Evaluate Vantage

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Big readouts ahead for small biotechs

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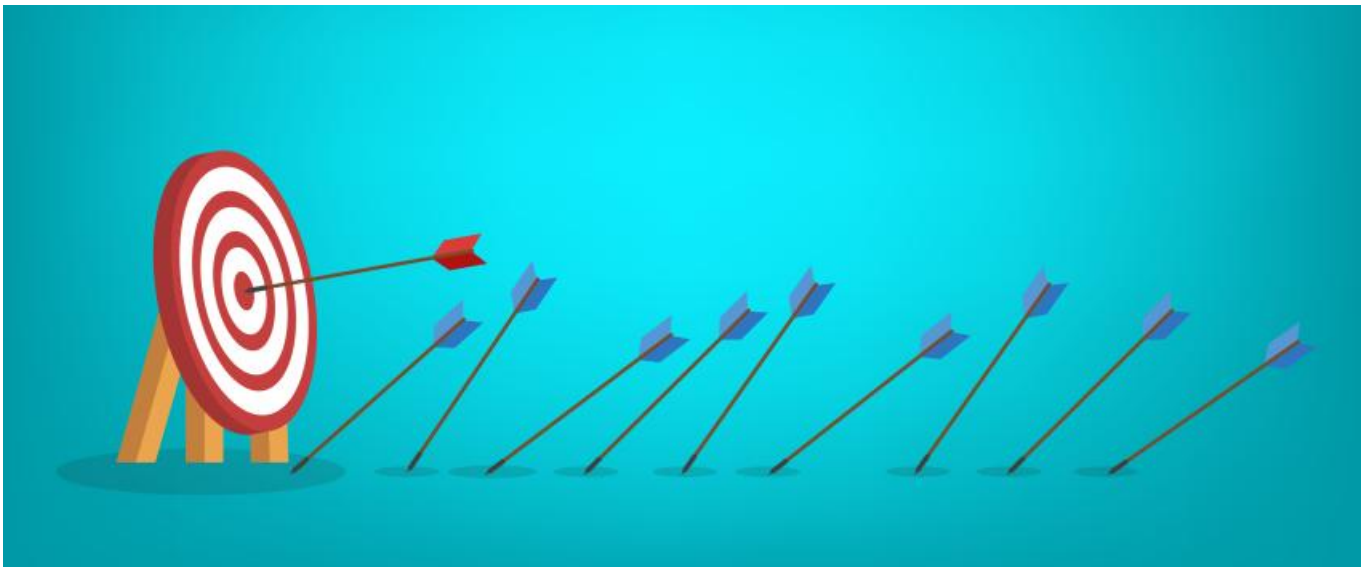

Nash data are due for Terns and Inventiva, as Marinus aims to expand its rare disease offering.

Having already looked at the key upcoming clinical catalysts for big pharma and large biotech groups, here *Evaluate Vantage* dives into approaching events for developers with a market cap under $1bn.

Amid a rebound in hopes for Nash breakthroughs, Terns is due to report data with Tern-501 as a monotherapy, and in combination with Tern-101. In the same space, Inventiva is combining its Nash therapy lanifibranor with a SGLT2 inhibitor in an attempt to mitigate weight gain issues. Elsewhere, Marinus needs a win with its Gaba modulator, intravenous ganaxolone, to open a bigger market.

Next up in Nash

Several mechanisms are in play in the mid-stage Nash pipeline, and one contender, **Terns,** is gearing up to report data from the phase 2a Duet study. The company is testing several doses of **Tern-501**, a thyroid hormone receptor beta agonist, on its own and in combination with **Tern-101**, a farnesoid X receptor agonist. Terns claims that this is the first trial assessing the combination of these mechanisms in the liver disease.

The primary endpoint concerns Tern-501 monotherapy and is the relative change from baseline in liver fat content as measured by MRI protein density fat fraction at week 12, versus placebo. The endpoint is also used as a secondary measure for the combination arms.

Other thyroid hormone receptor beta agonists have set the bar, and investors will compare Terns's data to precedents set by Madrigal and Viking. Madrigal has begun a rolling submission for resmetirom and Viking's VK2809 has shown reductions in liver fat of up to 48%, adjusted for placebo, with Nash resolution data expected next year.

