

Big pharma picks Immunocore as a cell therapy player to watch



[Jacob Plieth](#)

A low-key clinical trial agreement with Lilly has drawn attention to Immunocore's twist on engineered T-cell receptors – an approach that is itself seen as the next big thing after CAR-T.

Immunocore, a private UK biotech, already has a separate discovery alliance with Lilly, as well as similar deals with GlaxoSmithKline, Roche and AstraZeneca. This kind of big pharma endorsement marks it as a serious contender in a field where T-cell therapies are hot, and should have investment bankers salivating at the prospect of a very significant flotation.

Not that IPO plans are something the company has revealed much about, preferring instead to focus on building alliances around its technology. But the blueprint is CAR-T companies like Juno Therapeutics and Kite Pharma, and a fellow UK T-cell receptor (TCR) company, Adaptimmune, which raised \$191m in a Nasdaq IPO last month.

How they are related

The comparison between Immunocore and Adaptimmune is even closer than might appear at first sight. The two groups own equity in each other, share some investors and until last year had the same chief executive – James Noble.

Their technologies are both derived from Avidex, a UK business bought by Medigene back in 2006. Two years later Medigene spun out the TCR work, which it deemed non-core, into Adaptimmune and Immunocore.

The two approaches are distinct, however. Adaptimmune, in common with several important cell therapy players, is genetically altering patients' T cells to cause them to express a TCR against a tumour cell antigen, thus directing the immune system to attack the tumour.

Immunocore, meanwhile, is focused on a soluble version of the TCR, which acts as a sort of bispecific agent: one part of the generated protein is specific for the tumour antigen, while the other binds to and activates T cells. Thus T cell-mediated killing is achieved in both cases, but in different ways.

The TCR approach has some similarity with CAR-T, though the latter uses a chimaeric receptor rather than a natural one. Because CAR-Ts use an antibody motif they are not, like TCRs, restricted to antigens expressed on immune system cells, though TCRs are thought able to target a wider range of antigens.

Both rely on antigens uniquely expressed on tumours, to avoid off-tumour, on-target effects. This is where Immunocore's first target of choice, gp100, might run into difficulties since it is expressed in the skin, eyes and ears, as well as on melanoma cells; early academic studies of a gp100 TCR found profound eye and ear toxicity.

Still, four big pharma partners counts for a lot. [Today's deal](#) will see Lilly, a late entrant to immuno-oncology, and Immunocore collaborate on running studies of IMCgp100 combined with galunisertib and merestinib.

Selected TCR-based projects

Company	Project	Detail	Trial ID
NCI (NIH)*	NY-ESO-1 TCR	Phase II in various tumours	NCT01967823
	HPV-16 E6 TCR	Phase I/II in cervical cancer	NCT02280811
	MAGE A3/A6 TCR	Phase I/II in various tumours	NCT02111850
	MAGE A3 TCR	Phase I/II in various tumours	NCT02153905
	SSX2 TCR	Pre-IND	-
	KRAS TCR	Pre-IND	-
Juno Therapeutics	WT-1 TCR	Phase I/II in NSCLC	NCT02408016
UCL/Cell Therapy Catapult	WT-1 TCR	Phase I/II in leukaemia	NCT01621724
Adaptimmune	NY-ESO-1 TCR**	Phase I/II in multiple myeloma	NCT01892293
		Phase I/II in ovarian cancer	NCT01567891
		Phase I/II in melanoma	NCT01350401
	MAGE A10 TCR	Breast cancer IND due 2015	-
Immunocore	IMCgp100	Soluble TCR. Phase I in melanoma	NCT01211262
Medigene	-	First clinical study planned 2016	-

**CRADA with Kite Pharma; **partnered with GSK. Source: company filings.*

Immunocore faces formidable competition, but is crucially differentiated by developing soluble TCRs. Kite Pharma claims to be one of the most advanced engineered TCR players via a co-operative R&D agreement with the NIH's National Cancer Institute, and recently [bought the private Dutch company T-Cell Factory](#), which gave it a technology for generating TCRs.

Interestingly Novartis, the most advanced CAR-T company, seems not to be pursuing engineered TCRs, instead [directing its CRISPR gene editing approach](#) at next-generation CARs. And after discarding the Avidex assets Medigene, too, is now planning a comeback of its own into TCRs, via the acquisition of Trianta Immunotherapies.

With the benefit of hindsight one of the most galling aspects for Medigene must be how little it stands to benefit from Immunocore's success. At one point Medigene held a 17.5% interest, but this was capped at £2.8m (\$4.4m) and was [subsequently converted](#) into an uncapped 3% equity stake.

If Immunocore floats the biggest beneficiaries would be Adaptimmune investors and affiliates, who hold some 97% of the equity - not to mention, of course, the investment bankers.

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Evaluate HQ
[44-\(0\)20-7377-0800](tel:+14152073770800)

Evaluate Americas
[+1-617-573-9450](tel:+16175739450)

Evaluate APAC
[+81-\(0\)80-1164-4754](tel:+8108011644754)

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