

Amgen finally Navigates a win



[Madeleine Armstrong](#)



The asthma project tezepelumab shows an effect in both eosinophilic and non-eosinophilic patients.

After [recent disappointing readouts](#), Amgen has at last caught a break. The company, alongside its partner AstraZeneca, reported a top-line hit today with one of its big late-stage pipeline hopes, the asthma project tezepelumab.

Full data from the pivotal Navigator trial are yet to be revealed, but the TSLP inhibitor has apparently done well in both the eosinophilic and non-eosinophilic asthma subtypes. The latter is the big prize owing to an unmet need – currently approved monoclonal antibodies, like Sanofi/Regeneron's Dupixent, primarily target the eosinophilic phenotype.

Top of the cascade

TSLP (thymic stromal lymphopoietin) is a cytokine that sits at the top of multiple inflammatory cascades; the theory is that by hitting this target tezepelumab could have a benefit in all asthma patients, regardless of their subtype.

Today's top-line release appears to support the idea. The companies said Navigator, which enrolled a roughly equal proportion of patients with high (≥ 300 cells/ μl) and low eosinophil blood counts, not only met its primary endpoint of annualised asthma exacerbation rate over one year in the overall population, but also hit in the low eosinophil subgroup.

The companies also said that "similar reductions" in exacerbation rates were seen in patients with very low eosinophil counts of less than 150 cells/ μl .

"This is the first time we've seen a clear clinical impact irrespective of blood eosinophil count. That's the important takeaway," said Professor Andrew Menzies-Gow of the Royal Brompton Hospital in London, Navigator's lead investigator, in a media call, declining to elaborate further on the effects seen in each group.

The full data will be reported at a medical meeting next year. Safety will also be closely watched – [there have been concerns that inhibiting the action of TSLP could raise the risk of infections](#), and a case of Guillain-Barré syndrome was seen in phase II.

All Amgen and Astra are saying for now is that there were "no clinically meaningful differences" in safety between the tezepelumab and placebo groups. "I think everyone will be pleasantly surprised," Ruud Dobber, president of Astra's biopharmaceuticals business unit, added.

Unmet need

The companies plan to file tezepelumab, the most advanced anti-TSLP antibody, with regulators in the first half of next year. A broad approval would give them white space to move into – non-eosinophilic disease accounts for around half of severe asthma cases.

Oral corticosteroids are a mainstay of therapy here, but Professor Menzies-Gow noted that although these are “cheap in terms of their up-front costs”, they come with significant short-term and long-term side effects.

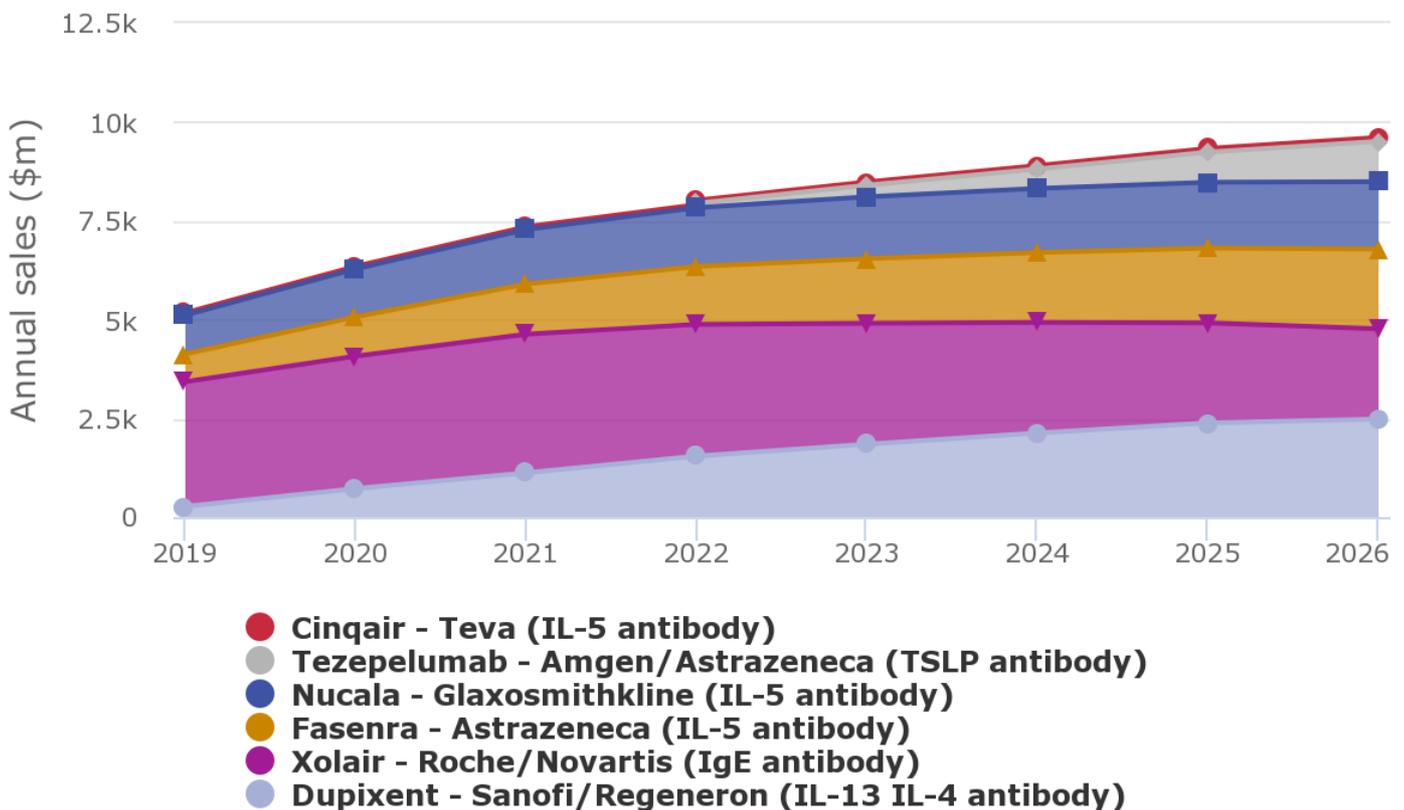
Navigator allowed the use of oral steroids, but it is unclear yet what proportion of patients were taking these. An ongoing [phase III trial, Source](#), is evaluating whether tezepelumab can reduce the use of oral corticosteroids; data are due before the end of this year.

Tezepelumab could also be a threat to other MABs that are currently approved for eosinophilic asthma, Professor Menzies-Gow believes. “People with high eosinophil counts don’t all respond as well as we’d like to current biologics.”

Current asthma antibodies, such as Dupixent and the IL-5 inhibitors, have shown reductions in annual asthma exacerbation rates of 50-70%, Leerink analysts noted.

Meanwhile, the phase II [Pathway trial](#) of tezepelumab found a [reduction in annual asthma exacerbation rates of 62-71%](#) versus placebo. If Navigator can get close to that, Amgen, whose stock opened up 4% today, will really have something to celebrate.

Forecasts for the asthma antibodies



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