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Merck KGaA Suffers Another Late-Stage Loss

by Elizabeth Cairns

After the Phase III failure of xevinapant, the German group will need to cut deals and do better in a rare cancer if it is to turn its fortunes around.

To lose one late-stage asset may be regarded as a misfortune; to lose two looks like carelessness. *Merck KGaA* has followed the Phase III failure of its multiple sclerosis candidate evobrutinib six months ago with the discontinuation of the pivotal trial of xevinapant in head and neck cancer.

The Phase III TrilynX study was evaluating the apoptosis protein inhibitor plus chemoradiotherapy in patients with unresected locally advanced squamous cell carcinoma of the head and neck. It was canned following an interim analysis by the study's independent data monitoring committee, which found that it would be unlikely to meet its primary endpoint of prolonging event-free survival compared with chemoradiotherapy alone.

The company has also shelved the other Phase III trial of xevinapant, X-Ray Vision, testing the agent against placebo

Key Takeaways

- Merck has called off two Phase III trials of xevinapant in head and neck cancer after one failed an interim futility analysis.
- It now has just one Phase III asset left, the tenosynovial giant cell tumor candidate pimicotinib.
- Companies working on similar drugs to xevinapant include Novartis and Ascentage Pharma.

on a background of radiotherapy in patients who have undergone surgery for the same disease.

In fairness, head and neck cancer is an intractable tumor type. *Merck & Co., Inc.*'s Keytruda is approved first-line, but only in more advanced disease. In the TrilynX setting nothing has toppled chemoradiotherapy as the standard of care, despite many attempts with new approaches including immunotherapy.

Jefferies analysts wrote that they expect an impairment of around €60m ($64m) related to the study termination to hit Merck's profit & loss in the second quarter. The group took a €95m impairment after the evobrutinib failure in December. (Also see "*Merck KGaA Wants Your Drugs*" - Scrip, 7 Mar, 2024.)

Hard Times

The TrilynX cancellation increases Merck's dependence on its sole late-stage product still standing. Pimicotinib is a colony stimulating factor-1 antagonist intended for the rare cancer tenosynovial giant cell tumor. Its Phase III trial, MANEUVER, could report in 2026.

Moreover, the company is gazing over the patent cliff for its multiple sclerosis drug Mavenclad (cladribine). The purine analog's US patent will expire in October 2026, and Merck needs to make up for the shortfall.

The company is already working hard to accelerate its dealmaking, hoping to fill its pipeline with more promising compounds. Presumably it will now redouble these efforts but investors may recall that xevinapant itself came via a deal, Merck having licensed it from Debiopharm in 2021 in a pact worth €188m upfront. (Also see "*Merck KGaA Bags Exclusive Rights To Develop, Sell Debiopharm's Xevinapant*" - Scrip, 1 Mar, 2021.) Merck is now expected to write off the majority of this upfront fee.

Merck is focused on late-stage deals – those for products that have proved their concept – and is potentially looking at targets in the low-single-digit billions of Euros range.

Reverberations

But the disappointment of TrilynX could have ramifications beyond Merck. According to *Evaluate Pharma*, *Novartis AG* has also been working on an apoptosis protein inhibitor, though this does not appear to be in any active trials. The most recent trial of LCL161, a 50-patient Phase II study in polycythemia vera and myelofibrosis, concluded two years ago.

Suzhou, China-based *Ascentage Pharma Group Corporation* is running two Phase II trials of a similarly acting compound, APG-1387, one in combination with toripalimab in patients with advanced solid tumors and another in pancreatic cancer. Data could come this year and the company doubtless has an anxious wait.

Sino Biopharmaceutical Limited has recently started a Phase I/II study of its apoptosis protein inhibitor, TQB3728, in locally advanced non-small cell lung cancer. This too could yield data in 2024.