Future of the JAK Inhibitor Class in RA - Takeaways from Our NYC Doc Day

Summary

At the Stifel NYC Doc Day, we hosted two U.S.-based KOLs to discuss the future of JAK inhibitors (jakinibs) in rheumatoid arthritis (RA): a former chair of the FDA Arthritis Advisory Committee, and a clinician handling ~450 RA patients. Both predicted jakinibs will secure ~30-40% of the total RA drug market in 10 years, with ABBV's (NR) Rinvoq and PFE's (NR) Xelzanz competing for majority share, and GLPG's (Buy; $188 TP) filgotinib and LLY's (NR) Olumiant battling over the remainder. KOLs think ABBV's marketing expertise will make Rinvoq an immediate player, while PFE's established presence and Xeljanz' longer track record will fuel continued solid growth. LLY's Olumiant will remain handicapped by a more restricted post-TNF label. KOLs think filgotinib will generally face an uphill climb given expected fourth-to-market status and comparative safety advantages (i.e. lower thrombosis rate in non head-to-head studies) they view as insufficiently differentiating to drive outsized gains.

Key Points

Exhibit 1: KOL feedback roughly in-line with our existing filgotinib RA assumptions

Drug	KOL est. % peak share	Est. WW total RA market size in 2030 ($B)	Implied peak jakinib sales ($B)	Comment
Rinvoq	15%	$30	$4.5	Superior to Humira head-to-head
Xeljanz	11%	$30	$3.3	Rheums most faimilar - approved 2012
Olumiant	2%	$30	$0.6	Label restricted to post-TNF failures
Filgotinib	8%	$30	$2.4	Stifel FY30 est. ~$2.5B
Jakinib total WW RA market	36%		$10.8	

Source: KOL feedback and Stifel estimates

KOLs cautious views on filgotinib potential in RA is unsurprising and consistent with our long-held modeling assumptions: For instance, per Exhibit 1 above, our KOLs predict that the jakinibs will garner ~30% to 40% share of the world-wide RA drug market within 10 years, which translates into ~$10B in peak jakinib sales, by our estimates. Of that, our consultants predict that ABBV's Rinvoq and PFE's Xeljanz will battle for dominate share. While recently approved Rinvoq was shown to be superior to injectable Humira in the head-to-head SELECT-COMPARE study, Xeljanz's long established presence in RA (approved 2012) has allowed physicians to gain significant experience/comfort with the drug. Our KOLs think GLPG's filgotinib (fourth to market; largely undifferentiated on safety/efficacy, in their view) and LLY's Olumiant (label restricted to TNF failures) will be left fighting for remaining market share. Our filgotinib RA revenue build forecasts peak WW sales of roughly $2.5B, which represents just 8% of the estimated total WW RA market, which we view as reasonable given the market dynamics, and in-line with our KOL views.

Jakinib market to grow substantially over the next 10 years, per KOLs: Our consultants currently treat approximately 15% to 20% of their RA patients with jakinibs (mostly Xeljanz, a small amount of Olumiant, just getting started with recently approved Rinvoq), and they see that percentage increasing to between 30% and 40% within the next 10 years (primarily at the expense of injectable TNFs). This shift is expected to be driven by an ongoing trend toward use of oral jakinibs after methotrexate and ahead of injectable TNFs. However, while patients generally prefer orals over injectables (often influenced by DTC advertising), KOLs point out that out-of-pocket expenses can sometimes be significantly higher for oral medicines - particularly in the Medicare population where not all patients have part D coverage, and for those who do, the donut hole can be a patient cost issue.

PFE's Xeljanz and ABBV's Rinvoq to battle for market dominance, while Olumiant to see limited use: When it comes to choosing between the currently approved jakinibs (Xeljanz, Olumiant, and Rinvoq), our consultants believe that rheumatologists will likely weigh their long-standing experience/comfort level with Xeljanz (approved since 2012) against the "new/improved" Rinvoq (which demonstrated head-to-head superiority over Humira in the SELECT-COMPARE study vs. Xeljanz which only showed non-inferiority to Humira in its study). While the SELECT-COMPARE results are not included in the Rinvoq prescribing label, KOLs believe that at a minimum, ABBV will be able to discuss and highlight the superiority data with rheumatologists - which could cause physicians to infer (perhaps unjustly given no head-to-head study of Rinvoq vs. Xeljanz), that Rinvoq is superior to Xeljanz. On Olumiant, our KOLs agreed that the drug's marginal efficacy/safety at the approved 2mg dose, coupled with its comparatively narrow prescribing label (restricted to TNF failures) will continue to render it as more of a salvage therapy - limiting RA market share.

Continued below...

