EDISON

Oryzon Genomics

Regulatory update

FDA aligns on Phase III BPD plans

Pharma and biotech

Oryzon Genomics has confirmed the FDA's alignment with its proposed Phase III programme for vafidemstat in borderline personality disorder (BPD). Notably, the FDA acknowledged agitation and aggression (A/A) as a therapeutic indication and, as such, the State-Trait Anger Expression Inventory 2 (STAXI-2) Trait Anger may be used as a primary endpoint for Phase III (PORTICO-2). We note that vafidemstat showed statistically significant benefit by this measure in the prior Phase IIb PORTICO trial. We view the news as encouraging and believe there is a sizeable opportunity for Oryzon to develop an effective treatment for BPD, for which there are currently no approved drugs. Next steps are to submit a full trial protocol for PORTICO-2 to the FDA (expected within Q125), before a potential trial launch from H225, contingent on regulatory clearance and providing that there are no other delays.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/22	15.7	(6.3)	(0.07)	0.0	N/A	N/A
12/23	14.2	(6.1)	(0.06)	0.0	N/A	N/A
12/24e	8.6	(4.9)	(0.05)	0.0	N/A	N/A
12/25e	31.6	15.5	0.28	0.0	6.5	N/A

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

Following its end-of-Phase II meeting with the FDA, Oryzon has announced the receipt of positive feedback. The FDA confirmed that STAXI-2 Trait Anger may be used as the primary endpoint for Phase III, and secondary endpoints will involve patient-rated and clinician-rated scales, such as the Clinical Global Impression – Severity A/A (CGI-S A/A) subscale and Borderline Evaluation of Severity over Time (BEST) scale, both of which were used in the prior Phase IIb PORTICO trial, as well as the CGI-S full scale (not used in PORTICO). It was noted that the FDA will require further information to demonstrate that STAXI-2 Trait Anger constitutes a clinically meaningful endpoint, alongside similar research to justify the choice of secondary endpoints. Management is planning to conduct a qualitative research study on a subset of the PORTICO-2 patients to provide validation of the proposed endpoints. The study protocol will be submitted to the FDA for review and feedback prior to initiating PORTICO-2. Psychometric properties and performance of the endpoints will also be shared with the FDA prior to the initiation of the Phase III trial.

It is estimated that the Phase III PORTICO-2 trial will recruit c 350 participants, who will be randomised (1:1) to receive vafidemstat or a control, across an 18-week treatment duration. Subject to the FDA accepting the protocol, PORTICO-2 will be one of two registrational trials required before filing for approval. We believe a key goal of the Phase III programme will be to build on the positive results from the prior Phase IIb PORTICO trial, which provided a robust foundation, in our view. As a reminder, this trial confirmed the safety of vafidemstat and, in terms of efficacy, the candidate was favoured over placebo in all measures. Notably, the secondary endpoints were met with statistical significance. The STAXI-2 Trait Anger data showed a 58.6% relative reduction in A/A with vafidemstat compared to placebo at weeks 8–12 (p=0.0071), with p values at weeks 10 and 12 of p=0.006 and p=0.016, and relative reductions of 92.1% and 57.1%, respectively. For a more detailed discussion of the final PORTICO data, please read our prior update note.

2 October 2024

Price	**€1.81**
Market cap	**€116m**
Net debt (€m) at 30 June 2024	3.2
Shares in issue	64.0m
Free float	82%
Code	ORY
Primary exchange	Madrid Stock Exchange
Secondary exchange	N/A

Share price performance

Business description

Oryzon Genomics is a Spanish biotech focused on epigenetics. Iadademstat is being explored for acute leukaemia, small-cell lung cancer and neuroendocrine tumours. Vafidemstat, its central nervous system asset, has completed several Phase IIa trials and a Phase IIb trial for borderline personality disorder (now the lead programme), and is in a Phase IIb trial for schizophrenia.

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