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The other shoe drops for Immunic

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Failure of a vital catalyst in psoriasis leaves Immunic's approach at risk of obsolescence.

As if being overtaken by a rival mechanism of action had not been enough, Immunic now has to contend with clinical failure. The company's RORγ inverse agonist IMU-935 yesterday flunked its proof-of-concept trial in psoriasis, an event SVB Securities had recently described as Immunic's most important near-term catalyst.

Things might not be as bad as the group's stock opening off 70% this morning suggests, and Immunic has an important card up its sleeve, thanks to IMU-935's apparently wide therapeutic window. But the concern is that it will now simply be left behind by Tyk2 inhibitors and Dice Therapeutics' IL-17 inhibitor rival.

If this happens Immunic will not be the first oral psoriasis contender to fall by the wayside. The space has seen Lilly scrap a small-molecule anti-IL-17 project, while Boehringer Ingelheim, Astrazeneca and Lead Pharma/Sanofi have all terminated assets with the same modality as Immunic's IMU-935.

Psoriasis trials of selected small molecules with activity to lower IL-17			
Project	**Company**	**Pharmacology**	**Status**
DC-806 (S011806)	Dice Therapeutics	IL-17 inhibitor	Ph1 showed 44% mean PASI reduction in pts on high dose
LEO 153339	Leo Pharma	IL-17 inhibitor	Ph1 in healthy volunteers completes Nov 2022
IMU-935	Immunic Therapeutics	RORγ inverse agonist	Failed to beat placebo in ph1
BI 730357	Boehringer Ingelheim	RORγ antagonist	Discontinued in ph2
LY3509754	Lilly	IL-17A inhibitor	Abandoned in ph1 after undisclosed liver findings
AZD0284	Astrazeneca	RORγ inverse agonist	Ph1 terminated after preclinical findings
SAR441169	Lead Pharma/ Sanofi	RORγ inverse agonist	Terminated in ph1
Source: company statements & clinicaltrials.gov.			

After market close yesterday Immunic said interim analysis of mean four-week PASI score reductions had shown no separation between two IMU-935 treatment arms, 150mg once or twice daily, and the placebo cohort.

The study in question, which does not have a clinicaltrials.gov listing and is being run in Australasia and Bulgaria, remains blinded, and the company "only has access to very limited information".

However, it has seen enough to be able to say that the two active arms performed in line with expectations. Unfortunately, placebo recipients appear to have done just as well, and this "unexpected high placebo rate" thus scuppered any potential benefit the trial might have shown.

Despite the setback, Immunic is continuing with the psoriasis indication for IMU-935, which is separately in phase 1 in prostate cancer. In the company's favour is that the oral small molecule has shown favourable safety, with no dose-limiting toxicities, thanks to which it has the flexibility to consider higher doses and/or longer treatment duration.

Context is important, of course; oral treatment of psoriasis is becoming competitive, with Amgen's PDE-4 inhibitor Otezla set to come under pressure from Tyk2 inhibitors. The first of these, Bristol Myers Squibb's Sotyktu, was approved last month with an unexpectedly clean label.

Not surprisingly, Immunic traded down on that approval, as did Dice Therapeutics, which has a competing oral psoriasis project, the IL-17 inhibitor DC-806. But Dice soon struck Immunic another blow, when DC-806 yielded phase 1 data showing efficacy in line with Sotyktu on a cross-trial basis – albeit from only seven patients on the highest dose.

Similar but different

There is a mechanistic similarity between IMU-935 and DC-806. While the latter hits IL-17 directly, the Immunic project inversely agonises RORγ, an effect said to block the differentiation of helper T cells into IL-17-producing cells. This effectively also lowers IL-17 levels, but with less scope for toxicity, Immunic hopes.

Dice's early success with the high DC-806 dose comprised a 44% mean reduction in four-week PASI score, against 13% for placebo. Those now awaiting full data from Immunic will want to know how close to a total 44% PASI reduction IMU-935 has come, and by how much the placebo response is above the typical 15-25%.

Immunic says it has enough cash to last into the fourth quarter of 2024. However, this is only thanks to a $60m private placement, done just 11 days ago at $4.34 per share. Today the stock is trading below $3 – a cautionary tale for investors attracted by an equity fund raising on the eve of an all-important binary clinical outcome.

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