EDISON

Oryzon Genomics

HOPE-2 clearance, new Phase II study in PMS

Regulatory update

Healthcare

29 September 2026

Oryzon has received European Medicines Agency authorisation to initiate HOPE-2, a Phase IIa study of vafidemstat in Phelan-McDermid Syndrome (PMS), a rare genetic condition associated with autism. The single-centre, single-arm, open-label trial will enrol 12 adult patients in Spain. Safety and tolerability are the primary objectives, while secondary measures will assess anger and aggression, repetitive behaviour and wider symptoms. Treatment will run for 12 weeks, with a possible extension to 24 weeks for participants showing clinical benefit. Regulatory clearance moves the programme closer to first dosing and adds a genetically defined population to Oryzon's central nervous system (CNS) pipeline. HOPE-2 is partly funded through VANDAM (a Med4Cure project), with the Spanish PMS association helping identify participants. While this represents a relatively small study, we believe an encouraging outcome would be an early efficacy signal, though determination of meaningful clinical benefit will come from subsequent studies, should initial results be supportive.

Year end	Revenue (€m)	PBT (€m)	EPS (€)	DPS (€)	P/E (x)	Yield (%)
12/24	7.4	(5.6)	(0.06)	0.00	N/A	N/A
12/25	10.9	(5.6)	(0.03)	0.00	N/A	N/A
12/26e	20.0	(7.5)	(0.05)	0.00	N/A	N/A
12/27e	73.8	42.4	0.54	0.00	5.1	N/A

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

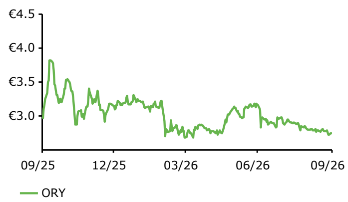
PMS is caused by deletions or mutations affecting SHANK3, a gene involved in communication between nerve cells. It can cause developmental delay, intellectual disability and limited speech. Aggression can be a major burden for patients and carers. Oryzon cites US prevalence of about one in 7,300 people. No medicine is approved specifically for PMS or aggression in PMS, although drugs approved for irritability associated with autistic disorder may be prescribed off label. As such, we believe there is a meaningful opportunity for Oryzon in this space.

Vafidemstat has been designed to inhibit LSD1, an enzyme that regulates gene activity, intended to modulate transcriptional programmes involved in neural plasticity, neuroinflammation and neuronal excitability. Oryzon has conducted studies in mice lacking SHANK3, with results showing that LSD1 inhibition improved social behaviour and aggression. Its Phase IIa REIMAGINE findings in people with autism spectrum disorder also support vafidemstat's potential application in PMS. The preclinical evidence provides a biological rationale, though we acknowledge that activity in human PMS patients is yet to be tested.

Beyond the primary safety and tolerability objectives, HOPE-2 will also assess aggression using the Aberrant Behavior Checklist (ABC) Irritability Subscale and the Clinical Global Impression of Severity – Anger and Aggression scale. Other measures include the Repetitive Behavior Scale-Revised, the PMS Assessment of Severity and the ABC Subscales: Stereotypic Behaviour, Hyperactivity/Non-compliance, Inappropriate Speech and Social Withdrawal, collectively, providing a comprehensive early test of potential efficacy in this new CNS condition.

Price	**€2.76**
Market cap	**€233m**
	$1.14/€
Pro forma net cash at 30 June 2026 (including €12m raise in July 2026)	€17.0m
Shares in issue	84.3m
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 haematological diseases, including AML and sickle cell disease, alongside other indications. CNS asset vafidemstat has completed several Phase IIa trials and a Phase IIb trial in BPD (Phase III in preparation). It is also involved in a Phase IIb trial for schizophrenia, and management has regulatory clearance for an additional Phase II trial in Phelan-McDermid Syndrome.

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