Evaluate Vantage

December 17, 2020

Key upcoming clinical catalysts for biotech

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Early 2021 will see rare diseases dominate for biotech, with Sarepta revealing key data on its gene therapy play.

An earlier analysis by *Evaluate Vantage* concentrated on upcoming big pharma data reveals; here, we take a look at the clinical results due for biotech companies with a market cap of $2bn and above.

Rare diseases dominate, with the likes of Alnylam and Alexion – soon to become part of Astrazeneca – gearing up for data. Probably the most eagerly awaited readout, though, concerns **Sarepta's** first placebo-controlled trial of **SRP-9001**, a micro-dystrophin gene therapy for Duchenne muscular dystrophy.

Roche paid $750m upfront to secure ex-US rights to SRP-9001 at the end of last year. With an NPV of $7.6bn, according to *Evaluate Omnium*, '9001 is one of biotech's most valuable pipeline projects, but before its lofty sales expectations can be realised it first needs to perform in the clinic.

The phase II trial, called Study 102, has enrolled 41 boys aged 4-7 with DMD. The primary outcomes are the change in quantity of micro-dystrophin protein expression at week 12 and the change in North Star Ambulatory Assessment (NSAA) total score at week 48.

So far '9001 has shown promise – in four patients. In a phase I trial, microdystrophin expression levels were 74-96% of normal at week 12, and there was a mean seven-point improvement on NSAA at two years. In terms of rivals, Sarepta's project looks more effective that Pfizer's gene therapy PF-06939926, albeit comparing two different trials involving small numbers of patients.

Three patients taking '9001 experienced elevated γ-glutamyl transpeptidase, a liver enzyme, in the first three months post-treatment, which resolved with steroids. Despite this, the safety profile of Sarepta's project looks cleaner than those of rival gene therapies.

Three serious events occurred in Pfizer's phase Ib trial of PF-06939926, with two said to be due to complement activation; still, these resolved quickly and a phase III study recently started recruiting. A phase I/II study of Solid Biosciences' SGT-001, meanwhile, was halted due to a series of adverse events, but dosing is expected to resume in the first quarter of next year.

More convenient

Alnylam's vutrisiran, a subcutaneous follow-on to the group's intravenous amyloidosis therapy Onpattro, is due to report phase III data soon. 164 patients in the Helios-A study, who have hereditary transthyretin amyloidosis with polyneuropathy, are being given vutrisiran once every 12 weeks or Onpattro once every three

weeks.

The primary endpoint of the study is change from baseline in the modified neurologic impairment score at nine months. Results from the vutrisiran arm will be compared against the placebo arm of the phase III Apollo-A study, which led to Onpattro's approval in polyneuropathy patients.

In order to compete with Pfizer's once daily Vyndaqel tablet, Alnylam needs to show its projects can improve cardiac measures − Vyndaqel is on the market for the cardiomyopathy subtype, a bigger indication. Pfizer's project is also approved outside the US for polyneuropathy.

In cardiomyopathy patients, Alnylam's Helios-B study of vutrisiran is still recruiting, and the Apollo-B study of Onpattro is expected to read out in 2022.

Copper target

Alexion's late-stage Wilson disease project, **ALXN1840**, probably did not feature highly on Astra's wish list when it agreed to pay $39bn for the biotech group, but a win here would be a bonus.

Alexion gained the project through its $855m takeout of the Swedish company Wilson Therapeutics in 2018.

Wilson disease is an autosomal recessive metabolic disease characterised by copper build-up in the liver or brain, and ALXN1840 is said to work as a copper-protein binding agent. The phase III study in 215 Wilson disease patients is designed to show ALXN1840's superiority versus copper-chelating agents followed by zinc maintenance. Alexion notes that the current standard of care can be burdensome as it involves multiple tablets and fasting, and does not address the neurological symptoms of the disorder.

The primary endpoint looks at the change from baseline to week 48 in non-ceruloplasmin-bound copper levels. Secondary measures include effects on neurological status and clinical symptoms.

Alexion's project, however, does not address the underlying genetic mutation causing the disease. A phase I/II study of VTX-801, a gene therapy for Wilson disease, is expected to start early next year. The project is a collaboration between Vivet Therapeutics and Pfizer, which acquired an equity interest in the private gene therapy company in 2019.

