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Sanofi seeks to build on COPD win

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Full Dupixent data confirm the drug's blockbuster potential in the lung disease, but the French drug maker is thinking even bigger.

Topline Dupixent data in COPD triggered a big bounce in Sanofi's share price earlier this year, and the full results, presented at a medical conference over the weekend, did not disappoint. The group also announced yesterday that a second project in pivotal development for the lung disease had passed an interim analysis.

That asset is itepekimab, an IL-33 targeted MAb that is being developed for former smokers, that Sanofi reckons could more than double its addressable COPD population, over Dupixent's segment. Itepekimab is the most advanced project in a big push from the developer in COPD and asthma, with several important readouts from various assets due in the coming years.

Dupixent is laying the groundwork, however, and full data from the Boreas trial at the American Thoracic Society meeting confirmed the agent's efficacy in patients with type 2 inflammation. High eosinophil levels are a marker of this type of inflammation, a marker that guided recruitment into Boreas.

In the trial Dupixent performed better than placebo in every subgroup measured, with an across-the-board benefit driving the impressive 30% relative reduction in exacerbations. Lung function improvements were seen despite the drug not being a bronchodilator, a surprising finding, according to Boreas's primary investigator, Dr Surya Bhatt, associate professor of medicine at University of Alabama.

"It tells me that probably [Dupixent is] a disease modifier," he told investors on a Sanofi call yesterday. "I think there are other pertinent things that are going on in the lung and structural changes...abnormalities are being improved."

The big issue for investors now is whether Sanofi, and its partner Regeneron, can file for accelerated approval based on this single trial. Executives on the call refused to be drawn other than saying they were "looking forward to speaking with regulators". An identical trial called Notus reads out in the first half of next year.

Sanofi's respiratory bets		
Trial	**Setting**	**Status**
Dupixent: anti IL-4/IL-13 Mab		
Boreas study	Moderate-to-severe COPD with type 2 inflammation	30% reduction in annualised exacerabtions vs placebo
Notus study	Moderate-to-severe COPD with type 2 inflammation	Topline readout H1 2024 (no interim analysis in trial design)
Itepekimab: anti-IL-33 MAb		
Aerify-1	Moderate-to-severe COPD (former smokers)	Topline read out 2025
Aerify-2	Moderate-to-severe COPD (former and current smokers; latter secondary population)	Topline readout 2025
Amlitelimab: anti-OX40L		
Tide-Asthma	Moderate-to-severe asthma	Phase 2b readout 2024
Rilzabrutinib: BTK inhibitor		
Proof-of-concept trial	Moderate-to-severe asthma	Phase 2b readout 2024
SAR443765: bispecific nanobody targeting IL-13 and TSLP		
Phase 1b	Asthma	Phase 2b programme to start later this year
Source: Sanofi presentation.		

As for itepekimab, which is only being developed in COPD, Sanofi also has high claims. It describes the biologic as having high binding affinity with among the longest half-lives and bioavailability of the IL-33 class, with no immunogenicity signals seen. Astrazeneca is also working on a similar project.

It has not been plain sailing with this asset, however, which failed in a phase 2a trial that recruited a wider COPD population, encompassing both former and current smokers. The pivotal programme focuses on former smokers, the group in which itepekimab showed a clear benefit, although the second trial has a current smoker cohort.

Smoking status was a prespecified subgroup in the mid-stage trial, but news that Aerify passed an interim analysis is reassuring nonetheless. Sanofi executives would not expand on the situation beyond saying it was “a meaningful interim analysis”.

Given itepekimab’s potential market – it seems to work in both patients with and without type 2 inflammation – success in this programme would be a big win for Sanofi. SVB Securities speculated that a 20% exacerbation rate reduction versus placebo could be the minimum bar that was crossed at the interim, concluding that they would not be surprised if Aerify read out in the same ballpark as Boreas’s 30% relative reduction.

As for earlier-stage assets, a few asthma projects were highlighted, sourced from partners. The Kymab-originated amlitelimab is being tested in both type 2 and non-type 2 patients, the second group being particularly in need of more options, according to Sanofi.

Rilzabrutinib is a BTK inhibitor that the company is targeting at poorly controlled patients in the pre-biologics space. Executives said they had seen no liver safety signals across any trials – the project is also being studies in a wide range of autoimmune conditions.

Finally, SAR-765 is a bispecific nanobody targeting IL-13 and TSLP, two binding domains that create the potential for “the most effective biologic for asthma”, Naimish Patel, head of immunology and inflammation for Sanofi, said.

Presumably a product of the Ablynx platform, cross-trial comparisons suggest SAR-765 is more potent than agents that address only TSLP or IL-13 alone, Patel claimed. Sanofi believes the project has the potential to preserve lung function and modify disease – although these claims are a long way from being proven.

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