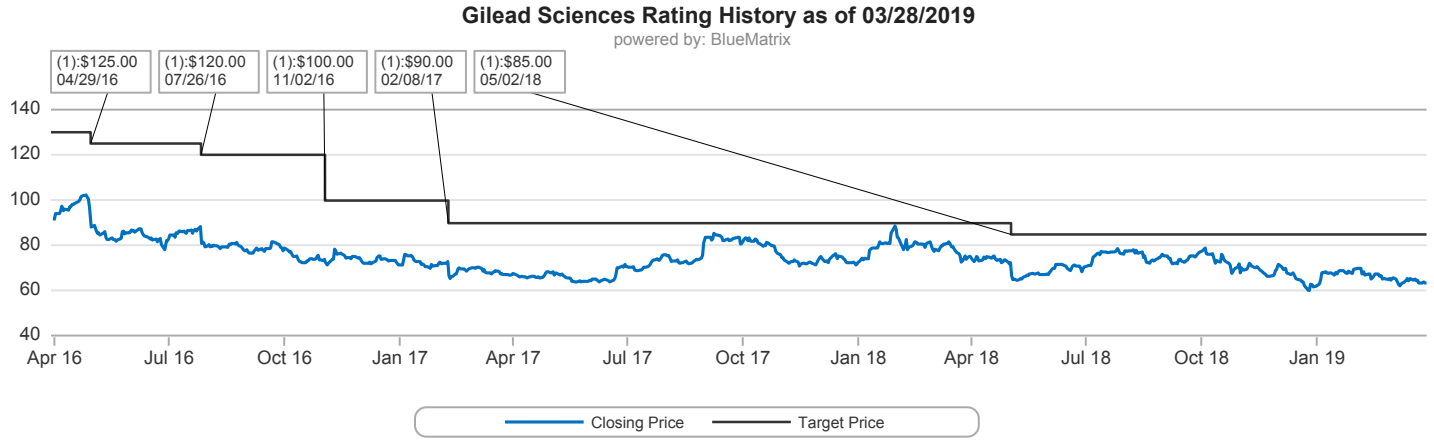

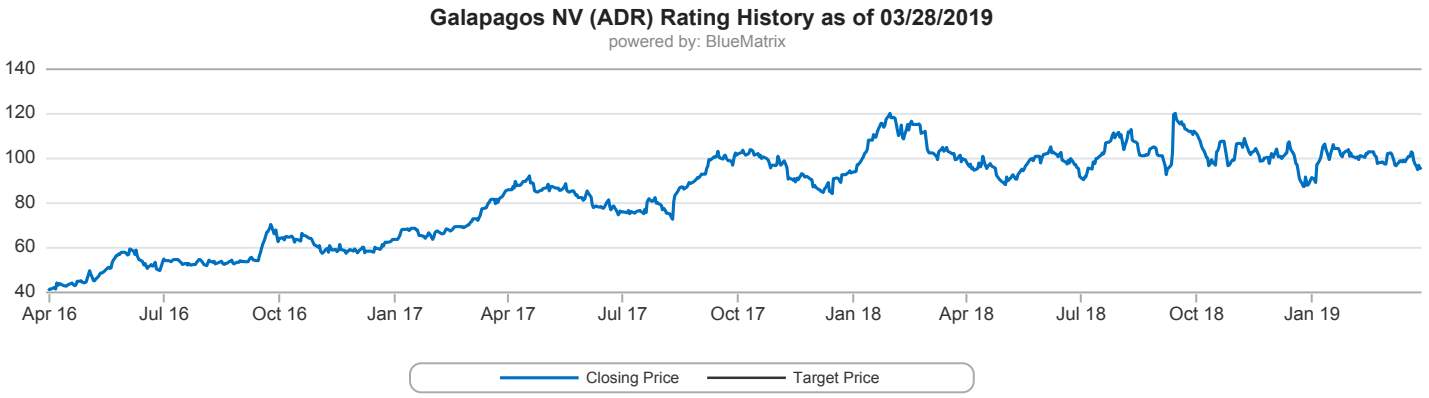

Initiated Coverage - 06/08/2015 - Rating Outperform

Legend for Price Chart:

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