Check out the table below for a full list of upcoming catalysts with consensus forecasts from *EvaluatePharma*. *Evaluate Vantage* has separately assessed expected catalysts for big pharma.

Q1 clinical catalysts (excludes Covid-19 data)					
Project	**Company**	**Therapy area**	**Q1 clinical catalyst**	**2026e indication sales ($m)**	**Not cov**
SRP-9001	Sarepta/Roche	Duchenne muscular dystrophy	Ph2 Study 102	2,901	See
CTX001	Vertex/Crispr	Beta-thalassaemia, sickle cell disease	Updates during 2021 from Climb-Thal-111 and Climb-SCD-121	1,306	Pror data – Cr ano
Vutrisiran	Alnylam	ATTR amyloidosis	Ph3 Helios-A early 2021	1,290	See
Repotrectinib (TPX-0005)	Turning Point Therapeutics	Solid tumours (harbouring ALK, ROS1, or NTRK1-3 rearrangements)	Trident-1 at IASCLC World conference on lung cancer on January 31	1,087	Initi sho com resp vs R Rozl Pfize but evid grea dura (Tur on t

	Q1 clinical catalysts (excludes Covid-19 data)				trac whe
Zuranolone (Sage-217)	Sage Therapeutics/ Biogen	Major depression, postpartum depression	Four ph3 studies due to report in 2021	970	Biog $1.5 righ zura Sag (Bio adv to $
Roctavian (valoctocogene roxaparvovec)	Biomarin	Haemophilia A	Ph3 52-week data from 301	937	EMA 1yr app aske data givi Aug
AT-GAA	Amicus	Pompe disease	Ph3 Propel Q1	637	San Neo dem non- to S (My faile sup ph3 Prop pow dem sup SoC
Mitapivat	Agios	PK deficiency	Pivotal data (Activate-T)	591	Acti in p rece regu tran met end Acti mor affe pati regu rece tran (Agi pre-
APL-2 (systemic pegcetacoplan)	Apellis	PNH	Ph3 Prince H1	554	Trea naïv Pdu pati had Soli
IMVT-1401	Immunovant	Warm autoimmune haemolytic anaemia, thyroid eye disease	Data from ph2a Ascend Waiha due Q1, ph2b Ascend Go-2 due H1	357	Sub anti (Ph3 mya grav star
ALXN1840	Alexion (now Astrazeneca)	Wilson disease	Ph3 due H1	322	See
					Prel

Q1 clinical catalysts (excludes Covid-19 data)

Bempegaldesleukin + Keytruda	Nektar	[illegible]	[illegible]	[illegible]	data Prop (~3
Relugolix	Myovant	Endometriosis	One-year efficacy and safety data from Spirit Extension	167	Kee for thro ever coul labe
Rozanolixizumab	UCB	Chronic inflammatory demyelinating polyneuropathy	Ph2 H1	123	Sub anti ph3 mya grav unti
Troriluzole	Biohaven	Mild-to-moderate Alzheimer's disease	Ph2/3 T2 Protect AD	114	(*Alz cata off a dom Biog*
Relacorilant + nab-paclitaxel	Corcept	Ovarian cancer, pancreatic cancer	Ph2 ovarian, Ph3 Reliant pancreatic H1	100	Sec gen Korl Korl Teva
VX-864	Vertex	Alpha-1 antitrypsin deficiency	Ph2 H1	-	Z-AA said stru dist VX-8 saw liver in p bee disc (*Clin setb bare wea*
ARGX-110 (cusatuzumab) + Vidaza	Argenx/Johnson & Johnson	Newly diagnosed AML unfit for intensive chemo	Ph2 top-line Culminate early 2021	-	Anti deal Cila imp resp in e (*Arg deli*
Camidanlumab tesirine (Cami, ADCT-301)	ADC Therapeutics	Relapsed or refractory Hodgkin lymphoma	Pivotal ph2 interim H1	-	Tria June its c was pati bee with Barr

Sources: EvaluatePharma, company releases, analyst notes, clinicaltrials.gov

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