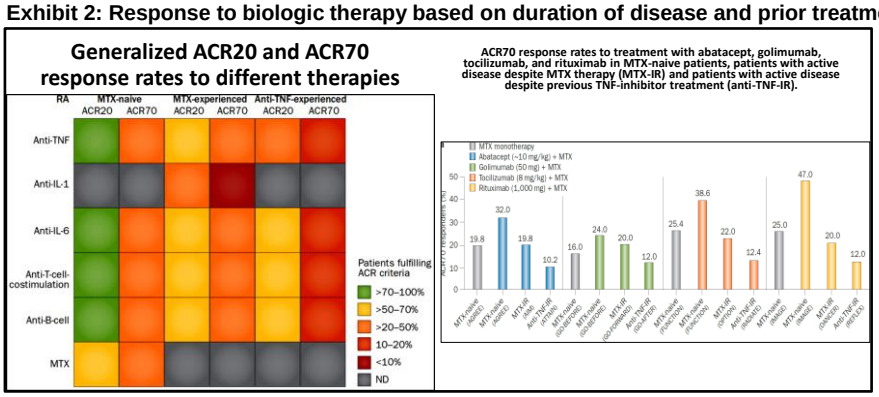
Note, irrespective of the biological target, all effective therapies achieve similar therapeutic effects in patients with RA, with none of them able to induce remission in a majority of patients. Additionally, responses to biologic therapies for RA decrease depending on the patient population: early RA, methotrexate-naive; established RA, methotrexate-experienced; or late RA, anti-TNF experienced. Hence, treatment through the inhibition of the JAK pathway might deliver some compelling advances as is being demonstrated with data from the baricitinib clinical programs.

**Exhibit 2: Response to biologic therapy based on duration of disease and prior treatment**




**Source: Nat. Rev. Rheumatol. February 2015**

While the current market is dominated by biologics, physician feedback suggests growing comfort with the emerging safety profile of JAK-inhibitors coupled with convenience of once or twice daily oral regimens will shift prescription habits over the next five to ten years. Safety profile was one of the key concerns which led to the tepid launch of Xeljanz, in our view.

**Exhibit 3: RA commercial landscape overview**

| | | | | 2015 Sales | |
|---|---|---|---|---|---|
| Drug | Lead Company | Type | Indication | U.S., billion | Global, billions |
| Humira | Abbvie | mAb | RA/Plaque Psoriasis/Psoriatic arthritis/Crohns | $ 8.4 | $ 13.9 |
| Enbrel | Amgen | mAb | RA/Plaque Psoriasis/Psoriatic arthiritis | $ 5.1 | $ 9.0 |
| Remicade | JnJ | mAb | RA/Crohns/ Psoriasis/UC/Plaque Psoriasis/ Psoriatic arthritis | $ 4.5 | $ 6.8 |
| Orencia | BMY | mAb | RA | $ 1.3 | $ 0.6 |
| Actemra | Roche | mAb | RA | $ 0.6 | $ 0.9 |
| Simponi | JnJ | mAb | RA/Psoriatic arthiritis/UC | $ 0.7 | $ 0.6 |
| Cimzia | UCB | mAb | RA/Crohns/Psoriatic arthiritis | $ 0.7 | $ 0.4 |
| Xeljanz | PFE | Jak/Oral | RA/UC/Plaque psoriasis | $ 0.5 | |

**Source: Bloomberg and Janney Montgomery Scott, LLC**

The success of baricitinib (anticipated launch during 2017) and the emergence of ABBV's ABT-494 along with GILD/GLPG's filgotinib increase the share-of-voice for oral RA treatments. While baricitinib is at least two years ahead of filgotinib, filgotinib selective JAK1 inhibition might deliver a superior hematologic safety profile, which could overcome any shortcomings from the likely twice daily regimen (if only the 100 mg BID dose were to be approved). However, this is an unlikely scenario (Exhibit 5), as Galapagos/Gilead have the option of co-developing the 100mg and 200 mg QD dose, where the clinically meaningful ACR50 and ACR70 rates are in the same ballpark as baricitinib, in our view.

Given the multitudes of options available to physicians the major goal of therapy is now remission or at least low disease activity (LDA). LDA is best reflected through the achievement of the ACR criteria for 70% improvement (ACR70 response). However, robust ACR70 responses are relatively rare and is typically an outcome in <10% of patients who are have had disease progression on synthetic DMARDs and between 10% and 20% of patients post anti-TNF therapy, Exhibit 2.

