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Significant readouts for small players

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Praxis and Relmada target depression as Athira and Taurx tackle Alzheimer's.

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

Praxis hopes to differentiate its Gaba-A modulator from Sage/Biogen's offering in depression, while Relmada is looking to position its NMDA receptor antagonist in the same space. Also, Alzheimer's data are expected for Athira and Taurx, both of which are keen to draw a line under earlier tribulations.

Lifting the mood

While Sage and Biogen have dominated the news flow in depression recently, several smaller companies are trying to get in on the act, including **Praxis** with its Gaba-A modulator **PRAX-114**.

Investors will see data in June from Praxis's Aria monotherapy trial as well as Acapella, a dose-ranging adjunctive study. In both trials PRAX-114 is given once daily for 28 days and the primary endpoint is the change from baseline in HamD-17 score at day 15.

Sage/Biogen's zuranolone, another Gaba-A modulator, has yielded mixed results in depression, with questions over long-term efficacy and clinical meaningfulness, and side effects including somnolence and dizziness. PRAX-114 is said to have higher selectivity for extrasynaptic receptors than zuranolone, potentially offering a more marked effect and improved tolerability.

Another company here is **Relmada**, which is developing **REL-1017**, an (S)-enantiomer of methadone that works as an NMDA receptor channel blocker. First up will be monotherapy data with REL-1017 25mg once daily for 28 days in the phase 3 Reliance-III trial. Two adjunctive studies will read out later in the year; the primary endpoint of all three is change in MADRS score at day 28.

In a phase 2 adjunctive study REL-1017 25mg daily showed a statistically significant 8.7-point benefit over placebo at day 7, and a 9.4-point difference at day 14, one week after dosing ended. In phase 2 REL-1017 was given as a powder, rather than the tablets dosed in phase 3.

Phase 3 is designed to detect a two-point change, with Mizuho analysts noting that Relmada hopes for a benefit of at least three points.

Alzheimer's bandwagon

Since data on big pharma's Alzheimer's MAbs are not expected until later in the year, smaller players are hoping to attract some attention. First up is **Athira**, which is still reeling from last year's departure of its chief executive officer and founder, Leen Kawas, over misconduct that had occurred during her doctoral research.

Now phase 2 data are expected from the Act-AD study in which **fosgonimeton** (ATH-1017) is given daily via a 40mg or 70mg subcutaneous injection versus placebo. The project is said to enhance the activity of hepatocyte growth factor and its receptor, MET, a pathway involved in normal brain function.

Act-AD enrolled 77 patients with mild-to-moderate Alzheimer's disease. The primary outcome is the change in event-related-potential P300 latency at 26 weeks, said to be a functional measure of working memory processing speed. Secondary endpoints include measures of cognition.

In a small phase 1b trial the P300 latency data showed a 73ms improvement over placebo, which Stifel analysts note was considerably bigger than that seen with prior cognition-enhancing drugs.

A phase 3 study, Lift-AD, is under way and was upsized from 300 to 420 patients to strengthen powering for secondary endpoints and possibly allow it to act as a single pivotal trial.

Meanwhile, the private company **Taurx** is taking a different approach to Alzheimer's with its Tau aggregation inhibitor **TRx0237**. Topline data from the phase 3 Lucidity study will be reported in May, with full results expected at the Alzheimer's Disease International conference in June.

Lucidity has enrolled 598 patients with mild-to-moderate disease who are not receiving cholinesterase inhibitors or memantine. Participants are given either 8mg or 16mg TRx0237 per day, versus placebo, and co-primary efficacy endpoints measure Adas-cog11 and ADCS-ADL23.

However, this project has previously failed in phase 3. At the time Taurx blamed the fact that patients in the control arm received a low dose of TRx0237 to maintain blinding, as the project discolours urine. The low dose could also have been effective, the company claimed.

In the upcoming Lucidity study placebo patients will get a urinary discolourant rather than active drug.

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

Clinical catalysts in Q2 2022 (excludes Covid-19 data), market cap under $1bn					
Project	**Company**	**Therapy area**	**Q2 clinical catalyst**	**2026e indication sales ($m)**	**Note/Vantage coverage**
Ocaliva	Intercept	Advanced fibrotic (F2/3) Nash	Ph3 Regenerate re-analysis	903	CRL in 2020, re-analysis will include re-reading biopsy slides & 18mth biopsies from an additional ~500 patients; Reverse study in compensated cirrhotic Nash due Q3
REL-1017	Relmada	Major depressive disorder	Ph3 monotherapy Reliance-III mid year	449	See text
Eftilagimod alpha (+ Keytruda)	Immutep	PD-L1 unselected 2L PD-1/PD-L1 refractory NSCLC	Ph2 Tacti-002 Part B April 1 at Esmo ELCC	444	Soluble Lag3 dimer *(Second-quarter catalysts for the smaller players)*
PRAX-114	Praxis Precision Medicines	Major depressive disorder	Ph2 Acapella for adjunctive treatment, Ph2/3 Aria monotherapy	374	See text
VRDN-001	Viridian	Thyroid eye disease	Proptosis reduction data POC	348	Intravenous IGF-1R MAb, has SC version also in development (VRDN-002, first-in-human data mid-year)

Clinical catalysts in Q2 2022 (excludes Covid-19 data), market cap under $1bn					
TP-03	Tarsus	Demodex blepharitis	Ph3 Saturn-2 April	344	Saturn-1 was positive, filing pending Saturn-2 data (*Tarsus eyes a new market*)
CTP-543	Concert	Moderate-to-severe alopecia	Ph3 Thrive-AA1	295	Jak inhibitor, second ph3 Thrive-AA2 due Q3; Lilly's Olumiant filed, Pfizer's ritlecitinib in ph3
ATA188	Atara	Progressive multiple sclerosis	Ph2 Embold study	289	Remyelination project, EBV-targeted T-cell therapy (*A remyelinating agent remains a distant hope*)
Reproxalap eye drop	Aldeyra	Dry eye	Ph3 Tranquility-2 mid year	240	Study tweaked after failure of first ph3 (*Aldeyra needs more Tranquility*)
VS-6766 +/- defactinib	Verastem	Low-grade serous ovarian cancer	Ph2 Ramp-201 part A top-line	214	Check for toxicity (*AACR 2020 – Verastem reveals the logic behind its Kras deal*)
FTX-6058	Fulcrum	Sickle cell disease	Ph1b	138	6mg data, ≤3mth; Fulcrum says it could take 3-5 mth to see maximum HbF induction (Leerink)
RP-L201	Rocket	Leukocyte adhesion deficiency-1	Ph2 (9 patients)	67	Rocket to pursue full approval (vs accelerated using CD18 expression) by collecting survival data; Q2 update might not cover all patients
Fosgonimeton (ATH-1017)	Athira	Alzheimer's disease	Ph2 Act-AD topline	-	See text
PLN-74809	Pliant	Idiopathic pulmonary fibrosis	Ph2a Integris-IPF mid year	-	Ph2 showed receptor occupancy via imaging but this needs to translate into clinical benefit (*Pliant "win" still leaves a lot to prove*)
LMTX/ TRx0237	Taurx (Private)	Alzheimer's disease	Ph3 Lucidity topline data due May 26, full data expected at ADI conference June	-	See text
Atrasentan	Chinook	IgAN patient cohort	Ph2 Affinity ERA congress May, basket trial	-	Preview of atrasentan's profile before topline data from Align ph3 study in IgA nephropathy, expected 2023

Source: clinicaltrials.gov, Evaluate Pharma & company releases.