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Small Galapagos setback prompts a bigger loss of sentiment



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A mid-stage clinical failure raises more doubts about Galapagos's pipeline and the wisdom of Gilead's \$5bn deal last year.

Even though Galapagos's GLPG1972 was an under-the-radar asset that barely featured in sellside models, its failure in knee osteoarthritis yesterday has laid the company low.

Galapagos stock came off 7% this morning, likely reflecting a broad loss of sentiment. The setback, in the [phase II Rocella study in which GLPG1972 failed to beat placebo on either the primary or secondary 52-week endpoints](#), will erode trust in Galapagos's pipeline, which [just last year got a \\$5bn windfall from Gilead](#).

Since then filgotinib has received a US complete response letter that could delay its approval in rheumatoid arthritis until 2022. Even if it is approved this delay will hand Abbvie - which had earlier pulled out of a deal over filgotinib - valuable extra time to build market share for its competitor, Rinvoq.

Though another Galapagos asset to which Gilead now has rights, ziritaxestat, scored an early clinical win in scleroderma last year, Gilead has yet to see any direct benefit from its \$5bn bet.

AdamTS-5

GLPG1972 is an inhibitor of AdamTS-5, a zinc metalloendopeptidase implicated in osteoarthritis via degradation of aggrecan, a structural cartilage proteoglycan, and the industry pipeline reveals few similarly acting assets.

However, the same mechanism is used by Merck KGaA's M6495, which just 10 days ago was licensed to Novartis for €50m (\$59m) up front.

Selected AdamTS-5 inhibitor projects

Project	Company	Development notes
GLPG1972	Galapagos	Small molecule; failed ph2
M6495	Merck KGaA (ex Ablynx (Sanofi))/ Novartis	Nanobody; two ph1 trials completed
AGG-523	Pfizer	Small molecule, also hit AdamTS-4; discontinued ph1 (poor PK)
RBM-010	Taisho/Ribomic	ssRNA aptamer; preclinical
CRB0017	Mylan	MAB; discontinued preclinical
GSK-2394002	Glaxosmithkline	MAB; discontinued preclinical (CV effects)
Unnamed	Oscotec	Preclinical, likely discontinued

Source: EvaluatePharma & company disclosures.

For the Galapagos/Gilead collaboration the big hope now rests on the mysterious “Toledo” programme. Nothing is known about the novel inflammatory targets on which these projects act, though [patent filings suggest that they might be SIK1, 2 and 3 kinases](#).

Apparently multiple assets will be taken forward and disclosed only when progress is made, and thus last year Galapagos started a phase I trial of GLPG3312, the first Toledo compound. No data have been revealed, but the asset has quietly been discontinued, according to Galapagos’s latest investor update.

Subsequently GLPG3970, a compound “acting on two Toledo family members”, was taken into phase II, and the first data are expected in 2021. Before the end of 2020, meanwhile, several more proof-of-concept studies will be launched; Gilead has an option over ex-European rights after completion of phase II.

Analysts expect Galapagos to reveal more about the Toledo projects on October 27. Investors and Gilead will pay close attention.

The Gilead and Galapagos engagement

Project	Deal details	Mechanism/uses
Filgotinib	50/50 share of global development costs & profits in certain European countries; 20-30% royalties in ex-Galapagos territories	Jak inhibitor; US CRL for RA
Ziritaxestat	Gilead has full rights, \$395m milestone due on US approval	Autotaxin inhibitor; ph2a success in scleroderma; ph3 in IPF
GLPG1972	Gilead option over US rights for up to \$550m after ph2b; Servier has ex-US rights	AdamTS-5 inhibitor; failed ph2 in osteoarthritis
GLPG3312	"Toledo" programmes; Gilead has option over ex-Europe rights for \$150m per programme, 20-24% royalties	3 undisclosed inflammatory targets; discontinued after ph1 (no data)
GLPG3970		2 undisclosed inflammatory targets; in ph2 for UC & RA
GLPG4399		Undisclosed inflammatory target; ph1 to start in 2020
GLPG4605		Undisclosed inflammatory target

Source: Company statements.

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