Farnesoid X receptor agonists have a poor track record. The most prominent example is Intercept's Ocaliva, which the company finally gave up on in Nash earlier this month.

A second company expecting Nash data is **Inventiva**. Monotherapy data on the pan-PPAR agonist **lanifibranor** has previously been reported in patients with type 2 diabetes and nonalcoholic fatty liver disease and separately in Nash. Lanifibranor produced Nash resolution and fibrosis improvement, but a weight gain signal was evident.

To mitigate the impact on weight, as well as effects on metabolic metrics, Inventiva's upcoming study includes a combination arm of lanifibranor plus the SGLT2 inhibitor Jardiance. The phase 2a Legend trial has enrolled

patients with Nash and type 2 diabetes and the primary measure is absolute change in HbA1c from baseline to week 24.

Lanifibranor's phase 3 study, Nativ3, will not report for several years but does include patients currently on a stable regimen of SGLT2 inhibitors or GLP-1 agonists.

Expansion

Marinus will report interim data from its phase 3 study in refractory status epilepticus. Marinus's whole clinical pipeline revolves around ganaxolone, a Gaba modulator. The therapy is given in intravenous form in the upcoming study, while an oral suspension is approved as Ztalmy for a rare form of genetic epilepsy. A win for **intravenous ganaxolone** would open a bigger market for the company.

Status epilepticus is a condition where a seizure lasts longer than five minutes or a person has more than one seizure within a five-minute period. Status epilepticus can occur in people with epilepsy or in people who have experienced a stroke or head injury, or because of drug or alcohol abuse.

In the phase 3 Raise study ganaxolone was added to standard of care; patients had already failed on two or more antiseizure medications. Ganaloxone was administered by continuous infusion for 36 hours, followed by 12-hour taper.

An interim readout is set to occur after the enrolment of 82 patients and is >90% powered for 40% delta versus placebo. According to TD Cowen analysts Marinus anticipates a placebo rate of no higher than 20-25%. The co-primary measures are the percentage of patients reporting cessation of status epilepticus within 30 minutes, and no progression to intravenous anaesthesia for at least 36 hours following therapy initiation.

In a small open-label phase 2 study the median time to cessation was five minutes, and no patient required escalation to anaesthetics within 24 hours from infusion initiation. There were two cases of severe sedation, noted as treatment emergent serious adverse events.

The table below contains a list of upcoming catalysts, with consensus forecasts from *Evaluate Pharma*. Readouts specifically in the fourth quarter are excluded.

Small biotech's clinical catalysts in Q3/H2 2023					
Product	**Company**	**Therapy area**	**Q3 clinical catalyst**	**2028e indication sales ($m)**	**Note/ Vantage coverage**
Anavex 2-73	Anavex	Paediatric Rett syndrome	Ph2/3 Excellence H2	631	Muscarinic & sigma-1 receptor agonist also being tested in Alzheimer's and Parkinson's diseases
Dyne-101, Dyne-251	Dyne	Myotonic dystrophy type 1 (DM1), Duchenne muscular dystophy (DMD) (amenable to exon 51 skipping)	Ph1/2 Achieve (DM1, Dyne-101), Deliver (DMD, Dyne-251) H2	390	Initial data from multiple ascending dose portion of studies
Lanifibranor +/- Jardiance	Inventiva	Non-cirrhotic Nash and type 2 diabetes	Ph2a Legend Q3	314	See text
Intravenous ganaxolone	Marinus	Refractory status epilepticus	Ph3 Raise H2	302	See text
Sebetralstat (KVD900)	Kalvista	HAE	Ph3 Konfident, Konfident-S (OLE) H2	262	Oral plasma kallikrein inhibitor, had safety issues with a similar product KVD824
Tern-501 +/- Tern-101	Terns	Nash	Ph2a Duet topline Q3	-	See text
Narsoplimab	Omeros	IgAN	Ph3 Artemis-IgAN, 9 month proteinuria data mid year	-	Competitive space (*Novartis takes the helicopter view on Chinook*)

**On the market already in different treatment line/indication setting. Sources: Evaluate Pharma, analyst notes, clinicaltrials.gov.*