Evaluate Vantage

April 23, 2020

The crucial data readouts coming soon for small biotechs

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Coronavirus aside, biotech companies including Akebia, Blueprint, Genfit and TG Therapeutics are set for some important data readouts in the next couple of months.

While the Covid-19 pandemic continues to dominate the headlines and cause delays to some clinical programmes, a number of important data readouts are expected soon from small biotech companies.

Phase III data in chronic kidney disease patients are due with **Akebia's vadadustat**. First up are results in dialysis patients, with non-dialysis data mid-year. Japanese phase III trials found vadadustat to be non-inferior to darbepoetin alfa, with one case of fatal myocardial ischaemia considered possibly related to the project.

Cardiac safety remains a big question mark for the HIF-PH inhibitors. Fibrogen's similarly acting asset, roxadustat, also has lingering safety questions and has a PDUFA date set for December. Akebia's US partner Vifor is expected to use its priority review voucher for vadadustat, so could steal a march on the competition.

Blueprint's Ayvakit is already approved for treating gastrointestinal stromal tumours driven by specific mutations – a niche population. The Voyager study tests it head to head against Stivarga in patients previously treated with Gleevec and one or two other tyrosine kinase inhibitors. Topline data will supplement the fourth-line GIST submission, which has a PDUFA date next month, as well as supporting expansion into third-line use. Blueprint is ahead of competitor Deciphera, which has an August PDUFA for the similarly acting ripretinib in fourth-line disease.

TG Therapeutics' Unity-CLL study has suffered a number of delays, and now an interim PFS readout is expected. The trial pits **ublituximab and umbralisib** – TG's anti-CD20 antibody and PI3K delta inhibitor respectively – against Roche's Gazyva plus chlorambucil. Notably the study does not include Roche/Abbvie's highly efficacious newcomer, Venclexta, so might lack real-world relevance, and its earlier failure to show an ORR benefit has already made hitting PFS a long shot.

Readout of **Genfit's** Resolve-It trial of **elafibranor** has also been pushed back several times. Odds of success for the Nash trial are low given elafibranor's phase II flop and the discontinuation of Cymabay's similarly acting seladelpar. In February Genfit said it would sit on the blinded dataset until the second quarter "to incorporate the latest FDA insights". This might be to allow Reduce-It's endpoints to be tweaked at the last moment – permissible before unblinding – should evidence emerge that this would increase the trial's chances of showing an effect on Nash.

Earlier this month **Akero** reported impressive results in the first cut of a mid-stage Nash trial of its pipeline lead, **AKR-001**, and shares climbed 23%. Relative reductions in liver fat were 63-72% versus baseline for the three AKR-001 doses tested, with a numerical dose response; all three hit statistical significance versus placebo recipients, who showed a 0% reduction. Biopsy data, a more robust measure, are expected this quarter.

Mavacamten, Myokadia's lead project, is a small molecule that reversibly binds to myosin, intended for the treatment of hypertrophic cardiomyopathy, an inherited condition that causes a thickening of the cardiac muscles. Mavacamten showed promising results in the open-label phase II Pioneer-HCM trial in 21 patients with the obstructive form of the condition, where blood flow out of the heart is restricted.

There were marked reductions in post-exercise LVOT gradient – the difference between ventricular and aortic pressure – at 12 weeks versus baseline, the primary endpoint. The 220 patient Explorer-HCM study is placebo-controlled and has a combined primary endpoint of clinical response, improvement on a heart failure scale and an increase in exercise capacity.

Towards the end of last year **Kadmon** reported a positive interim analysis of the pivotal phase II Rockstar trial of **KD025** in chronic graft-vs-host disease. At two months the project easily cleared a 30% objective response rate threshold, and unless results substantially deteriorate when six-month data are released this quarter, or an unexpected safety issue rears its head, a green light for patients who have received at least two prior lines of therapy looks likely.

For consensus forecasts on the above and a few extra second-quarter events, please see the table below.

Selected Q2 clinical catalysts for biotech ($250m-$5bn market cap) (excludes Covid-19 data)					
Project	**Company**	**Therapy area**	**2024e indication sales ($m)**	**Q2 clinical catalyst**	***Evaluate Vantage* note/story link**
Mavacamten	Myokardia	Obstructive hypertrophic cardiomyopathy	920	Pivotal phase III Explorer-HCM	See text
Vadadustat	Akebia/ Vifor/Otsuka	Anemia due to CKD	766	Phase III data Inno2vate data Q2 (dialysis patients), Pro2tect data mid year (non-dialysis)	*Pivotal data on Akebia's anaemia project please, but safety concerns linger*
ABI-H0731	Assembly Biosciences	Hep B	532	Additional interim analyses from phase II study 211	*AASLD 2019 – Assembly asks investors to keep the faith*
Elafibranor	Genfit	Nash	531	Phase III Resolve-It	*Genfit's latest delay could see a last-minute endpoint change* *Genfit's liver disease Hail Mary approaches*
KD025	Kadmon	Chronic graft-vs-host disease	464	Top-line from the primary analysis of pivotal Rockstar study	*Kadmon sets a high bar in an increasingly competitive space*
Ayvakit/avapritinib	Blueprint Medicines	Fourth-line GIST	410	Plans to lock the Voyager trial database in April, PDUFA set for May 14	*Blueprint beats Deciphera to the punch*
Umbralisib and ublituximab	TG Therapeutics	CLL	323 (combined revenues)	Interim PFS analysis expected in May, phase III Unity-CLL	*TG shrugs off another delay, but history is against it* *Upcoming events – TG's long-awaited outcome*
AXS-05	Axsome	Alzheimer's disease agitation	91	Phase II/III Advance-1	Treatment-resistant depression trial with AXS-05 recently missed its primary endpoint, *Axsome trips up*
Troriluzole	Biohaven	Obsessive compulsive disorder	66	Phase II/III NCT03299166	The glutamate modulator is also being tested in mild-to-moderate Alzheimer's
AKR-001	Akero	Nash	-	Biopsy data from Balanced study	*Akero's success gives a new Nash mechanism hope*
Source: EvaluatePharma sales by indication data; company releases; analyst notes; clinicaltrials.gov.					

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