Osteoarthritis program gets off its knees GLPG NA

Galapagos and partner Servier announced the launch of the 800-patient phase II trial with ADAMTS-5 inhibitor GLPG1972 in knee osteoarthritis (protocol here), named ROCCELLA after Galapagos island moss. Notably, the trial reflects the latest thinking in OA drug development like selecting the primary endpoint of cartilage thickness measured by MRI, which is better suited to demonstrate the disease-modifying effect of the drug and limits the variability of a conventional endpoint of pain and incorporating biomarkers to select the appropriate OA subpopulation for pivotal studies. In our view, GLPG1972 has solid mechanistic and biomarker rationale to demonstrate measurable slowdown in cartilage degradation, but the major win would be to establish a positive trend in functional endpoints/pain - a goal that has not been reached by any other disease-modifying drug so far. We currently value the OA program only €2/share due to the early stage of development, but given its potential blockbuster status, we view GLPG1972 as a meaningful driver to Galapagos' case contributing €14/share value on a non-risk adjusted basis.

Trial design follows the latest thinking in OA. The randomized double-blind phase II trial will evaluate 3 doses of GLPG1972 vs. placebo in 800 patients with knee osteoarthritis (OA) with the aim to demonstrate a slowdown in cartilage degradation on MRI over 52 weeks for at least one dose. The trial will also evaluate functional endpoints (i.e. WOMAC) and pain (currently a registration endpoint) as secondary. The inclusion criteria are pretty similar to the latest trials with disease-modifying OA drugs (e.g. Merck's sprifermin), recruiting patients with established knee OA and pronounced pain requiring NSAIDs. The trial population does not seem to specifically enrich for early-stage OA (n.b. degradation of aggrecan precedes degradation of collagen in the cartilage), but will evaluate biomarkers to aid identification of clinical responders and combat heterogeneity of the disease for the phase III trials.

The data could come in 2020. Considering the lack of disease-modifying therapies for OA and based on sprifermin phase II experience, we expect the trial to complete recruitment within a year and deliver topline results already in H2'20, which should support the partnering discussions for the US rights.

GLPG1972 is one of the most promising OA drugs in development. GLPG1972 inhibits ADAMTS-5, an enzyme cleaving the major structural component of cartilage aggrecan, that emerged as the key target to slow down or prevent cartilage degradation. Moreover, aggrecan prevents collagen II degradation, therefore ADAMTS inhibition may impact overall cartilage protection. GLGP1972 showed up to 50% reduction in ARGS, a biomarker of aggrecan degradation in OA patients, in line with 60% in healthy volunteers. There are no precedents for clinical efficacy, as earlier attempts to target ADAMTS-5 had failed due to pharmacokinetics and potential safety concerns, but GSK's patent (US 20130336989A1) noted that a ~50% ARGS reduction in patients cartilage could be considered a good response to ADAMTS-5.