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Why Immatics could soon become the next listed cell therapy player

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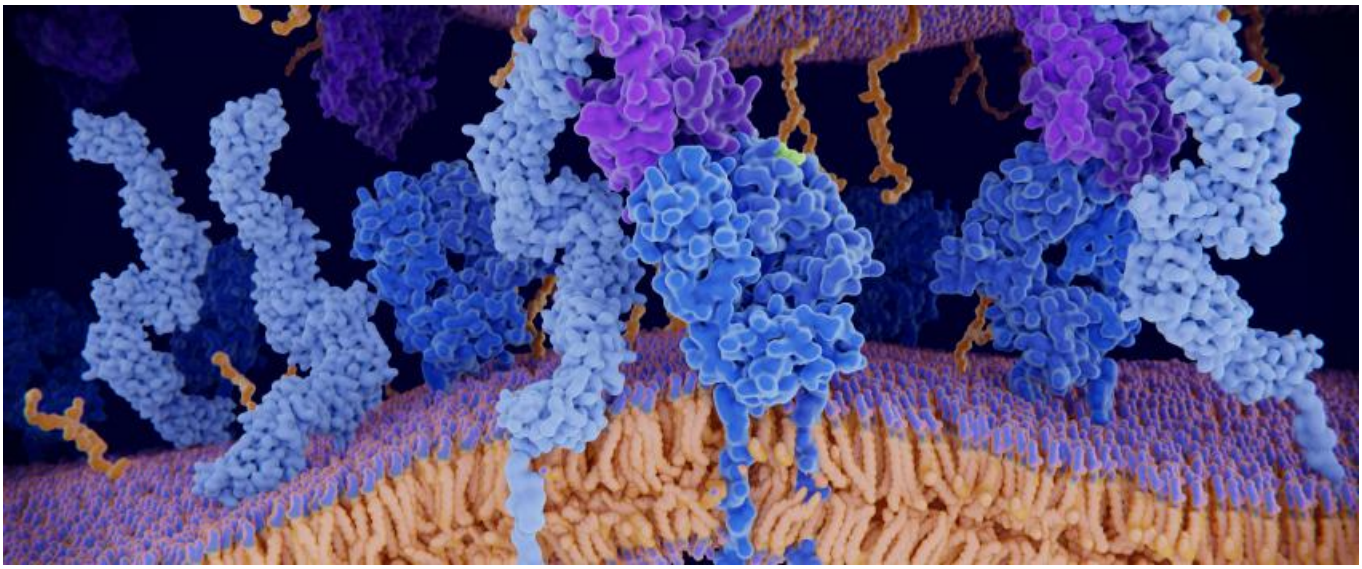

Immunocore and Adaptimmune could shortly have a publicly listed rival.

Cell therapies still have much to prove commercially – but this has not stopped early-stage players raising impressive amounts of cash. One of these, Germany's Immatics, could soon be eyeing the public markets after a $58m funding round last year and a $54m deal with Genmab last week.

"Clinical trials need money – and the next deal or financing round could include an IPO," the group's chief medical officer, Carsten Reinhardt, tells EP Vantage. Such a move could see Immatics beat its nearest rival, Immunocore, to a public listing.

Like the UK-based cell therapy player Autolus, which floated on Nasdaq in June, Immatics will probably eschew a European listing, Mr Reinhardt adds. "It's pretty clear that if we decided to go that route, it's most likely a Nasdaq IPO."

The Genmab deal, though involving preclinical projects, has given Immatics another strong endorsement after earlier tie-ups with Amgen, Roche and Morphosys. Partners have been enticed by a technology that could enable internally expressed cancer antigens to be targeted – and this means hitting solid tumours.

Under the Genmab agreement three undisclosed intracellular targets have been selected; work will focus on developing binders against these – Genmab generating antibodies, Immatics making affinity-enhanced T-cell receptors (TCRs).

"I'm biased towards TCRs, but we are kind of agnostic in our collaboration," says Mr Reinhardt. Either way, the aim is to incorporate these binders in bispecifics targeting the desired antigen at one end and (most likely) CD3, to recruit T cells, on the other.

Amgen's Blincyto is an example of a typical bispecific antibody, in this case a Bite (bispecific T-cell engager), and Immatics' Amgen deal also includes work to develop Bites.

As well as the projects covered by the Genmab deal, and two separate targets involved in the Amgen collaboration, Immatics is also solely developing a proprietary project that has an undisclosed target, codenamed AG008-01, on which it presented data at the AACR meeting in April.

CAR-T vs TCR

In a way the Genmab deal unites two opposing factions of the cell therapy world: proponents of CAR-T, and those who those who believe in TCRs.

CAR-T, using the ScFv binding region of an antibody, is an approach that hits cell-surface proteins. Internally processed antigens, meanwhile, are displayed on a cell's major histocompatibility complex (MHC) and can therefore normally only be hit with a TCR; such TCRs can be artificially engineered.

Each approach has its pros and cons. CARs are universal for a given antigen, but are generally thought incapable of targeting internal proteins, which limits the range of cancers in which they can be used. "Most of the current targets used for antibody or CAR-T therapies are cell-surface proteins – those are only 15-20% of all cancer-specific proteins," says Mr Reinhardt.

TCRs, meanwhile, are designed to target internally processed antigens, but they are limited by the fact that in humans many different haplotypes of the MHC exist, and each TCR product has to be matched. Most work, including at Immatics so far, has focused on the most common haplotype, A2, present in 40% of the Caucasian population.

Cheaper and easier?

Of course, a bispecific approach, whether based on antibodies or TCRs, could offer a cheaper and easier alternative to cell therapy, though efficacy with conventional Bites has so far not matched that seen with CAR-T.

And while there are other companies working on engineered TCRs – Adaptimmune, Gilead and Celgene to name three – Mr Reinhardt reckons only Immunocore and Immatics have developed TCR-based bispecifics to a point where they might be ready for clinical trials.

The Immatics and Immunocore approaches are similar, except the former uses a larger bispecific construct – 100kD versus 70kD – that Mr Reinhardt reckons gives better pharmacokinetic properties and a longer half-life: "I guess [Immunocore is] working on longer half-life versions, just like Amgen is working on longer Bite versions."

The rest of Immatics' in-house pipeline derives from a 2015 deal with MD Anderson (*Immatics answers the call from MD Anderson, August 26, 2015*). This includes ACTolog, an approach generating tumour-infiltrating lymphocytes with defined target specificity, and ACTengine, a technology developing typical engineered TCRs.

Perhaps most intriguing is the early-stage ACTallo platform, which expresses engineered TCRs on gamma-delta T cells. Unlike normal alpha-beta T cells this subgroup of cells presents very low risk of graft-versus-host disease, and thus could form the basis of an off-the-shelf therapy. The mispairing of alpha and beta subunits between the endogenous and engineered TCR – a problem that can render alpha-beta engineered TCR approaches ineffective – is also avoided.

The gamma-delta field has been getting crowded lately: others in the space include the Puretech Health subsidiary Nybo Therapeutics, Gadeta, Gammadelta Therapeutics, Incysus, Lymphact and Medinet.

Immatics' fundraising track record – as well as its ability to attract big pharma names – shows the level of interest in its technology.

But it still has a long way to go. Mr Reinhardt will not be drawn on when a Genmab-partnered bispecific might hit the clinic, but says that Immatics would expect a proprietary bispecific project to be IND-ready in two to three years.

Still, it is not unusual these days to see preclinical-stage companies going public, particularly those in hot areas like cell therapies – and Immatics might soon join their ranks.