Evaluate Vantage

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Biotech’s important first-quarter data

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Kodiak, Biomarin and Argenx prepare for clinical catalysts.

After delving into big pharma readouts, *Evaluate Vantage* has pulled out the key first-quarter catalysts for biotech companies with a market cap of $1bn and up. Kodiak is eyeing up the wet AMD market with KSI-301, but the project's longer-acting potential needs proving.

Biomarin, meanwhile, will report two-year data with its haemophilia gene therapy valrox, which has been tainted by waning efficacy. And with an FDA approval in the bag for intravenous Vyvgart, Argenx is expecting data from a more convenient subcutaneous formulation, which the company believes will be a much bigger seller.

Longer acting?

Kodiak is hoping to gatecrash a wet AMD market dominated by Regeneron and Bayer’s Eylea with its long-acting anti-VEGF biopolymer conjugate **KSI-301**.

Kodiak’s 550-patient phase 2b/3 Dazzle study tests 5mg intravitreal injections of KSI-301 every 12, 16 or 20 weeks after three monthly loading doses, versus 2mg Eylea given every eight weeks after three monthly initiating doses. The primary endpoint is mean change in best corrected visual acuity (BCVA) at one year.

Data from a 50-patient phase 1b study of KSI-301 showed 78% of subjects achieved a treatment-free interval of four months or more at year one. Pooled data from both 2.5mg and 5mg doses showed a increase in BCVA at week 52 of 5.7 letters. Most adverse events were mild.

Regeneron and Bayer are not resting on their laurels – they are developing a high-dose version of Eylea that could help keep competitors like Kodiak at bay.

Data from Eylea’s Pulsar study is expected later in 2022. This is testing 8mg at 12 or 16-week intervals, an advantage over the current eight-week regimen. But with Lucentis and Eylea biosimilars on the horizon, and numerous gene therapies in play, the stakes remain high.

Efficacy conundrum

Biomarin’s haemophilia A gene therapy **valoctocogene roxaparvovec (valrox)** has suffered numerous setbacks, including a rejection by the FDA in 2020 amid questions about durability, which remain unanswered.

In early 2022 investors will see two-year data from all participants in the pivotal Gener8-1 study,

with Biomarin aiming to refile valrox in the US in the second quarter.

Gener8-1, a single-arm study in 134 patients, found mean and median FVIII levels of 43% and 24% respectively at one year; however, these had fallen to 24% and 15% in the small number of patients followed for two years *(Pivotal valrox data give Biomarin déjà vu, January 11, 2021).*

Pfizer and Sangamo's rival gene therapy hasn't had an easy ride either. The companies recently reported a marked decline in FVIII levels with giroctocogene fitelparvovec over the long term in phase 1/2, and the therapy's phase 3 is on clinical hold due to concerns over very high FVIII levels.

Argenx's convenience

Argenx's efgartigimod, now called **Vyvgart**, became the first FDA-approved anti-FcRn project last week, with the intravenous version getting the go-ahead in generalised myasthenia gravis. Next up are data from the AdaptSc study, testing a subcutaneous formulation.

The non-inferiority study will compare the percent change in total IgG levels between intravenous and subcutaneous efgartimod at day 29. An indicator of what subcutaneous efgartigimod might need to match comes from Vyvgart's Adapt study, which yielded a 61.3% mean maximum reduction in IgG, one week after the fourth infusion.

Argenx has noted that it will require additional data from AdaptSC+, a long-term safety study, before filing the subcutaneous version. The company has not disclosed when data might be released.

UCB's similarly acting project rozanolixizumab, which is infused subcutaneously over an hour, is not far behind. The company is aiming for regulatory submissions from the third quarter of next year. Top-line data in myasthenia gravis was said to have met primary and secondary endpoints, although detailed numbers were not provided.

The following table contains a fuller list of catalysts.

Clinical catalysts in early 2022 (excludes Covid-19 data)				
Product	**Company**	**Therapy area**	**Clinical catalyst**	**Note/Vantage coverage**
Zuranolone (Sage-217)	Sage Therapeutics/ Biogen/ Shionogi	Major depressive disorder	Coral (50mg vs placebo, on top of sertraline) early 2022	Primary endpoint (HAMD-17 change from baseline) will be measured at day 3, instead of day 15 previously. NDA submission in MDD H2
KSI-301	Kodiak	Wet AMD	Ph2/3 Dazzle early 2022	See text
PD-L1 t-haNK + Anktiva	Immunitybio	3L pancreatic cancer	Ph2 Quilt 88 Cohort C data Asco GI January	Nant Cancer Vaccine, which includes Immunitybio's natural killer cells (PD-L1 t-haNK), IL-15 receptor agonist Anktiva, and aldoxorubicin, plus low-dose chemotherapy
Omecamtiv mecarbil	Cytokinetics	Acute heart failure	Ph3 Meteoric-HF early 22	Galactic-HF disappointed (*AHA 2020 – look out for the omecamtiv fault lines*)
Transcon PTH	Ascendis	Adults with hypoparathyroidism	Ph3 Pathway Q1	Filing expected Q3'22, using data from both the positive long-term 84-week OLE study, as well as 6-month data from Pathway
Valoctocogene roxaparvovec (valrox)	Biomarin	Haemophilia A	Pivotal Gener8-1 (2-year data) Q1	See text
ST-920 (isaralgagene civaparvovec)	Sangamo	Fabry disease	Ph1/2 Staar Q1	Gene therapy, prelim data showed promise in the first 4 pts with first 2 doses, 3rd cohort recruiting, updated results throughout 2022 (*Sangamo takes on 4D in Fabry*)
Bempegaldesleukin +/- Opdivo	Nektar	1L advanced melanoma	Ph3 H1	Propel study failed (+ Keytruda 1L met NSCLC) (*Esmo IO 2021 – Propel fails to propel Nektar*)
Subcutaneous efgartigimod	Argenx	Generalised myasthenia gravis	Ph3 AdaptSC bridging study H1	See text
Sparsentan	Travere Therapeutics	Focal segmental glomerulosclerosis	Additional estimated glomerular filtration (eGFR) data from ph3 Duplex H1	FDA knocked back Travere's plan to use proteinuria data to file for accelerated approval. Travere now plans to file in mid-2022 with eGFR data
CTX001	Cripsr/ Vertex	Beta-thalassaemia and sickle cell disease	Climb-SCD-121, Climb-Thal-111 updates over the year	CRISPR/Cas9 gene-edited therapy, filing expected YE
Source: clinicaltrials.gov, Evaluate Pharma, company releases.				

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