Hence, any new drug that does not reach these established levels of response has little place in future treatment armaments, unless it is effective in a population particularly refractory to existing treatments or it elicits comparably fewer adverse events. Preliminary data from filgotinib (DARWIN 1 and DARWIN 2) studies have been encouraging. Although cross trial comparisons have limited clinical value, in a similar population (when combined with standard therapy) the efficacy of the 200 mg once daily filgotinib regimen was on par with baricitinib 4 mg dose. Importantly, the 100 mg BID cohort appears to be numerically superior to baricitinib, without any dramatic increase in SAE's, and potentially increases dosing flexibility. Note, ACR70 responses for JAK inhibitors in a MTX refractory population is in the 20% to 30% range, which bodes well for adoption.

**Exhibit 4: Cross-study comparison of filgotinib, baricitinib, and ABT-494**

| MTX+ JAK | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Drug | Study | Cohort | N | ACR 20 | | ACR 50 | | ACR 70 | |
| | | | | 12-week | 24-week | 12-week | 24-week | 12-week | 24-week |
| filgotinib | DARWIN 1 | 50 mg OD | 82 | 11% | 13% | 17 | 18% | 8% | 13% |
| | | 50 mg BID | 85 | 14% | 18% | 19% | 18% | 11% | 15% |
| | | 25 mg BID | 86 | 12% | 14% | 13% | 18% | 6% | 12% |
| | | 100 mg QD | 85 | 17% | 18% | 24% | 29% | 12% | 24% |
| | | 200 mg QD | 86 | 24% | 31% | 28% | 33% | 16% | 20% |
| | | 100 mg BID | 84 | 35% | 38% | 40% | 38% | 23% | 30% |
| | | | | | | | | | |
| baricitinib | BEAM | 4 mg QD | 487 | 30% | 37% | 28% | 32% | 14% | 22% |
| | | | | | | | | | |
| ABT-494 | BALANCE-2 | 3 mg BID | NA | 15% | | 20% | | 16% | |
| | | 6 mg BID | | 23% | | 29% | | 24% | |
| | | 12 mg BID | | 32% | | 30% | | 9% | |
| | | 18 mg BID | | 27% | | 25% | | 21% | |
| | | 24 mg QD | | 32% | | 24% | | 18% | |

**Source: Company presentation, NEJM 2016, and Janney Montgomery Scott, LLC**

At peak, we are modeling ~25% market share for oral JAK-inhibitors, driven by convenience, safety and tolerability profile, and pricing. For filgotinib we are modeling 6% and 3%, market share in the U.S. and the EU., respectively (25% of the oral JAK opportunity), which could translate into ~$2B in peak sales and ~$530M (RA only) royalty for Galapagos.

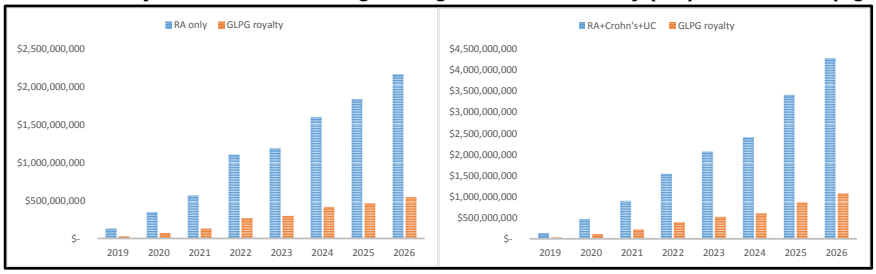
**Exhibit 5: Filgotinib commercial opportunity assuming low to mid-single digit adoption**

| | Cases | | Estimated peak adoption | | Annual Cost | | Commercial opportunity | | Peak revenue opportunity |
|---|---|---|---|---|---|---|---|---|---|
| | US | EU | US | EU | US | EU | US | EU | |
| RA | 1,290,000 | 1,548,000 | 6% | 3% | $ 20,000 | $13,000 | $ 1,548,000,000 | $ 603,720,000 | $2,151,720,000 |
| Ulcerative Colitis | 610,000 | 1,500,000 | 5% | 3% | $ 20,000 | $13,000 | $ 610,000,000 | $ 585,000,000 | $1,195,000,000 |
| Crohn's Disease | 565,000 | 1,100,000 | 4% | 3% | $ 20,000 | $13,000 | $ 452,000,000 | $ 429,000,000 | $ 881,000,000 |
| | | | | | | | | | $4,227,720,000 |

**Source: The CDC, The Journal of Crohn's and Colitis 2013, 7; 322 and Janney Montgomery Scott LLC estimates**

Additionally, if both Crohn's and Ulcerative Colitis opportunities come to fruition, filgotinib's peak revenue opportunity could exceed $4B globally and translate into ~$1B peak royalty stream for Galapagos, by our estimates.