Adam A. Walsh, M.D. | (617) 488-4626 | adamwalsh@stifel.com
Edwin Zhang, PhD | (212) 271-3787 | zhange@stifel.com
Neil Carnahan | (617) 488-4403 | neil.carnahan@stifel.com
Stifel Equity Trading Desk | (800) 424-8870

Filgotinib likely to have black box for thromboembolic events (TE) despite low rate in pivotal studies as FDA shifts towards class labeling: One of our KOLs was previously the Chair of the FDA Arthritis Advisory Committee and pointed out that FDA has clearly shifted towards class labeling for recently developed drug classes. This is consistent with the language in the recently approved Rinvoq label, which includes a jakinib class warning for thrombosis, DVT, and PE. We'd previously written that a superior event rate on TEs for filgotinib might allow the drug to avoid the black box warning included in the other jakinib labels. Both docs believe this is unlikely since a consensus theory behind jakinib-driven TEs is currently lacking and variability across patient populations in late-stage studies complicates TE comparisons between the different jakinibs. Thus, FDA is likely to view TEs as a jakinib class effect.

KOLs do not see filgotinib as differentiated on lower thromboembolic event rate due to lack of head-to-head data: While our KOLs acknowledge that filgotinib has demonstrated a lower rate of thromboembolic events (TE) than Rinvoq in their separate pivotal studies (0.1 TE per 100 PTE for filgotinib vs. 0.5 for Rinvoq), they do not believe this potential filgotinib safety advantage is sufficient to influence prescribing behavior upon filgotinib approval. They cite the lack of head-to-head data as the primary reason for this and view current cross-trial comparisons as unscientific and therefore unconvincing. With respect to other potential filgotinib safety advantages demonstrated in clinical studies (i.e. increases in Hb, decreases in platelets, etc.), our KOLs were similarly unimpressed and neither thought such safety data would be sufficient to meaningfully drive sales.

MANTA data (testicular tox study) necessary for our KOLs to get fully comfortable with filgotinib's safety profile: Both KOLs are aware of the ongoing MANTA studies and both indicated they would like to see those results (timing of data unknown at present) in order to have full confidence in the drug's safety profile prior to using it broadly in males. While GLPG has indicated MANTA results are not gating for FDA approval (FDA has seen MANTA un-blinded data available to date), KOL comments suggest that the MANTA data may in fact be gating in the minds of rheumatologists when it comes to widely prescribing the drug. Both KOLs pointed out that the existence of the MANTA study may give some physicians pause, particularly if the data are not yet disclosed at the time of the filgotinib launch. While we believe it will be, we assume there is at least a possibility that it won't be, given lack of guidance as to when the study will be completed.

Despite our KOLs' lukewarm views on filgotinib in RA, we remain positive on the long-term outlook for the drug as broad clinical development is underway in multiple indications, including potential blockbusters such as IBD: Filgotinib will be the fourth jakinib to market in RA and will take time to gain a foothold in the competitive space. Both KOLs believe supplanting the other jakinibs in RA will be difficult in the absence of head-to-head studies or dramatic differences in efficacy or safety (unlikely at this point in time, in our view). That said, we highlight filgotinib's potential in other large indications such as IBD (Crohn's and UC). For example, we expect enrollment to complete in the P3 SELECTION1 study (n=1,320) of filgotinib in Crohn's disease in 2H20 and anticipate a readout by early FY22 (50% PoS in our model; est. FY23 launch; unadjusted peak WW sales of $2.5B; unadjusted peak revenue to GLPG of $635M per GILD (NR) partnership agreement.

KOLs disagree on the importance of JAK selectivity: Our KOLs expressed divergent views on the importance of JAK selectivity, with one believing that selectivity may matter for safety/efficacy, and the other arguing selectivity has not demonstrated meaningful advantages to date.

Excellence in marketing may play a key role in determining winners/losers amongst the jakinibs: Per KOLs, ABBV's experience with Humira will make its Rinvoq a formidable opponent for the rest of the jakinib class. One KOL pointed out that while the company's Humira was third to market in the anti-TNF class, it was able to quickly compete with AMGN's (NC) deeply entrenched Enbrel. "Marketing is going to be the main driver of how this shakes out. ABBV has been a leader here above the other companies. Reps from all of these companies come to my office, these are all educated people, but ABBV has been able to do it better." Our consultants believe that LLY's Olumiant will be most likely to be impacted by ABBV's marketing muscle, as long-term experience and comfort with PFE's Xeljanz will take time to Rinvoq overcome.

Near-term jakinib uptake to be driven primarily by newly diagnosed patients: Both KOLs agreed that uptake of the jakinibs will steadily improve over time, with utilization likely peaking in the range of ~30-40% of RA patients. Uptake will likely be driven by the status of the patient. Our KOLs expect an increasing proportion of naive RA patients to start on jakinibs near-term, with the obvious benefit of oral delivery over injections partially driving the shift. Alternatively, they postulate that patients who are stable on their current treatments will switch more slowly over time, primarily as a result of loss of treatment response.

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