EDISON

Oryzon Genomics

Making headway towards Phase III in BPD

Regulatory update

Healthcare

20 October 2025

Oryzon Genomics has announced that it has received FDA feedback on its plans for the Phase III programme in borderline personality disorder (BPD) for its lead central nervous system (CNS) drug candidate, vafidemstat. Following the submission of the proposed protocol in June 2025, Oryzon now has written feedback regarding various components of the programme, including trial endpoints as well as non-clinical considerations. Management has communicated that this dialogue with the regulators has been constructive and will enable the company to re-submit a revised Phase III protocol in due course. We highlight that such interactions with the FDA are common in drug development, and perhaps unsurprising in this case where there is no regulatory precedent for BPD. Should the FDA clear Oryzon's revised protocol, it should strengthen the company's chances of bringing an effective new treatment option for patients with BPD, an indication that currently has no approved drugs.

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	8.9	(3.9)	(0.01)	0.00	N/A	N/A
12/26e	48.3	35.9	0.48	0.00	7.0	N/A

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

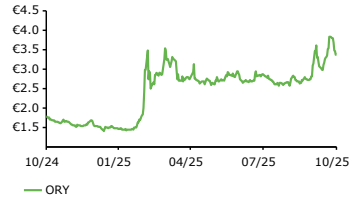
According to the announcement, Oryzon plans to incorporate the FDA's feedback into a revised Phase III protocol for vafidemstat in BPD. By aligning the regulators, this should strengthen the design of the programme, and improve the probability of success in bringing a new treatment option to BPD patients. We expect Oryzon to keep the market up to date regarding next steps, including when the protocol is re-submitted and when subsequent interactions with the FDA are underway.

BPD is a relatively neglected condition, with no FDA- or EMA-approved treatments specifically targeting the condition, despite its global prevalence of c 1–2%. At present, clinicians are limited to prescribing medications like antipsychotics and/or mood stabilisers off label, but this often has limited durability and is associated with undesirable side effects. We therefore see a potentially sizeable opportunity for Oryzon to address the unmet need in this space. We believe that the prior clinical data have been encouraging, and while the Phase IIb PORTICO trial did not meet the primary endpoints with statistical significance, key secondary endpoints were met with statistical significance, and, importantly, vafidemstat was favoured over placebo in all efficacy measures.

As a reminder, vafidemstat has been designed to address agitation and aggression, and while this is a common characteristic of BPD, it is also prevalent in other CNS conditions. Oryzon is exploring multiple other opportunities where vafidemstat may be of benefit, with the second-most advanced clinical programme being the EVOLUTION trial in schizophrenia. This is a double-blind, randomised, placebo-controlled Phase IIb trial. Insights from PORTICO have led to a revised protocol for EVOLUTION, with only 84 patients required to demonstrate meaningful benefit (previously 220). While the programme was previously limited to hospital sites across Spain, increased funding is enabling Oryzon to expand the trial to additional European sites. Other indications being explored include autism spectrum disorder based on prior clinical data (the Phase IIa REIMAGINE trial), highlighting the expandable opportunity for vafidemstat, in our view.

Price	**€3.37**
Market cap	**€269m**
Pro forma net cash/(debt) at 30 June 2025 (including the €13.3m grant income received in July 2025)	€26.3m
Shares in issue	79.9m
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 additional indications. 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, and management is preparing for an additional Phase II trial in autism spectrum disorder.

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