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Regeneron and Sanofi breathe easier on Dupixent

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After a knock in its approved dermatitis indication last week Dupixent needed a result in asthma – and it has delivered. A win in the phase III Liberty Asthma Quest trial boosted the drug's chance of approval for the new use, which could add another $1.4bn in sales by 2022, according to *EvaluatePharma* sellside consensus.

But with competition expected to heat up in asthma, as well as atopic dermatitis, Sanofi and Regeneron will need to stay ahead of rivals if Dupixent is to meet the $10bn-plus peak sales that some analysts are forecasting.

It looks like some investors are already factoring in increasing competition: Regeneron's share price fell 6% yesterday. There were also some worries that the phase III data fell short of that seen in phase II (*Event – Dupixent asthma data could seal a second blockbuster market, August 08, 2017*).

Competition is coming?

Regeneron and – particularly – Sanofi rely heavily on Dupixent living up to lofty expectations, but there are signs that its launch is not going as well as hoped, with second-quarter sales falling short of expectations.

And Regeneron's stock dipped 6% last week on news that Abbvie's rival atopic dermatitis contender, upadacitinib or ABT-494, had produced seemingly similar results in phase IIb. Upadacitinib, an oral Jak inhibitor, could have a convenience advantage over Dupixent, which is delivered via subcutaneous injection.

Even if upadacitinib prevails in the phase III it is not expected to become available until 2020, but this has not stopped analysts becoming more cautious about Dupixent's chances of dominating this market.

Equally, in asthma there are worries that Regeneron and Sanofi's product could be squeezed by Astrazeneca's anti-thymic stromal lymphopoietin antibody tezepelumab, which also reported positive phase IIb results last week (*Snippet Roundup: PI3Ks not dead, but PD(L)-1 multiple myeloma hopes falter, September 08, 2017*).

Notably, these data came in all patients, irrespective of eosinophil levels, the same population that Dupixent is targeting.

While Bernstein analysts noted that Dupixent might "still lead the market in both indications" they added: "It does suggest competition will be coming [and] some of the higher-end estimates for the drug may need to come down."

And breathe

At least Sanofi and Regeneron have now taken a step closer to approval in the key asthma indication, which is forecast to account for around 25% of Dupixent's sales.

The 1,900-patient Liberty Asthma Quest trial met its two co-primary endpoints, reducing the number of annual exacerbations and improving lung function over 12 weeks, measured by change in forced expiratory volume in one second (FEV1).

The companies only disclosed data for the 300mg dose of Dupixent; they said 200mg was "generally comparable on both exacerbations and FEV1" but did not say whether it hit significance. Both doses were given on top of standard asthma therapy.

Liberty Asthma Quest study results with 300mg dose of Dupixent			
Endpoint	**Overall population**	**Patients with ≥150 eosinophilic cells/microliter**	**Patients with ≥300 eosinophilic cells/microliter**
Reduction in exacerbations at 52 weeks	46%*	60%*	67%*
Improvement in FEV1 at 12 weeks	130ml (9%)*	210ml (11%)*	240ml (18%)*
*Source: company website; *p<0.001.*			

Encouragingly, the improvement with the 300mg dose was significant regardless of patients' eosinophil status, although Dupixent did perform better in those with higher eosinophil levels.

The companies took a chance in testing all comers, as the phase IIb trial of Dupixent primarily measured response in a high-eosinophil subgroup – but the study did hit secondary endpoints covering patients with low eosinophils too.

This risk appears to have paid off for Sanofi and Regeneron, as Dupixent should now get the go-ahead in the broad asthma population. The companies plan to submit a supplemental US BLA by the end of the year.

Top-five asthma therapies in 2022				
Product	**Company**	**Description**	**Status**	**2022e sales ($m)**
Xolair	Roche	Anti-IgE MAb	Marketed	2,238
Nucala	Glaxosmithkline	Anti-IL-5 MAb	Marketed	1,422
Dupixent	Sanofi/Regeneron	Anti-IL-4 & IL-13 MAb	Phase III	1,372
Breo Ellipta	Glaxosmithkline	LABA & corticosteroid inhaler	Marketed	1,302
Symbicort Turbuhaler	Astrazeneca	LABA & corticosteroid inhaler	Marketed	1,251
Source: EvaluatePharma.				

If approval follows, Dupixent should have the edge over existing injectable products like Glaxosmithkline's anti-IL-5 antibody Nucala, which is only approved in high-eosinophil patients. Even before the latest data, *EvaluatePharma* consensus had put Dupixent not far behind Glaxo's MAb in 2022.

However, with tezepelumab and potentially other novel agents on the horizon for broad use, Sanofi and Regeneron will need to make their headstart count.

Study	Trial ID
Liberty Asthma Quest	NCT02414854

This story has been updated to reflect Regeneron's share price fall on Monday.

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