Galapagos Puts Faith In Refocused Pipeline To Regain Investor Confidence

By Kevin Grogan 11 May 2021

Executive Summary

The Belgian biotech's president, Bart Filius, tells Scrip that exiting the metabolic disease and osteoarthritis space and focusing on inflammation makes sense to "bring a bit more balance in terms of risk into our portfolio."

After a very tough nine months, Galapagos NV has laid the foundations on the road to recovery by refocusing its research areas, targeting €150m in savings and seeking out late-stage assets to fill the gap between its approved rheumatoid arthritis drug Jyseleca and the rest of the pipeline.

Bart Filius, Galapagos president, mapped out the Belgian biotech's strategy to Scrip after the completion of a review of the business following a miserable spell which started in October 2020 when the osteoarthritis drug GLPG1972, an ADAMTS-5 inhibitor partnered with Servier, failed to significantly reduce cartilage loss in the Phase II ROCELLA trial. A couple of months later, partner and major stakeholder Gilead Sciences, Inc. walked away from US development of Jyseleca (filgotinib), which is approved in Europe and Japan, as it could no longer see a viable path to approval for the JAK inhibitor after a type A meeting with the US Food and Drug Administration to discuss a complete response letter issued in August when the agency surprisingly rejected the drug for rheumatoid arthritis. (Also see "Galapagos Knocked By Knee Osteoarthritis Fail" - Scrip, 16 Oct, 2020.) (Also see "Gilead Gives Up On Galapagos's Filgotinib In RA" - Scrip, 16 Dec, 2020.)

The latest blow, in February this year, saw the termination of the ISABELA Phase III program for ziritaxestat which was being evaluated in about 1,500 idiopathic pulmonary fibrosis (IPF) patients. A review of the oral autotaxin inhibitor concluded

that its benefit-risk profile no longer supported continuing these studies, and Galapagos and Gilead declared that all clinical trials for the drug would be discontinued, including the long-term extension of the Phase IIa NOVESA trial in systemic sclerosis. (Also see "Ziritaxestat Failure Could Spell End For Gilead/Galapagos Pact" - Scrip, 11 Feb, 2021.)

"The ziritaxestat setback was a big surprise, a big disappointment but it made clear the need to do something about our organization so we embarked on this exercise, driven first by the science," Filius told Scrip. "We went through our entire portfolio looking at all the different options and assets we have and knowing what we've seen from ziri, our conclusion was that it was probably sensible to bring a bit more balance in terms of risk into our portfolio."

He added that one of Galapagos's strengths had been in having a broad portfolio but that also "increases the risk that you spread yourself a bit too thin and we've felt it was necessary to focus on our two core areas of expertise, inflammation and fibrosis, and we've let go of metabolic disease and osteoarthritis."

The decision to exit the latter space "clearly has a direct link to the discontinuation of GLPG1972," Filius noted, and while continuing with inflammation and fibrosis, there has been some fine-tuning there. Specifically in IPF, "we decided to discontinue GLPG1205 which was a follow-on molecule to ziri, and which we had hoped could be also a good combination molecule. It is very tough to develop new therapies in that disease area but we needed to select one of two and we came to the conclusion that it was more logical to continue with GLPG4617," a Phase II-ready chitinase inhibitor for IPF licensed from OncoArendi Therapeutics last year.

On the clinical front, Galapagos is most enthusiastic about its broad Toledo program which consists of a series of salt-inducible kinase (SIK) inhibitors. The first Toledo compound, GLPG3970, is in five proof-of-concept trials and results from the first, in severe psoriasis, are expected later this year and a second SIK2/3 inhibitor, GLPG4876, has been selected for accelerated development from preclinical. Galapagos is also looking to start Phase II trials of its TYK2 inhibitor codenamed GLPG3667 for psoriasis.

Filius said that the changes should result in an overall spending cut of €150m, "which, depending how you do the math is between 20% and 25% of our annual cash spend. He stressed that roughly 80% of the spend was connected to trials or third-party expenses, and some job losses were inevitable, "we're in the process of reviewing that with workers councils and unions."

Jyseleca Launches Going To Plan

Another priority is to make a success of the Jyseleca launch in Europe, where approval came at the end of September last year. "We always have to wait a little bit, because reimbursement in Europe in all these countries takes ages to be honest," Filius said, noting that while the National Institute for Health and Care Excellence (NICE) backed broad use of the once-daily pill for both moderate as well severe active RA, a wider approval than more established JAK inhibitors, namely Pfizer Inc.'s Xeljanz (tofacitinib), Eli Lilly and Company's Olumiant (baricitinib) and AbbVie

Inc.’s Rinvoq (upadacitinib), "we're still a couple of weeks out before we're actually in the market in the UK." (Also see "Jyseleca European Launches Could Lift Gloom At Galapagos" - Scrip, 23 Feb, 2021.)

He added that the launch was going to plan in the Netherlands and Germany, where the country's Federal Joint Committee (G-BA) granted Jyseleca an additional benefit qualification "which is a good outcome for us and better than Xeljanz and Olumiant." The safety concerns about JAK inhibitors that arose again in January after a failed Phase IV post-marketing safety study of Xeljanz has led to delays to tighter scrutiny of the class in the US, which could help Galapagos in its bid for market share in Europe and Filius stressed that Jyseleca was differentiated on its safety profile, while still being competitive especially in the high dose." (Also see "What Will JAK Inhibitor Safety Jitters Mean For Drug Sales?" - Scrip, 7 Apr, 2021.)

Both the 200mg and 100mg doses of Jyseleca are approved in Europe, "which we think is important, because it gives doctors the chance to choose a lower dose for the elderly and the higher dose for the younger patients." Roll-out in the main European markets should be initiated by the end of the year and Filius said the company saw Jyseleca in Europe as a €500m opportunity; the European Medicines Agency's regulatory review of the drug for ulcerative colitis is ongoing, which will clearly boost sales potential if positive.

Search Is On For Late-Stage Assets

A major focus for Galapagos is to bring in later-stage products and while the cash burn for this year is forecast to be €580-620m, the company ended the first quarter with cash and equivalents of €5.11bn. Filius said, "Our Toledo program is, in all fairness, six to seven years out from commercialization so we need to fill the gap behind our first molecule. Ziri was supposed to fill that gap but that's no longer the case, so we're interested in business development (BD) opportunities."

He added, "It's always expensive to do BD but you need to look for the right assets, where there's a good fit to what Galapagos does. We're not going to be in a bidding war against big pharma on late-stage assets."

The BD situation is somewhat complicated by the fact that Gilead would have an option to the ex-EU rights to any additions to the portfolio, while it is also possible that Galapagos could also bag assets from its partner’s own pipeline to develop further. Filius told Scrip that "if it is virology or oncology, they would do it themselves but if it's in the inflammatory space, there are synergies and the partnership could work in two directions."

He concluded, "It's up to us to show to investors and analysts what we have to offer and the best way to do that is to show great data and progress in our pipeline. Currently our share price is under pressure after all the news over the last nine months and we need to regain that confidence by demonstrating the value that we have scientifically."