

New Genmab/Abbvie tie-up rings old bells



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Followers of Nordic Nanovector and Oxford Biomedica, among others, will pay close attention to an early focus of yesterday's deal.

For some seasoned biotech investors yesterday's broad alliance between Genmab and Abbvie will have rung old bells. While its headline focus is on the anti-CD20 bispecific epcoritamab, behind the scenes lie two other projects against antigens with which some will be very familiar: CD37 and 5T4.

The former is perhaps most famous as being the target of Betalutin, an asset according to whose fortunes Nordic Nanovector's stock has waxed and waned. 5T4, meanwhile, used to be a major focus of several Oxford Biomedica approaches, but was brought crashing to earth with the failure of Trovax's pivotal Trist study in 2008.

The CD37 approach, too, has seen discontinuations. As is to be expected, Genmab and Abbvie insist that their bispecifics, DuoHexaBody-CD37 (GEN3009) and DuoBody-CD3x5T4, are "potentially best in class" ([Genmab brings on Abbvie for bispecific boost, June 10, 2020](#)).

GEN3009 is a bispecific MAb by virtue of engaging two different epitopes on CD37, and Genmab says this is a unique approach; after showing promise in vitro it is in a [dose-escalation lymphoma study](#). DuoBody-CD3x5T4 is a T-cell-engaging bispecific, but an IND for it has only just been submitted.

Competition

There is more advanced industry work on the former antigen than the latter. In late 2016 Norway's Nordic Nanovector touched a record valuation of \$785m as Betalutin impressed in late-line lymphoma settings, but the realisation that work is still very early, coupled with delays, [have caused the stock to drift since](#).

Betalutin comprises an unusual approach, combining CD37 targeting with the radionuclide lutetium-177; a follow-up uses lead-212 as the radionuclide.

Debiopharm's naratuximab is a more typical antibody-drug conjugate, and was acquired from Immunogen three years ago; a phase II trial should end imminently. Among the disappointments are another ADC, from Seattle Genetics/Astellas, which was canned despite [showing promise in heavily pretreated non-Hodgkin's lymphoma in 2017](#).

Selected projects targeting CD37

Project	Mechanism	Company/institution	Clinical trial?
<i>Phase II</i>			
Naratuximab emtansine	Anti-CD37 ADC	Debiopharm (ex Immunogen)	Rituxan combo in r/r lymphoma
Betalutin	Anti-CD37 MAb-Lu-177 conjugate	Nordic Nanovector	Lymphoma trial with lilotomab (anti-CD37 MAb) pre-dosing
<i>Phase I</i>			
GEN3009	Anti-CD37 dual-epitope MAb	Genmab/Abbvie	First-in-human lymphoma
CAR37 T Cells	Anti-CD37 Car-T	Massachusetts General	Haem-onc trial yet to start enrolling
<i>Preclinical</i>			
NNV013	Anti-CD37 MAb-Pb-212 conjugate	Nordic Nanovector	-
<i>Discontinued</i>			
Otlertuzumab	Anti-CD37 MAb	Aptevo	Disc in Nov 2018 after lack of efficacy in T-cell lymphoma
AGS67E	Anti-CD37 ADC	Seattle Genetics/Astellas	30% ORR, 7/52CR
BI 836826	Anti-CD37 MAb	Boehringer Ingelheim/Xencor	4 studies completed, 1 terminated, 1 withdrawn
<i>Source: clinicaltrials.gov & EvaluatePharma.</i>			

Still, if some previous work on CD37 prompts doubts over the target, this is nothing compared with that on 5T4, a tumour antigen discovered by scientists at Cancer Research UK back in the 1990s.

5T4's most notorious casualty was Oxford Biomedica's Trovax, which crashed in phase III 12 years ago. To be fair this was a cancer vaccine, so its failure might have had more to do with the approach than the target, but Oxford has separately flirted with MAb, ADC and even Car-T formats against 5T4, none making significant progress.

A second big failure was Active Biotech's anti-5T4 ADC Anyara, whose phase II/III renal cell carcinoma study blew up in 2013 ([Anyara sounds the death knell for 5T4-targeted anticancers, January 29, 2013](#)). Remarkably, Active managed to offload Anyara to Neotx, which is now running a phase I trial in combination with Imfinzi.

The precedent for targeting CD37 and 5T4 might not be great, but at least Genmab and Abbvie can boast novel approaches to hitting these old-school antigens. All that remains is for them to show their worth in the clinic.

Selected projects targeting 5T4

Project	Mechanism	Company/institution	Clinical trial?
<i>Phase II</i>			
VTP-800	Anti-5T4 cancer vaccine	Vaccitech	Opdivo combo in prostate cancer
<i>Phase I</i>			
Anyara	Anti-5T4 ADC	Neotx (ex Active Biotech)	Imfinzi combo; failed ph2/3 in renal cancer
<i>Preclinical</i>			
DuoBody-CD3x5T4	Anti-5T4 bispecific MAb	Genmab/Abbvie	IND filed Q1 2020
ALG.APV-527	Anti-5T4/4-1BB bispecific MAb	Alligator/Aptevo	-
OXB-302	Anti-5T4 Car-T	Oxford Biomedica	-
UCART5T4	Anti-5T4 Car-T	Collectis	-
ASN004	Anti-5T4 ADC	Asana/Mersana	-
<i>Discontinued</i>			
Trovax-DC	Anti-5T4 cancer vaccine	Oxford Biomedica	Failed ph3 Trist study
PF-06263507	Anti-5T4 ADC	Oxford Biomedica/Pfizer	-
<i>Source: clinicaltrials.gov & EvaluatePharma.</i>			

This story has been updated to include Vaccitech's VTP-800.

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