Evaluate Vantage

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Sanofi’s oncology hopes crumble

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The discontinuation of amcenestrant piles more pressure on the group’s chief executive, Paul Hudson.

When Paul Hudson became Sanofi’s leader in 2019 making the group an oncology player was one of his main goals. Now, as the company fights various fires in its pipeline, that dream is looking very distant indeed.

News that the group was discontinuing its oral Serd amcenestrant was not that surprising given that project’s previous pivotal failure, but it still sent Sanofi’s stock down 5% this morning. If the company is now deprioritising oncology, as this and other recent moves suggest, what does this mean for Mr Hudson’s tenure, given he was the architect of Sanofi’s oncology push?

Walking away

In March amcenestrant flunked the Ameera-3 trial in ER-positive, Her2-negative breast cancer, but this and failures with other oral Serds were put down to a focus on all comers instead of on patients with ESR1 mutations.

One question is therefore why Sanofi has chosen to abandon amcenestrant completely, rather than carrying out a trial enriched for ESR1 mutants.

This is not the only recent indication that Sanofi might be going lukewarm on oncology: it recently handed back rights to Libtayo to Regeneron, just a year after claiming that the PD-1 laggard could challenge Merck & Co’s Keytruda in first-line non-small cell lung cancer.

True, several of Sanofi’s slew of recent deals have come in oncology, but the biggest of these, the $2.5bn purchase of Synthorx, is on shaky ground after initial data with the “not-alpha” IL-2 project SAR444245 disappointed.

Sanofi has so far kept the faith with ‘245, but it does not seem as bullish about this asset as it was even a few months ago. During its first-quarter results Mr Hudson talked up ‘245’s “best-in-class potential” and highlighted several mid-stage studies starting to read out this year. But in the second quarter Sanofi’s slide deck merely said a phase 3 decision on ‘245 was due by the end of 2022. It should be noted that acquiring Synthorx was one of Mr Hudson’s first moves as chief exec.

As for Sanofi’s late-stage pipeline, oncology is conspicuous by its absence. The only project of note, now amcenestrant has gone, is the anti-Ceacam5 antibody-drug conjugate tusamitamab ravtansine, which Sanofi hopes to file in second/third-line NSCLC next year.

Bolt Biotherapeutics recently discontinued a preclinical Ceacam5-targeting immune-stimulating antibody conjugate, BDC-2034, after deaths in non-human primate studies; however, Bolt blamed BDC-2034's binding to other Ceacam family members.

Hopes for tusamitamab ravtansine, at least measured by *Evaluate Pharma*'s sellside consensus forecasts, are not particularly high.

Aside from the aforementioned '245, Sanofi's mid-stage oncology hopes rest on alomfilimab, an anti-Icos MAb, and the Shp2 inhibitor SAR442720 – both mechanisms that have been marked by disappointments.

Pipeline "highlights"

The remainder of Sanofi's late-stage pipeline, outside of oncology, is not much to write home about either. There are big questions about tolebrutinib and rilzabrutinib, the oral BTK inhibitors gained via Sanofi's $3.7bn purchase of Principia, the universal haemophilia contender fitusiran and the COPD project itepekimab.

Indeed, the only real bright spots are the ultra-long-acting factor VIII therapy efanesoctocog alfa and the respiratory syncytial virus antibody nirsevimab. These look odds-on for approval, though there are still doubts about how big they can become.

Sanofi also has the Zantac litigation to contend with, although there was a sign today that fears around this might have been overblown, with the first case, against GSK, being dismissed.

With news like that, Sanofi should have been up today. The fact that it was not shows just how bad things have got for the company.

Sanofi's late-stage pipeline			
Project	**Description**	**Note**	**2028e sales ($m)**
Nirsevimab	Anti-RSV MAb (partnered with Astrazeneca)	Prevented RSV but did not reduce hospitalisation in ph3; filed in EU, other filings due in 2022	845*
Tolebrutinib (SAR442168)	Oral BTK inhibitor for MS (via Principia)	On clinical hold after drug-induced liver injury in ph3 trials	767
Amcenestrant	Oral Serd for breast cancer	Failed Ameera-3 Mar 2022; Sanofi discontinued development Aug 2022 following failure of Ameera-5 1L trial	591
Efanesoctocog alfa	Ultra-long-acting FVIII therapy for haemophilia A (via Bioverativ)	Hit in phase 3 Xtend 1 Mar 2022	579
Tusamitamab ravtansine (SAR408701)	Anti-Ceacam5 ADC (licensed from Immunogen)	Recently partnered with Innovent Biologics in China; Bolt recently discontinued its Ceacam5-targeting project BDC-2034 following preclinical tox findings	368
Itepekimab	Anti-IL-33 mAb for COPD (partnered with Regeneron)	Failed ph2; ph3 Aerify-1 & Aerify-2 ongoing in former smokers	224
Fitusiran	RNAi targeting antithrombin for haemophilia A & B (licensed from Alnylam)	Concerns about blood clot risks, Sanofi still trying to find the right dose	194
Rilzabrutinib (PRN1008)	Oral BTK inhibitor for various immune-mediated diseases (via Principia)	Failed ph3 in pemphigus, various other indications still in play including ITP	185
Venglustat (GZ402671)	Glucosylceramide synthase inhibitor for Gaucher type 3, Fabry & GM2 gangliosidosis	Filings delayed vs previous expectations; ph3 in Gaucher & Fabry began 2022	128
VRVg (VerorabVax)	Rabies vaccine	Ph3 was due to complete Mar 2022	-

**Sanofi to book revenues, Sanofi and Astrazeneca share costs & profits. Source: Evaluate Pharma & company presentation.*

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