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ABBV 4Q: Upa 15mg Dose Only? Safety Concern?

Quick Note

We have received investors Qs on ABBV's 4Q earnings call last Friday, in relation to its NDA upadacitinib in moderate to severe rheumatoid arthritis (RA); submitted Dec 20, 2018. On the call, ABBV indicated that it will seek an upadacitinib label in RA at the 15mg dose (low dose). The 15mg and 30mg data is part of its NDA submission, and the higher-dose data, even if not part of the label, may help inform safety. We believe this disclosure is interesting, considering FDA's approval of baricitinib's (Olumiant) low-dose only and the overall approval/CRL fiasco (note), which centered on concern around higher-dose safety. *We note that this seemingly cautious approach by ABBV is potentially due to safety, especially considering the comparable DVT/PE rates between baricitinib and upadacitinib (both are JAK1/JAK2 selective inhibitors).* Safety remains a *clear differentiator for filgotinib, given lower rates of DVT/PE across doses.* **Next Up:** 1Q19 GLPG's FINCH 1 & 3 P3 readouts in MTX-naïve and MTX-IR settings (see our expectations here). *Reiterate Buy.*

- **15mg Low-Dose Selection, a Cautionary Hedge? Olumiant's FDA Precedent.** FDA approved Olumiant (baricitinib, another JAK1/JAK2 inhibitor-like upadacitinib) at the (lowest) 2mg dose in later lines of RA therapy (post-TNF) with a black-box label (note), largely due to concerns of thrombotic events (DVT/PE). Though upadacitinib's DVT/PE rates are similar to baricitinib's, the rates do not appear to be dose-dependent (an advantage over baricitinib's dataset).
- **Lower Dose Only Leaves Efficacy and Market Opportunity on the Table?** We anticipate that the lack of a high-dose option for upa could limit the opportunity, given the Olumiant launch to date, noting the 4mg (high dose) is the most utilized dose in the EU, where launch is well under way. High-dose upa (30mg) will, of course, be available off-label if not approved, though potentially expensive (as 15mg x 2), as pricing is likely set on 15mg, and thus at the mercy of payers, which could favor on-label high-dose filgotinib. We believe that upa's 30mg dose continues to represent the best comparator to filgotinib's 200mg (high dose), as noted in our recent FINCH 1 & 3 readout expectations here, and that GLPG/GILD will seek a label for both high and low doses in RA. Further, depending on the review, ABBV could continue to explore activity of upa at higher doses in different RA settings and combinations.
- **Higher-Dose Upadacitinib Concerns Could Limit UC Opportunity?** If concerns remain about higher-dose upa, or come across in a 3Q19 ADCOM (anticipated by ABBV), upa utilization may be limited in the lucrative IBD market. In ulcerative colitis (UC), upadacitinib was tested up to 45mg in a Ph2b trial (U-ACHIEVE), demonstrating dose-dependent efficacy up to the highest dose. We have previously highlighted GLPG and filgotinib's clear leadership position as the first-in-class, best-in-class, and likely *first to market JAK1 selective inhibitor for IBD*, which we view as attractive and subject to less "horse race" debate than the RA market.

Instinet, LLC, Equity Research

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Rating Remains	**Buy**
Target Price Remains	USD 140.00
Closing price 25 January 2019	USD 102.59

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Further, Xeljanz's (another JAK inhibitor on the market) recommended dose for UC is twice that of mod-sev RA (label).

- **Filgotinib Safety Advantage to Be Revealed 3Q19/Early 4Q19 Upa ADCOM Color?** We remain cautious on upa's safety language in the label and into a likely ADCOM meeting, expected ~1mo prior to PDUFA, placing it 3Q19/early 4Q19 of this year.

ABBV Call Upadacitinib's Dose/NDA Quotes

- "Across the SELECT clinical program, both doses of upadacitinib performed extremely well and demonstrated a strong benefit/risk profile."
- "Based on our analysis of the data generated across the registrational program, we believe the 15-milligram dose represents the best dose for the RA indication, as it delivered maximal efficacy across a wide range of studies, drove strong results on important structural endpoints, and demonstrated superiority to HUMIRA in our head-to-head study."
- "Thus, this dose provides the differentiation we were seeking when we designed our program."
- "it's common for filings like this, for new molecular entities in RA to go to an ADCOM, so it's certainly possible."