EDISON

Oryzon Genomics

Regulatory update

A step closer to a new treatment paradigm in BPD

Healthcare

24 June 2025

Oryzon Genomics has submitted the Phase III clinical trial protocol to the FDA for its lysine-specific demethylase 1 (LSD1) inhibitor, vafidemstat, in borderline personality disorder (BPD), marking a major step towards developing its lead programme as a potential first-in-class therapy for aggression in BPD. The primary endpoint will be the previously defined STAXI-2 Trait Anger score, where vafidemstat had demonstrated statistically significant improvement in the previous Phase IIb study. The key secondary endpoint will be the score on the clinician-rated Modified Overt Aggression Scale (OAS-M). The study design incorporates guidance from the FDA and input from US psychiatric key opinion leaders (KOLs), which we believe significantly derisks the Phase III programme. We expect FDA clearance in Q325, with Phase III to commence in 2026, potentially under a partnering agreement. Our valuation remains unchanged following the announcement.

Year end	Revenue (€m)	PBT (€m)	EPS (€)	DPS (€)	P/E (x)	Yield (%)
12/23	14.2	(6.1)	(0.06)	0.00	N/A	N/A
12/24	7.4	(5.6)	(0.06)	0.00	N/A	N/A
12/25e	38.9	39.3	0.55	0.00	4.9	N/A
12/26e	43.3	32.0	0.43	0.00	6.3	N/A

Note: PBT and EPS are normalised, excluding intangibles, exceptional items and share-based payments.

We believe that the study protocol submission (in line with the Q225 timeline) is a key development for Oryzon, with the Phase III trial now in sight. The Phase III PORTICO-2 study will be a potentially pivotal randomised, double-blind, placebo-controlled trial and will enrol 350 patients across multiple sites to study vafidemstat or placebo for an 18-week treatment duration. While the STAXI-2 Trait Anger score had been previously defined as the primary endpoint, we note that the key secondary endpoint, OAS-M, is a clinician-defined scale used widely to assess aggressive behaviour in psychiatric indications.

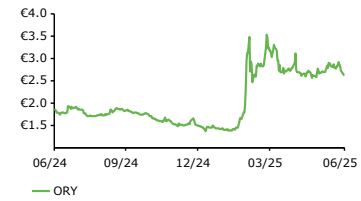
Management plans to present a detailed discussion on the trial design and the unmet need in the BPD space in a dedicated KOL webinar scheduled for 9 July 2025. While BPD is a serious psychiatric condition (afflicting c 1–2% of the global population), there are currently no FDA- or European Medicines Agency-approved treatments specifically targeting the condition. Aggression (the target for vafidemstat) is a key clinical feature of BPD (affecting c 70% of all patients), with the FDA acknowledging it as a therapeutic target, following the positive end of Phase II meeting in Q424.

Based on feedback from regulators, the Phase III programme may require either one or two clinical trials to be run in parallel or sequentially. While clarity will come with the FDA clearance of the programme (we expect this in Q325), our model conservatively assumes that two separate trials may be required, with trial commencement in 2026, potentially under an outlicensing partnership.

Vafidemstat is a central nervous system (CNS)-optimised LSD1 inhibitor, a histone-modifying enzyme forming parts of complexes implicated in the regulation of genes associated with various CNS conditions and cancers. We believe that with additional exploratory potential in autism spectrum disorder (clinical trial planned as part of the Med4Cure grant), ADHD and Alzheimer's, vafidemstat offers optionality across multiple neuropsychiatric indications with high unmet need.

Price	**€2.72**
Market cap	**€212m**
Pro forma net cash at 31 March 2025 (including proceeds from the April 2025 equity raise and grant income)	€31.2m
Shares in issue	78.5m
Free float	82.0%
Code	ORY
Primary exchange	MADRID
Secondary exchange	N/A

Share price performance



Business description

Spanish biotech Oryzon Genomics is focused on epigenetics. Iadademstat is being explored for acute leukaemias, small-cell lung cancer and neuroendocrine tumours. Central nervous system asset vafidemstat has completed several Phase IIa trials and a Phase IIb trial in borderline personality disorder (Phase III clinical trial protocol submitted to the FDA). It is also currently involved in a Phase IIb trial for schizophrenia.

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