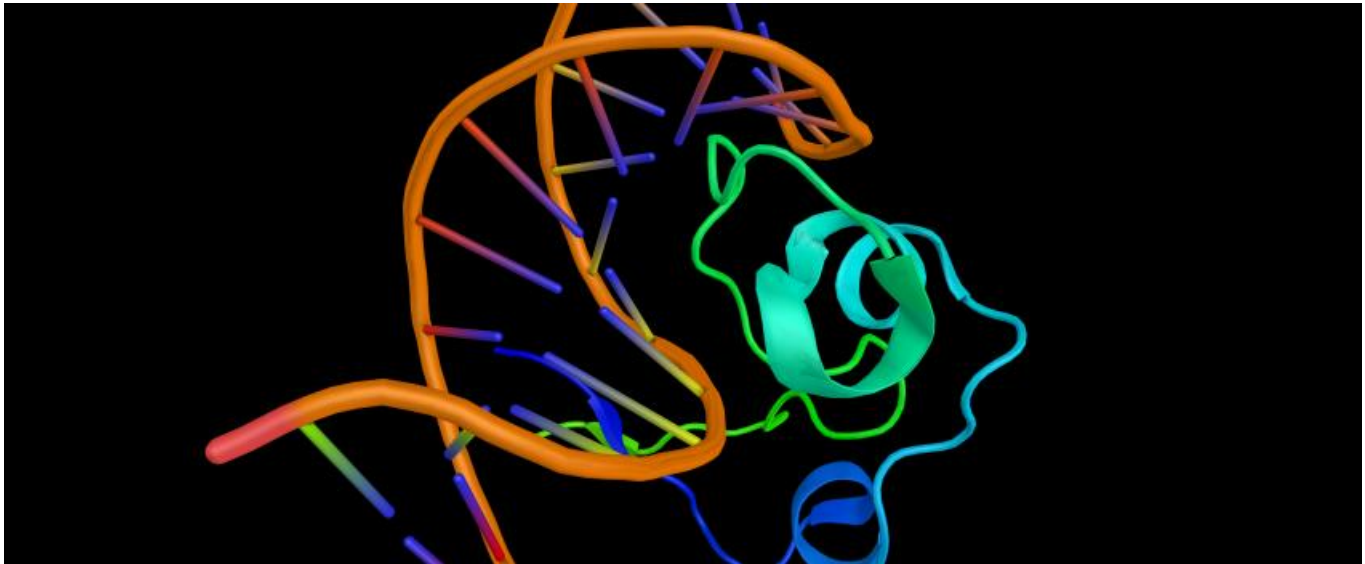


February 28, 2020

## Another preclinical thumbs-up for Sangamo's zinc fingers



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### **The deal between Sangamo and Biogen marks another endorsement of a gene-editing technology that many had written off years ago.**

The transformation of zinc-finger nucleases from an outdated also-ran to a gene-editing technology that could be at least the equal of trendy Crispr has been remarkable, and yesterday's deal sees Biogen become the latest to buy into the technique's leading exponent, Sangamo.

The \$350m that has changed hands on signing puts the neurology-focused tie-up among the industry's biggest deals struck without a single patient having been treated. Biogen already has form here, having given \$1bn to Ionis under a 2018 preclinical CNS tie-up, while Sangamo has now received a combined \$698m for assets that at the point of being partnered had never seen a human subject.

Biogen and Sangamo have long worked together, having in 2014 struck one of these preclinical alliances, focusing on sickle cell disease and beta-thalassaemia. That cell therapy asset is now in phase I/II trials, after Biogen spun it into the Bioverativ business now owned by Sanofi.

But it was Sangamo's 2017 tie-up with Pfizer, covering haemophilia A, that marked the watershed for zinc-finger nucleases ([Sangamo's gene therapy gets Pfizer stamp of approval, May 11, 2017](#)). This was also a watershed for Sangamo itself, marking the start of a 10-month period in which its stock surged 450% to peak at \$26.35.

#### **\$9.21 per share**

Perhaps such a precedent makes yesterday's Biogen deal seem less impressive. Its \$225m equity element is being done at just \$9.21 per share, but then Sangamo has fallen considerably from its March 2018 peak; today the shares opened up 30%.

