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Novavax keeps investors waiting

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Those wanting to see whether the US government was right to give Novavax $1.6bn two weeks ago will have to wait a little longer.

Investors and governments desperate for progress with a vaccine against the new coronavirus have this week received an abundance of riches. But they will have to wait until the end of the month for data from Novavax, a company that has unexpectedly managed to secure the biggest award to date from Project Warp Speed – $1.6bn.

The company did present today at a virtual session of the International Society for Vaccines, but in the event this amounted to a summary of preclinical findings. For now investors will have to continue picking apart the minutiae of clinical results unveiled yesterday by Astrazeneca, Biontech/Pfizer and Cansino, and disclosed earlier by Moderna.

Novavax bulls have been primed, however. Speaking at the scientific session, the group's head of R&D, Greg Glenn, confirmed that clinical results for the trial of its NVX-CoV2373 vaccine would include detail on antibody as well as T-cell responses. Both will be key to determining how the company stacks up against the competition (*Covid-19 vaccine contest turns to T-cell responses, July 20, 2020*).

What Novavax needs to show to justify its valuation is a separate question, of course. The company's market cap today stands at $8bn, backed merely by NVX-CoV2373 data generated in non-human primates.

Novavax had secured its $1.6bn of Warp Speed funding just two weeks ago, and it seemed puzzling that the US government did not wait to see clinical data before making such a large award (Novavax shares enter Warp Speed with cash injection, July 7, 2020). It is unclear whether the funding is tranched or contingent on milestones.

Warp Speed bonanza – summary of disclosed awards				
Date	**Company**	**Project**	**Detail**	**($m)**
30 Mar	Johnson & Johnson	(no code)	Adenovirus type 26 vaccine; ph1 starting 22 Jul, ph3 27 Jul 2020	465
16 Apr	Moderna	mRNA-1273	mRNA vaccine in ph1; ph3 starting 27 Jul 2020	483
21 May	Astrazeneca	AZD1222	Chimp adenovirus vaccine in ph1; ph3 starting 14 Aug 2020	1,200
7 Jul	Novavax	NVX-CoV2373	Nanoparticle vaccine; ph1 data late Jul; ph3 starting 15 Oct 2020	1,600
7 Jul	Regeneron	REGN10933 + REGN10987	MAb "cocktail" in ph1 & ph3; NB, not a vaccine	450

Novavax's clinical trial tests two NVX-CoV2373 doses, 5µg and 25µg, the latter with or without an adjuvant, in 131 volunteers. Data are expected by the end of July, said Mr Glenn.

For its part, the Chinese group Cansino yesterday saw the scientific publication of clinical data for its Covid-19 vaccine Ad5-nCoV. This trial is by far the largest of any vaccine to read out so far, having been conducted in 382 volunteers assigned one of two doses or placebo.

However, the paper did not alter the view that data are disappointing; seroconversion of neutralising antibody responses occurred in only 59% and 47% of subjects in the two active cohorts. At a time when three competitors are seeing neutralising antibodies at potentially relevant levels in 100% of recipients, albeit in smaller trials, this seems underwhelming.

A key new aspect of Cansino's data was detail on T-cell responses. It is thought that a vaccine will have to show these, along with generating neutralising antibodies, to yield effective and long-lasting immunity, though of course no one knows what levels of each will actually result in such immunity.

Cansino did report T-cell responses to Ad5-nCoV in 90% and 88% of patients in the two dosing groups, but did not specify whether these concerned CD4+ or CD8+ T cells. Also, relative to the response levels cited by Biontech/Pfizer relating to BNT162b1 the Cansino levels seem modest.

Cross-trial comparison of Covid-19 vaccine data					
Project (company)	**Doses**	**Study**	**Neutralising antibodies at relevant levels**	**T cells**	**Toxicity**
BNT162b1 (Biontech/Pfizer)	10-30µg prime & boost, 100µg single	NCT04368728	Seen in 36/36 volunteers	No data	Grade 3 AEs in 2/36 (vs none for placebo); no serious AEs
BNT162b1 (Biontech/Pfizer)	1-50µg prime & boost, 100µg single	NCT04380701	Seen in 48/48 volunteers	RBD-specific CD8+ responses in 29/36; mean 1.04% of cells	"Occasional" grade 3 reactogenicity; no serious AEs
AZD1222 (Astrazeneca)	5n10 viral particles, single or prime & boost	NCT04324606	Seen in 32/35 volunteers, rising to 35/35 after boost	Unspecified T-cell responses in 43/43; mean ~0.1% of cells	No serious or grade 3 AEs (vs 1 serious in control)
mRNA-1273 (Moderna)	25-250µg prime & boost	NCT04283461	Seen in 45/45 volunteers	Very modest; S-specific CD8+ responses seen in 2 outliers, at 0.1-0.2% of cells	No serious or grade 3 AEs
Ad5-nCoV (Cansino)	1n11 or 5n10 viral particles, single	NCT04341389	Seen in 210/382 volunteers	Unspecified T-cell responses in 342/382; mean ~0.01% of cells	Grade 3 AEs in 10/382 (vs none for placebo); no serious AEs
Source: scientific paper preprints, NEJM & Lancet. RBD=receptor-binding domain.					

CD8+ T-cell responses to Moderna's mRNA-1273 also look very modest so far. One caveat with the Cansino data is that Ad5-nCoV is being dosed singly; most rivals opt for a prime-and-boost strategy, and indeed the Cansino study's authors suggest an additional dose to improve efficacy.

The possible effect of an adjuvant is also not yet known. The Novavax data should be the first to show whether this might be another way to increase the potency of certain Covid-19 vaccines.