Evaluate Vantage

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Smaller companies set for third-quarter catalysts

Joanne Fagg

The third quarter will see important data for Travere, Radius and Sio Gene, among other small developers.

Evaluate Vantage's final article in a series of previews exploring key clinical readouts concerns companies with a market cap under $1bn. Previously, we outlined key catalysts for big pharma and larger biotechs that are expected to happen in the third quarter.

Travere hopes to take on a rare kidney disease with pivotal data due from the Sparsentan trial, while Radius is lining up results from its oral Serd elacestrant; comparisons could be made to imminent data from Sanofi's more advanced amcenestrant. Elsewhere, Sio Gene is hoping a 12-month readout from its gene therapy AXO-AAV-GM1 will show durability, in the setting of GM1 gangliosidosis.

Rare disease

August will see data from **Travere's Sparsentan** in IgA nephropathy, a rare kidney disease. The Protect study is in 380 patients, and results are due from an interim analysis of at least 280 patients after 36 weeks of treatment to evaluate the primary endpoint: change in urine protein/creatinine ratio from baseline.

The analysis is designed to support a potential submission for accelerated approval; a secondary measure, rate of change in estimated glomerular filtration rate over 58 weeks, will serve as the confirmatory endpoint.

Protect is 90% powered to detect a 30% difference in proteinuria between sparsentan and irbesartan, an angiotensis II receptor antagonist. Sparsentan is said to work by inhibiting both endothelin receptor type A and angiotensis II receptor type 1.

There are no approved therapies for IgA nephropathy but Calliditas's Nefecon could become the first in the US with a Pdufa date of September 15 for the FDA's decision. Nefecon, an oral formulation of the steroid budesonide, showed a placebo-adjusted 27% reduction in proteinuria in phase 3 and a significant improvement in eGFR versus placebo.

Other competitors include Novartis who reported phase 2 data recently with iptacopan, an oral complement inhibitor. The high dose led to a 23% reduction in proteinuria, versus placebo, and a phase 3 study is underway.

Giving up its Serd

With the readout of Sanofi's third-line registrational study with amcenestrant imminent, interest in oral

selective oestrogen receptor degraders, or Serds, has been rising. Roche and Astrazeneca also have candidates but small biotech **Radius Health** is expected to report next.

Radius's Emerald study seems to allow both second and third-line patients with ER+, Her2- breast cancer, with **elacestrant** monotherapy being tested against standard of care, which includes Faslodex or an aromatase inhibitor.

The co-primary endpoints are PFS in patients with oestrogen receptor 1 (ESR1) mutations and all comers. ESR1 mutation is a key resistance mechanism to endocrine therapy.

Several failures in this space means that this remains a high risk read out; Radius itself has backed away from the project, selling worldwide rights to elacestrant to Menarini for just $30m upfront last year. The deal came after Radius decided to focus on endocrine diseases, rather than oncology.

Durability

Sio Gene's AXO-AAV-GM1 has already shown early promise at 6 months in GM1 gangliosidosis, a rare inherited lysosomal storage disorder. Next up are 12 month results from the phase 1/2 study, which will be an important test of durability, a key issue for gene therapies.

At 6 months beta-galactosidase activity was restored to, on average, 38% of normal, in five patients with juvenile or late-infantile disease. GM1 gangliosidosis patients are deficient in beta- galactosidase, leading to a build-up of toxic gangliosides in neurons and other cells.

There were also promising signs on clinical assessments including those measuring mobility, and there were no serious adverse events related to the gene therapy. Both the six month data and the upcoming 12 month results are from the low-dose cohort.

Sio is some way ahead of competitors in this disease; Passage Bio's PBGM01 will report one month data in the fourth quarter, while the first patient was recently dosed with Lysogene's LYS-GM101. Early next year Sio expects to report 12 month data from the first two patients treated with a higher dose.

The table below contains a fuller list of upcoming catalysts with consensus forecasts from *Evaluate Pharma. Vantage* has previously looked at clinical data expected for big pharma and biotech companies.

