

Sanofi does a spring clean



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The French company has taken a look at its R&D portfolio, and made some radical changes in oncology and diabetes.

Buried deep in today's fourth-quarter financials report from Sanofi is a slide detailing R&D pipeline changes, making it clear that the French group has been paying attention to recent trends in immuno-oncology, but also containing a few surprises.

Out go anti-Lag-3 and CTLA-4 approaches in oncology, and a pivotal combo study in first-line lung cancer has been canned, presumably as realisation dawned that competing against Keytruda was a non-starter. Among the surprises, an anti-BCMA bispecific enters phase I in multiple myeloma, just two days after Novartis and Gilead spelled out their reservations about competing in this crowded field.

On Tuesday Gilead took an extraordinary \$820m charge to write off its anti-BCMA CAR KITE-585 in the face of fierce competition, while Novartis moved to strengthen its own asset, MTV273, by taking it forward in combination ([Novartis and Gilead's multiple myeloma CARs diverge](#), February 6, 2019).

Today Sanofi highlighted the recent start of recruitment into a phase I trial of REGN5458, a Regeneron-partnered anti-BCMA bispecific. This will have to contend with GSK2857916, an antibody-drug conjugate from Glaxosmithkline. Glaxo has vowed that '7916 will be the first BCMA-targeting project to come to market.

Dual duels

If there is still space to compete in BCMA the same can apparently not be said about GIP/GLP1 mechanisms in diabetes. Lilly last year [surged ahead in developing LY3298176](#), a novel GIP and GLP1 agonist, and Sanofi's similarly acting offering, SAR438335, has been jettisoned from phase I.

In phase II discontinuations out goes SAR425899, a glucagon and GLP1 dual agonist for obesity and diabetes that had competed against Novo Nordisk's NN9277. And, on the day that the Ablynx-derived Cablivi got US approval with a [surprisingly benign label](#), Sanofi canned another Ablynx asset, the anti-RSV nanobody ALX0171.

There was good news this week for Sanofi when isatuximab [scored a hit in the phase III Icaria-MM trial](#) in multiple myeloma. While this anti-CD38 MAb faces the tall order of challenging Darzalex, Sanofi is moving forward with two phase II combo trials, one with Roche's anti-PD-L1, Tecentriq, and the other with its own anti-PD-1 drug, Libtayo.

Lung cancer scrap

It is Libtayo, which posted sales of \$15m in its first quarter on the market, that could attract most attention from investors today: Sanofi is scrapping its phase III trial in combination with Yervoy in first-line NSCLC patients expressing PD-L1 at 50% or above.

In this use Merck & Co's Keytruda has a stranglehold, which will soon be broadened to include lower PD-L1 expressers. Similar PD-(L)1/CTLA-4 approaches from AstraZeneca and Bristol face a desperate battle for relevance ([Bristol makes investors squirm a little more, January 24, 2019](#)).

There is bad news for followers of Oxford Biomedica, whose myosin VIIA gene therapy UshStat [Sanofi is discontinuing in phase II](#), and for Immuteq, a major player in the Lag-3 mechanism. Sanofi's Libtayo combination with REGN3767, an anti-Lag-3 MAb, is being scrapped in phase I; other anti-Lag-3s include Bristol's relatlimab and Merck & Co's MK-4280.

And, in addition to ending Libtayo's Yervoy combination, the anti-PD-1 MAb's combo with the in-house CTLA-4 inhibitor REGN4659 has bitten the dust, also in NSCLC. This will be taken as yet another vote of no-confidence in CTLA-4, and in the idea of trying to compete in lung cancer.

Selected Q4 2018 pipeline changes for Sanofi

In...			
Project	Target	Move	Relevant for
Isatuximab + Tecentriq	CD38 + PD-L1	Start of phase II in solid tumours	Darzalex, MOR202
Isatuximab + Libtayo	CD38 + PD-1	Start of phase II in lymphoma	Darzalex, MOR202
REGN5458	BCMA	Start of phase I in multiple myeloma	GSK2857916, MTV273, bb2121, JCARH125
BIVV003	Bcl 11A gene therapy	Start of phase I in sickle cell	Sangamo (partner)
SAR443060	RIP1 kinase	Start of phase I in ALS & Alzheimer's	GSK3145095 (oncology)
...out			
Libtayo + Yervoy	PD-1 + CTLA-4	Discontinuation of phase III in 1L NSCLC	Opdivo, Imfinzi, Bavencio
SAR425899	GLP1 + glucagon	Discontinuation of phase II in diabetes	NN9277
SAR438335	GLP1 + GIP	Discontinuation of phase I in diabetes	LY3298176, NN9423
SAR439794	TLR 4	Discontinuation of phase I in peanut allergy	Viaskin Peanut, AR101
REGN3767	Lag-3	Discontinuation of monotherapy & Libtayo combo	GSK2831781, IMP731, relatlimab, MK-4280
REGN4659	CTLA-4	Discontinuation of monotherapy & Libtayo combo	Yervoy, tremelimumab, AGEN1884, MK-1308
UshStat	Myosin VIIA gene therapy	Discontinuation of phase I in Usher syndrome 1b	Oxford Biomedica (former partner)
SAR228810	Protofibrillar amyloid-beta	Discontinuation of phase I in Alzheimer's	Gantenerumab, aducanumab, BAN2401

Source: company presentation.

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