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Gout flop leaves Sobi red-faced

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SEL-212 fails to beat Krystexxa in phase II, but why did Sobi pay $100m for the asset in June and then put it into phase III?

The failure of a vital head-to-head study of Selecta/Sobi's gout project SEL-212 is another lesson to biotech about something that should be obvious: do not go into phase III without first clearly showing the scientific and business rationale of doing so.

It makes Sobi (Swedish Orphan Biovitrum) in particular look rather rash: Sobi had licensed in SEL-212 for $100m up front just four months ago. Perhaps Sobi can say it took a risky punt at a price that did not break the bank, but why the companies decided to initiate a pivotal study last month is harder to fathom.

SEL-212 had in fact raised pretty substantial doubts well before yesterday's failure to beat Krystexxa head to head. Back in 2017 a phase II trial failed, with fewer than half of 79 patients able to maintain serum uric acid levels despite a complex "3+2" treatment cycle (*Selecta feels the pain of gout, November 8, 2017*).

The failure to demonstrate a suitable dosing schedule should have rung alarm bells, but in the meantime a separate phase II trial, Compare, took on major importance. This pitted SEL-212 head to head against Krystexxa, Horizon Therapeutics' recently anointed gout market leader.

Go Compare

It was Compare that flopped yesterday. The companies said SEL-212 failed to beat Krystexxa in lowering serum uric acid to below 6mg/dl for at least 80% of the time at months three and six combined, Compare's primary endpoint.

There was a numerical benefit, 53% versus 46%, but this did not come close to hitting statistical significance (p=0.181). Mizuho analysts said this setback would significantly reduce SEL-212's US commercial opportunity, while Stifel wrote to clients that there was now no reason to buy Selecta shares, which this morning fell 35%.

Evidently Selecta/Sobi's plea to look at a per-protocol assessment of 59 subjects rather than all 83 enrolled patients fell on deaf ears. The companies argued that the Covid-19 pandemic had caused protocol deviations in the intent-to-treat population; a per-protocol analysis came closer to meeting statistical significance, with p=0.056.

The groups also claimed a win if only the three-month point was considered, though the resulting p value of 0.019 can only be nominal, since the primary analysis had failed. If anything, however, such a three-month effect harks back to the earlier phase II flop and SEL-212's inability to maintain long-term serum uric acid

levels.

Selected studies of SEL-212		
Trial	**Design**	**Primary endpoint**
Phase II		
3+2 dosing study	79 subjects, various doses	Safety & tolerability (but failed to maintain SUA <6mg/dl beyond wk12 in most subjects)
Compare	83 subjects, vs 87 on Krystexxa	SUA <6mg/dl for ≥80% of mths 3 & 6 combined (failed)
Phase III		
Dissolve I	105 subjects, 2 doses vs placebo	SUA <6mg/dl for ≥80% of mth 6 (has 6mth extension)
Dissolve II (starts end 2020)	105 subjects, 2 doses vs placebo	SUA <6mg/dl for ≥80% of mth 6
SUA=serum uric acid. Source: Selecta, Sobi & clinicaltrials.gov.		

Krystexxa comprises pegloticase, a recombinant uricase, while SEL-212 combines the therapeutic uricase enzyme pegsiticase/pegadricase with an immune tolerance technology.

The former is due to sell $897m in 2026, according to *EvaluatePharma* sellside consensus, while before yesterday's failure the latter carried a forecast of $411m. Annabel Samimy, a Stifel analyst covering Horizon, wrote that the competitive threat to Krystexxa was now removed.

Selecta and Sobi said they would explore the impact of Covid-19 further once they had the full Compare dataset in hand. The also insisted that the numerical findings supported SEL-212's pivotal programme, comprising two trials, Dissolve I and II, which are expected to generate topline results in the second half of 2022.

Both pivotal studies pit SEL-212 against placebo, so hopes of success should be relatively high, and indeed SEL-212 might well be approvable. But without a demonstrated advantage against an established market leader it will have a mountain to climb.