Evaluate Vantage

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The next triggers in Covid-19 vaccine development

Jacob Plieth

Pfizer/Biontech's preprint might prove academic as investors look to pivotal study designs and readouts.

The latest scientific paper preprint – now the typical way for Covid-19 vaccine data to be released – has shed more light on Biontech/Pfizer's decision to take BNT162b2 into phase III, but things have already moved on.

Investors will focus on the next triggers in this fast-moving field, including pivotal data from Astrazeneca's AZD1222, and the first phase I results from a crop of relative laggards, including Curevac, Glaxosmithkline and Johnson & Johnson. The last is notable for this week raising the target enrolment into its proposed phase III study from 30,000 to a massive 60,000 volunteers.

Ensemble, the pivotal trial of J&J's Ad26.COV2-S, was previously thought to be starting on September 26. But its clinicaltrials.gov entry has revealed double the enrolment target, across hospitals in the US, South America, South Africa, the Philippines and Ukraine, and a start date of September 5.

The phase III study of Astra's AZD1222 is under way as of four days ago, in 30,000 high-risk individuals. While this has a formal primary completion date of December 2020 analysts believe that initial results, the first data from a pivotal Covid-19 vaccine study, could come sooner, perhaps in October.

Meanwhile, the fourth quarter should see pivotal data from Moderna's mRNA-1273 and Biontech/Pfizer's BNT162b2, as well as perhaps from Novavax's NVX-CoV2373, though like Ad26.COV2-S the last will not begin phase III until next month. NVX-CoV2373 recently generated its first clinical results, confirming its place in the Covid-19 vaccine race.

Obviously the metric investors should be looking for in phase III is how effective a vaccine actually is at offering protection from infection. This has been impossible to gauge from phase I data, which only looked at neutralising antibody generation or T-cell stimulation – measures that may or may not translate into a real protective effect.

Selected vaccines in development for Covid-19				
			US Warp Speed financing	
Company/org	**Vaccine**	**Status**	**R&D**	**Dose orders**
Gamaleya Research Inst	Gam-COVID-Vac	Ph1 completed; approved in Russia	-	-
Moderna/NIAID	mRNA-1273	Ph3 under way (n=30,000)	Up to $955m	$1.50bn (100m doses)
Biontech/Pfizer	BNT162b2	Ph3 under way (n=29,481)	-	$1.95bn (100m doses)
Biontech/Pfizer	BNT162b1	Ph1 data reported		
Astrazeneca/ Uni of Oxford	AZD1222	Ph3 under way (n=30,000)	$1.20bn (300m doses; split not specified)	
Cansino Biologics	Ad5-nCoV	Ph2 under way	-	-
Curevac	CVnCoV	Ph2 started Aug 2020	-	-
Johnson & Johnson	Ad26.COV2-S	Ph3 starts 5 Sep 2020 (n=60,000)	$456m	$1.00bn (100m doses)
Novavax	NVX-CoV2373	Ph3 starts 15 Oct 2020 (n=30,000)	Up to $1.60bn (100m doses; split not specified)	
Inovio	INO-4800	Immune responses claimed in ph1	-	-
Dynavax/Clover/GSK	SCB-2019	Ph1 data possible Aug 2020	-	-
Imperial College	LNP-nCoVsaRNA	Ph1 started Jun 2020	-	-
Vaxine	Covax19	Ph1 started Jun 2020	-	-
GSK/Medicago (M Tanabe)	?	Ph1 started Jul 2020	-	-
Anges	AG0301-COVID19	Ph1 started Jun 2020	-	-
Zydus Cadila	ZyCoV-D	Ph1 started Jul 2020	-	-
Genexine	GX-19	Ph1 started Jul 2020		
Arcturus	ARCT-021	Ph1 started Aug 2020	-	-
Merck & Co (ex Themis)	V591/TMV-083	Ph1 started Aug 2020	-	-
IMV	DPX-COVID-19	Ph1 starts "summer" 2020	-	-
GSK/Sanofi	?	Ph1 starts Sep 2020; ph3 starts 25 Nov 2020 (n=30,000)	$1.10bn*	$1.00bn (100m doses)
Translate Bio/Sanofi	?	Ph1 starts Q4 2020	-	-
Merck & Co/Iavi	V590	Ph1 starts 2020	$38m	-
*Source: WHO list, EvaluatePharma & company statements. *award is for up to $2.1bn, "more than half" of which is for development.*				

A case in point is Biontech/Pfizer's BNT162, which comprises four separate vaccines. BNT162b1 was first to generate clinical data, but it was BNT162b2 that went into phase III, the companies explaining that b2, which codes for the full S-protein, had shown better tolerability than b1, which codes for a receptor-binding domain, while generating similar neutralising antibody titres.

Yesterday this was backed up by a scientific preprint of the results of a small head-to-head trial of these two projects. This described a little less injection site pain, and fewer side effects like chills and fatigue, with b2 versus b1; immunogenicity, meanwhile, was broadly similar.

Beyond the pivotal front runners, more early trials of Covid-19 vaccine are swiftly getting under way. One of the most closely watched is Curevac's CVnCoV, which has swiftly moved into phase II, and in the fourth quarter should yield data from a phase I trial in 168 volunteers.

This is an important asset given Curevac's recent Nasdaq flotation, which swiftly brought about a fourfold share price increase and an $11bn valuation. Curevac yesterday said it had held exploratory talks to provide the EU with up to 405 million doses of its mRNA vaccine, though it did not reveal a possible price.

Many investors are also watching Gam-COVID-Vac, an adenovirus vaccine developed by Gamaleya Research Institute that has completed two phase I studies. No wonder that this has become an intriguing asset: no human data on it have yet been released, but remarkably it received regulatory approval in Russia 10 days ago.