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Crucial clinical events for the smaller players

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Data are due in the fourth quarter for Aldeyra, Aeglea and Radius, among other small developers.

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

Aeglea's lead project, pegzilarginase, will yield pivotal results in an ultra-rare disease, and Radius hopes to validate its Serd elacestrant ahead of the competition. Meanwhile, Aldeyra's reproxalap, which has already prevailed in allergic conjunctivitis, will see data in the bigger, and more crowded, indication of dry eye disease.

Aldeyra's two phase 3 dry eye studies, Tranquility and Tranquility-2, include 300 patients each and are based on a chamber challenge model with dry air. In the two-day regimen patients receive either topical **reproxalap** or vehicle four times on day one, then on day two they are dosed just before entering the chamber and again 45 minutes afterwards.

The primary measure is ocular redness, assessed over 90 minutes in the dry eye chamber. Earlier this year the redness measure was met in an allergic conjunctivitis study (*Aldeyra eyes the future, April 27, 2021).* Reproxalap inhibits reactive aldehyde species, which are said to be elevated in numerous inflammatory diseases.

Aldeyra is not the only group trying to take on current dry eye drugs such as Abbvie's Restasis and Novartis's Xiidra. Bausch already had one win with its lipid modulator Nov03, and is expected to report data from the second study in the fourth quarter, while an approval decision on Oyster Point's nasal formulation of Chantix, OC-01, is due in October.

Rare disease target

Pivotal phase 3 data are expected from **Aeglea**'s lead project, **pegzilarginase**, a recombinant arginase 1 enzyme designed to lower levels of arginine in patients with arginase 1 deficiency (Arg1-D).

Current treatments for the rare progressive disease include severe dietary protein restriction, amino acid supplementation and ammonia scavengers.

Aeglea's Peace study, in 32 Arg1-D patients aged two years and older, involves weekly intravenous infusions of pegzilarginase for 24 weeks versus placebo. The primary endpoint is change from baseline in plasma arginine concentration, with mobility assessments as a secondary measure.

56-week data from a small earlier study were encouraging, with all 13 patients achieving plasma arginine levels under 200µM, the target set in disease management guidelines. The median plasma arginine level was 99µM, compared with 389µM at baseline.

Regarding mobility assessments, the overall response rate was 85% and meeting these secondary endpoints in the pivotal study will be important.

Serd validation

Elacestrant, Radius/Menarini's selective oestrogen degrader, is due to yield data soon in advanced breast cancer, setting up a showdown with Sanofi's competing project amcenestrant. Readout from Sanofi's Ameera-3 study had been expected earlier in the year, but has been delayed.

Radius's Emerald trial, in second or third-line ER-positive/Her2-negative disease, tests elacestrant monotherapy versus 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.

Roche, Astrazeneca and Lilly are all also vying for Serd validation. Ongoing studies from the big pharma companies in first-line disease will start reporting in 2024 *(The search for a better Faslodex continues, July 26, 2021).*

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

Q4 clinical catalysts (excludes Covid-19 data)					
Product	**Company**	**Therapy area**	**Q4 clinical catalyst**	**2026e indication sales ($m)**	**Note/Vantage coverage**
Tymlos (abaloparatide SC)	Radius	Male osteoporosis	Ph3 Atom	329*	Results to be included in sNDA to add males to label; Stifel notes this will add ~10% to addressable population
Reproxalap ophthalmic solution	Aldeyra	Dry eye	Ph3 Tranquility, Tranquility-2 (confirmatory)	312	See text
Pegzilarginase (AEB1102)	Aeglea	Arginase 1 deficiency	Topline pivotal Ph3 Peace	252	See text
FLT190	Freeline	Fabry disease	Ph1/2 Marvel-1 by YE	251	Gene therapy
ME-401 /zandelisib	MEI Pharma	3L+ r/r follicular lymphoma	Ph2 Tidal	247	PI3k delta inhibitor; complete data from FL arm are to be submitted to the FDA to support accelerated approval
Etigilimab (OMP-313M32)	Mereo	Solid tumours	Phase 1b/2 Activate basket study + Opdivo	160	Anti-Tigit MAb, ~20 pts worth of response and biomarker data; interest in Tigit remains high *(Glaxo pays handsomely to join the Tigit chase)*
XEN1101	Xenon	Adult focal seizures	Ph2b X-Tole	148	Potassium channel modulator, adjunctive treatment
COM701 + Opdivo + BMS-986207	Compugen/Bristol Myers Squibb	Advanced solid tumours	Ph1/2 dose escalation	145	Bristol's Tigit, Compugen's anti-PVRIG MAb; Glaxo also has an anti-PVRIG SRF813 via Surface (No Surface

BMS-986207	Q4 clinical catalysts (excludes Covid-19 data)				Surface (*No Surface buyout, but Glaxo picks another cancer target*)
Elacestrant	Menarini/Radius	2nd/3rd-line ER+/Her2- breast cancer	Ph3 Emerald, versus standard of care	69	See text
COM902	Compugen	Advanced cancer	Ph1 monotherapy dose escalation	2	Anti-Tigit (Fc-silent)
Cosibelimab	Checkpoint/Fortress	Metastatic cutaneous squamous cell carcinoma	Cohort data in Ph1 registration enabling study	-	Anti-PD-L1 (*No fast way to eighth place for Incyte*)
PBGM01	Passage Bio	Early and late infantile GM1 gangliosidosis	Ph1/2 Imagine-1 safety and 30-day biomarker	-	Gene therapy, should also see data from Sio's AXO-AAV-GM1 in Q4 (*A three way battle beckons in GM1 gangliosidosis*)
ANVS401/ Posiphen	Annovis Bio	Alzheimer's and Parkinson's diseases	Ph2a full data early fall	-	*AAIC – speculative Alzheimer's groups fail to catch the Aduhelm wave*
ATL001/ clonal neoantigen T cell (cNeT) therapy	Achilles	NSCLC, melanoma	Ph1/2 Chiron and Thetis update	-	TIL therapy, data expected from 10 patients across the two studies who have received monotherapy
Vidutolimod (CMP-001)	Checkmate Pharmaceuticals	Head and neck squamous cell carcinoma	Ph2 before YE	-	TLR9 agonist; in combination with Keytruda

**Already approved. Sources: Evaluate Pharma, company releases, analyst notes & clinicaltrials.gov.*