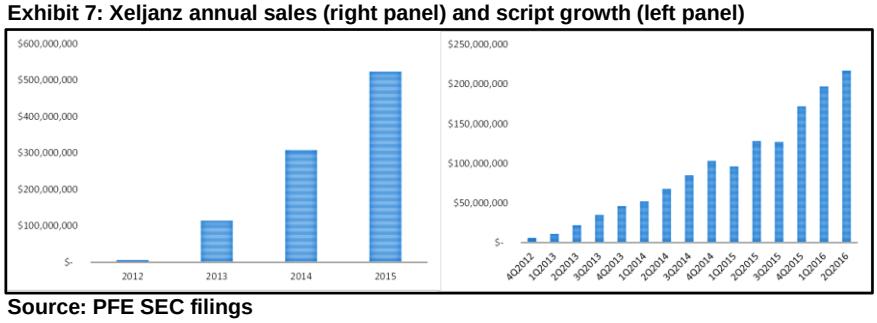
**Exhibit 6: Projected evolution of filgotinib global sales RA only (left) and RA+IBD (right)**




**Source: Janney Montgomery Scott LLC estimates**

Xeljanz was the first JAK (Tofacitinib inhibits JAK3 and JAK1 and to a lesser extent Jak2.) inhibitor approved for RA. While launch has been relatively slow compared to expectations, pace has picked up with sales approaching the $1B mark for FY16 primarily form the U.S. Anticipated approval in the EU during 2017 could drive adoption as physicians now have are going more comfortable on the safety profile of Xeljanz with available data from two long-term extension studies highlight no marked increase in malignancies compared to available therapies in this patient population.

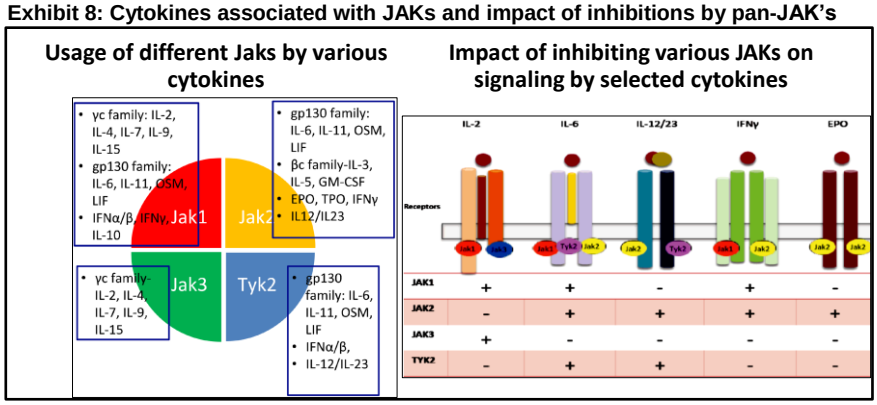
**Exhibit 7: Xeljanz annual sales (right panel) and script growth (left panel)**




**Source: PFE SEC filings**

## JAK-1 SELECTIVITY HAS YET TO PLAY OUT:

**Exhibit 8: Cytokines associated with JAKs and impact of inhibitions by pan-JAK's**




**Source: Adapted from the Ann Rheum Dis. 2013 April ; 72(0 2): ii111–ii115, by Janney Montgomery Scott LLC**

An important side effect of Jakinibs is serious bacterial, mycobacterial, fungal and viral infections. In the phase II, III and long extension trials of tofacitinib among opportunistic infections, tuberculosis (TB) was reported in 12 cases, 11 of which were initially negative on screening for TB, and 10 occurred in patients from endemic countries. Increased frequency of non-disseminated herpes zoster was also reported which may reflect reduction of NK cells by virtue of JAK1 or JAK3 blockade.

Jakinibs can cause anemia, thrombocytopenia and neutropenia, likely related to Jak2 inhibition, which is important for EPO signaling and the actions of colony stimulating factors. A concern regarding chronic treatment with Jakinibs pertains to the possibility of increased cancer risk. Interferons and NK cells are important in tumor surveillance and the blockade of their action provides the theoretical rationale for development of malignancies mandating increased clinical vigilance. The rate of lymphomas or other lymphoproliferative disorders in phase III and long extension studies of tofacitinib in RA was 0.07 per 100 patient-years, which is comparable with studies of other biologicals and the general RA population.


RESEARCH ANALYST CERTIFICATIONS AND IMPORTANT DISCLOSURES ARE ON PAGES 34 - 36 OF THIS REPORT