Q3 clinical catalysts (excludes Covid-19 data)					
Product	**Company**	**Therapy area**	**Q3 clinical catalyst**	**2026e indication sales ($m)**	**Note/Vantage coverage**
Lytenava/ ONS-5010	Outlook Therapeutics	Wet AMD	Pivotal Ph3 Norse Two	429	Ophthalmic formulation of Avastin, versus Lucentis
Rubraca	Clovis	1L ovarian cancer maintenance	Ph3 Athena, data from monotherapy arm H2	419*	Label extension, both Lynparza and Zejula are already well-entrenched in 1L ovarian cancer maintenance
Sparsentan	Travere Therapeutics	IgA nephropathy	Ph3 Protect due August	336	See text
Reproxalap ophthalmic solution	Aldeyra	Dry eye	Ph3 Tranquility, Tranquility-2 (confirmatory) H2	312	Pivotal hit in allergic conjunctivitis in April (*Aldeyra eyes the future*)
Korsuva oral	Cara	Chronic liver disease-associated pruritis	Ph2 due H2	304	Failed in atopic dermatitis, injectable version filed to treat itch in dialysis patients with August Pdufa (*Cara fails to convince, but pushes on anyway*)
					In Argon-1 1mg was

	Q3 clinical catalysts (excludes Covid-19 data)				
EDP-305	Enanta/Undisclosed partner	Nash	Interim Argon-2 (1.5 & 2mg)	253	not efficacious; 2.5mg was efficacious but caused unacceptable pruritus *(Enanta fails to convince with Nash win)*
Lenabasum	Corbus	SLE	Ph2 H2	220	Failed in systemic sclerosis, cystic fibrosis and dermatomyositis
STRO-002	Sutro	Ovarian cancer	Ph1 dose expansion data	187	Anti-FRα (folate receptor) MAb-drug conjugate, promising early data but issues with neutropenia *(Sutro bucks the folate trend)*
ADP-A2M4CD8	Adaptimmune	Solid tumours	Ph1 Surpass update at Esmo (Sept 17-21)	130	Next gen candidate, MAGE-A4 specific, CD8
XEN1101	Xenon	Adult focal seizures	Ph2b X-Tole	122	Potassium channel modulator, adjunctive treatment
Elacestrant	Radius/Menarini	Breast cancer ER+/Her2-	Ph3 Emerald H2	69	See text.
SLN360	Silence	Cardiovascular disease due to elevated lipoprotein a	Ph1 Apollo single ascending dose portion data H2	65	siRNA against apolipoprotein A, Astrazeneca signed a $80m cash-and-equity deal with Silence Therapeutics last March *(Astrazeneca throws Silence an $80m lifeline)*
Auto4	Autolous	TRBC1+ T cell lymphoma	Ph1 interim	50	Designed to treat peripheral T-cell lymphomas, where treatment options are severely limited
Ganaxolone (oral)	Marinus	Tuberous sclerosis complex	Ph2	39	Jazz's Epidiolex got approved in this setting last year *(Marinus finds a path forward in rare epilepsies)*
AXO-AAV-GM1	Sio Gene Therapies	GM1 gangliosidosis	Ph1/2 12-month data from low dose cohort H2 (5 patients)	24	See text.
Xpovio	Karyopharm	1L maintenance endometrial cancer	Siendo Ph3 topline H2	-	Label expansion
AR-15512					Stifel: Aerie expects AR-15512 to serve the need for immediate relief

Q3 clinical catalysts (excludes Covid-19 data)					
AR-15512 (AVX-012)	Aerie	Dry eye disease	Ph2b top-line [illegible]		(with no pain); current therapies for chronic DED have slow onset and poor compliance.
Veverimer	Tricida	Chronic kidney disease	Ph3 Valor-CKD interim H2	-	Veverimer received a CRL last August, Valor-CKD was supposed to be the confirmatory post-marketing study
IMR-687	Imara	b-thalassemia, sickle cell	Ph2b Forte, Ph2b Ardent H2	-	Disappointed in sickle cell, Ardent is testing a higher dose (*Imara disappoints in sickle cell disease*)

**On the market already in different therapy line. Sources: Evaluate Pharma, company releases, analyst notes & clinicaltrials.gov.*