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Dupilumab grabs atopic dermatitis head start

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Regeneron and Sanofi's dupilumab has exceeded analyst expectations in phase III trials and looks set to become the first systemic drug approved for atopic dermatitis. However, this was not enough to push up Sanofi's share price this morning, suggesting that success had been widely anticipated. Regeneron's stock, meanwhile, was up 4% at the time of going to press.

Even so, dupilumab's performance in the identically designed Solo-1 and Solo-2 trials will set a high bar for rival atopic dermatitis projects in its wake (see table below). Regeneron and Sanofi should have a couple of years' head start over competitors, helping dupilumab achieve 2020 sales of $2.5bn, *EvaluatePharma* consensus expectations – with two thirds of this coming in dermatitis.

Making it look EASI

The sellside forecasts have been steadily rising, and could go up further on the back of the latest data. Leerink analysts previously wrote that the Solo studies needed to show that 25-30% of patients achieved the primary endpoint, an investigator's global assessment (IGA) score of 0 or 1, representing clearing or near-clearing of skin lesions.

Meanwhile the mean improvement in the eczema area and severity index (EASI) score, a secondary endpoint, needed to be 45-55% or better.

Dupilumab, an injectable monoclonal antibody that inhibits interleukin-4 and 13, surpassed both of these goals, and results were also in line with phase IIb data (*Sanofi and Regeneron itching to move dupilumab into phase III, July 10, 2014*).

Although adverse events were generally low, one drawback could be a higher rate of conjunctivitis in the dupilumab arm. The Leerink analysts, however, do not believe that this is a cause for concern, and note that there was no mention of herpes infection, which had been slightly elevated with dupilumab in phase II.

16-week results from phase III Solo-1 and Solo-2 trials of dupilumab

Endpoint	Solo-1			Solo-2		
	Dupilumab	Placebo	p value	Dupilumab	Placebo	p value
Dose: 300mg weekly						
IGA=0 or 1	37%	10%	p<0.0001	36%	9%	p<0.0001
Improvement in EASI	72%	38%	p<0.0001	69%	31%	p<0.0001
Proportion of patients achieving EASI-75	53%	15%	p<0.0001	48%	12%	p<0.0001
Dose: 300mg every two weeks						
IGA=0 or 1	38%	10%	p<0.0001	36%	9%	p<0.0001
Improvement in EASI	72%	38%	p<0.0001	67%	31%	p<0.0001
Proportion of patients achieving EASI-75	51%	15%	p<0.0001	44%	12%	p<0.0001

The project is expected to get the go-ahead in 2017, while the next MAbs in line, Chugai's CIM331 and Roche/Chugai's lebrikizumab, should reach the atopic dermatitis market in 2019 or later, according to the Leerink analysts.

Even if rival drugs are approved these might have trouble capturing market share if their pivotal trial results do

not live up to those from Solo-1 and Solo-2. The sector looks set to become pretty crowded, with no fewer than seven MAbs in development for eczema and dermatitis, according to *EvaluatePharma*.

MAbs in development in eczema/atopic dermatitis			
Project	**Company**	**Status**	**Mechanism of action**
Dupilumab	Regeneron/Sanofi	Phase III reported	Anti-IL-4/IL-13 MAb
CIM331/nemolizumab	Chugai	Phase II	Anti-IL-31 MAb
Lebrikizumab	Roche/Chugai	Phase II	Anti-IL-13 MAb
Stelara	Johnson & Johnson	Phase II	Anti-IL-12/IL-23 MAb
Cosentyx	Novartis	Phase II	Anti-IL-17 MAb
Tralokinumab	AstraZeneca	Phase II	Anti-IL-13 MAb
Tezepelumab	AstraZeneca/Amgen	Phase II	Anti-TSLP MAb

This is before counting other mechanisms of action such as histamine blockade, where Ziarco is soon expecting phase IIa results with its oral candidate ZPL-3893787 (*Upcoming events – Dermira and Ziarco to show some skin, April 1, 2016*).

Dupilumab is also in phase III development in asthma, an attractive market but one in which it will face more competition, noted Evercore ISI analyst Mark Schoenebaum. The relatively new sector of atopic dermatitis, where standard of care includes steroids and creams, is the chance for the drug to really make its mark – and the latest trial results should help it do so.

Study	**Trial ID**
Solo-1	NCT02277743
Solo-2	NCT02277769
Chronos	NCT02260986
Solo-Continue	NCT02395133
Paediatric safety study	NCT02612454
Open-label study	NCT01949311

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