This should not detract from the fact that it represents a considerable bet by Biogen. The group's focus will initially fall on three Sangamo assets to which it gains exclusive rights: ST-501 and ST-502, an anti-tau and  $\alpha$ -synuclein gene therapy for Alzheimer's and Parkinson's diseases respectively, plus an undisclosed CNS asset.

The overall CNS focus of this alliance also seems unusual, given how many of the preclinical deals that have attracted the most up-front cash have centred on oncology. Notably, however, perhaps the most valuable preclinical CNS alliance also featured Biogen, which gave Ionis \$375m in cash and bought an amazing \$625m

of equity under a [2018 tie-up covering a range of disorders](#).

Selected deals signed at the preclinical stage						
Project	Paying company	Source company	Deal date	Cash fee (\$m)	Equity stake (\$m)	Combined up-front (\$m)
Neurological diseases	Biogen	Ionis	20 Apr 2018	375	625	1,000
RTA 404	Abbott	Reata	12 Dec 2011	400	0	400
ST-501, ST-502 + undisclosed	Biogen	Sangamo	27 Feb 2020	125	225	350
ASP0892	Astellas	Immunomic	9 Oct 2015	300	0	300
JTX-2011	Celgene	Jounce	19 Jul 2016	225	36	261
Undisclosed	Celgene	Forma	1 Apr 2014	225	0	225
ADU-S100	Novartis	Aduro	30 Mar 2015	200	25	225
Alzheimer's research	Abbvie	Alector	24 Oct 2017	205	0	205
Immuno-oncology	Celgene	Agios	17 May 2016	200	0	200
mRNA cancer vaccines	Merck & Co	Moderna	29 Jun 2016	200	0	200
Bispecific Mabs	Incyte	Merus	21 Dec 2016	120	80	200
KITE-037	Gilead	Sangamo	22 Feb 2018	150	50	200
Undisclosed	Baxalta	Symphogen	4 Jan 2016	175	0	175
Immuno-oncology	Celgene	Nurix	16 Sep 2015	150	17	167
XmAb14045	Novartis	Xencor	28 Jun 2016	150	0	150

*Source: EvaluatePharma & company filings.*

With Biogen's growing dependence on aducanumab, its focus on the CNS and increasing desire to spend big on business development are understandable.

But the other side of the equation is no less remarkable. Sangamo, which in the wake of the hype about Crispr gene editing looked like it was being left behind with its outdated zinc-finger technology, has now used precisely that technology to bring in \$698m of cash - without using it to treat a single patient.

To date only two of its partnered gene therapy assets, in haemophilia A and beta-thalassaemia/sickle cell disease, have entered the clinic. A third, Gilead's zinc-finger edited allogeneic anti-CD19 Car, KITE-037, should get there this year.

No doubt the Biogen-partnered projects will now be advanced quickly. A \$350m bet will need clinical backing sooner rather than later.

	 <b>Biogen.</b>	 <b>GILEAD</b>	 <b>Pfizer</b>	 <b>Pfizer</b>	 <b>SANOFI</b>	 <b>Takeda</b>
<b>Target/ therapeutic area</b>	Neurological including AD, PD	Oncology anti-CD19 CAR-T	C9ORF72 ALS	Hemophilia A	Beta thalassemia, Sickle Cell disease	Huntington's disease
<b>Royalties (% on net sales)</b>	High-single to low double-digit	Single-digit	Mid- to high-single digit	Low teens to 20	Double-digit	Single-digit
<b>Upfront</b>	\$125M payment + \$225M in equity purchase	\$150M payment + \$50M in equity purchase	\$12M	\$70M	\$20M	\$13M
<b>Milestones</b>	Up to \$2.37B (\$925M pre-commercial, and \$1.445B for 1 <sup>st</sup> sale and sales thresholds)	Up to \$3.1B (\$1.3B through 1st sale, and \$1.8B sales thresholds)	Up to \$150M preclinical and commercial	Up to \$475M (\$300M for SB-525 and \$175M other)	Up to \$276M for both programs	-

A summary of Sangamo's deals, all done at the preclinical stage. Source: company presentation.