Evaluate Vantage

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Key data catalysts for the industry’s small players

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Intercept looks for redemption in Nash in the third quarter, while Kymera, Zealand and Anavex hope for share price boosts.

Evaluate Vantage has already previewed important upcoming third-quarter data for big pharma and large biotech groups. Now it is the turn of companies with a market cap under $1bn.

In a turbulent biotech market where positive news is often not rewarded, smaller companies hoping to avoid an even worse outcome this quarter are Intercept and Akero, which both have readouts in the notoriously tricky area of Nash. Elsewhere, Kymera hopes for no further trouble for its novel atopic dermatitis project, while Zealand wants to challenge Takeda with short bowel syndrome data.

One more time with feeling

Intercept hopes to defy expectations with two pivotal readouts for **Ocaliva** in Nash-related disorders.

The group has been struggling to get sales off the ground in the drug's approved indication of primary biliary cholangitis owing to toxicity-related label restrictions. Now it has a shot at label expansion, with the Reverse trial for Nash patients with cirrhosis and a reanalysis of the controversial Regenerate trial for advanced fibrotic Nash.

Regenerate was the basis of a filing by Intercept that resulted in an FDA complete response letter in Nash. Radout of Reverse has been delayed twice, having originally been expected at the end of 2021. Intercept was recently forced to sell ex-US Ocaliva rights to, and it will be in even more trouble if it cannot get a hit in Nash.

It is not the only company awaiting Nash data. **Akero Therapeutics’ efruxifermin**, an FGF21 analogue, should see the readout of the phase 2 Harmony trial. While the failures in Nash have been multiple, Pfizer at least has shown some confidence in Akero’s approach with a recent $25m equity investment.

Skin deep

Pfizer’s decision to end development of its Irak-4 inhibitor PF-06650833 in hidradenitis suppurativa was a blow to sentiment around **Kymera’s** similarly acting **KT-474.** However, the biggest threat to the small group's project could be QTc prolongation, which forced Kymera to increase the dosing period from 14 to 28 days in its phase 1 study in hidradenitis suppurativa and atopic dermatitis. At this point the effect appears to be mild and

below the threshold for an increased risk of arrhythmia.

Alongside any toxicity signals and inflammatory skin and plasma biomarkers, investors will also be looking for a similar, if not better, EASI-75 than the 40-50% seen with Dupixent and Cibinqo.

If the results are positive, and the QTc prolongation turns out to be transient, Kymera's partner Sanofi will likely take the project into phase 2. However, most investors view this asset as dead, Wells Fargo analysts have noted.

Second-chance saloon

Zealand Pharma recently refocused its R&D efforts to jumpstart its stagnant shares. Validation of this strategy could come with the pivotal readout from the Ease-SBS1 trial of **glepaglutide** in short bowel syndrome; the hope is that efficacy and convenience benefits will be shown over the market leader, Takeda's Gattex.

Both are injectable GLP-2 agonists, but glepaglutide only needs to be dosed once or twice weekly, compared with daily dosing for the Takeda drug. Jefferies analysts believe that this and the convenience of a ready-to-use injection could ensure strong take-up of the Zealand project. The expected entrance of a US generic version of Gattex in 2023 adds to the risks, however.

The table below contains a list of upcoming catalysts with consensus forecasts from *Evaluate Pharma.*

Clinical catalysts in Q3 2022, market cap under $1bn				
Product	**Company**	**Therapy area**	**Q3 clinical catalyst**	**Note/Vantage coverage**
Ocaliva	Intercept	Nash patients with compensated cirrhosis (F4), advanced fibrotic (F2/3) Nash	Ph3 Reverse, ph3 Regenerate re-analysis	See text
Ensifentrine	Verona	Maintenance treatment of COPD	Ph3 Enhance-2	PDE3/4 inhibitor, Enhance-1 data expected YE
REL-1017	Relmada	Major depressive disorder	Ph3 Reliance I adjunctive	Still awaiting registrational Reliance III monoRx data, due mid-year
Efruxifermin	Akero	Nash F2/F3	Ph2b Harmony	See text
Glepaglutide	Zealand	Short bowel syndrome	Ph3 Ease-SBS1	See text
Monalizumab + Erbitux	Innate/ Astrazeneca	Recurrent or metastatic head and neck cancer, post PD-(L)1 inhibitor	Ph3 Interlink-1 interim futility analysis	Innate will receive a €50m milestone on pre-defined (but undisclosed) clinical activity threshold
Vebicorvir +/- AB-729	Assembly (Arbutus)	Hep B	Ph2 H2 from two triple combination studies: -Vebicorvir + AB-729 + SOC Nrtl -Vebicorvir + Nrtl + interferon	Vebicorvir is an HBV core inhibitor, AB-729 is RNAi
ADX-2191	Aldeyra	Proliferative vitreoretinopathy, retinitis pigmentosa	Part 1 of ph3 Guard, ph2 in retinitis pigmentosa H2	Intraocular methotrexate injection, methotrexate is SOC but has no GMP-certified ocular injection formulation (Berenberg)
KT-474	Kymera/ Sanofi	Atopic dermatitis, hidradenitis suppurativa	Ph1 H2	See text
Anavex 2-73 (blarcamesine)	Anavex	Early Alzheimer's disease	Ph 2b/3 Anavex2-73-AD-004 topline H2	Blarcamesine hit in Rett syndrome this year after study endpoints were changed
Source: clinicaltrials.gov, company releases & Evaluate Pharma.				

Check out our podcast discussing third quarter catalysts here.

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