EDISON

Oryzon Genomics

Regulatory update

FDA green light for SCLC combination trial

Pharma and biotech

With the FDA investigational new drug (IND) application clearance, Oryzon can commence its Phase I/II cooperative research and development agreement (CRADA) trial sponsored by the National Cancer Institute (NCI; part of the National Institutes of Health) with Dr Noura Choudhury from the Memorial Sloan Kettering Cancer Center (MSKCC) as the principal investigator. This trial will evaluate iadademstat in combination with immune checkpoint inhibitors (ICIs) for the treatment of first-line extensive-stage small-cell lung cancer (SCLC). This is a key development for Oryzon as interim results from this study will influence the design of the company-sponsored Phase Ib/II STELLAR trial. The IND application for this is likely to be filed by end-2024 (trial commencing in 2025). ICIs atezolizumab and durvalumab are currently approved as first-line treatments in SCLC and Oryzon expects a combination with iadademstat to enhance immune activity in patients, increasing therapeutic efficacy. The CRADA-MSKCC trial will enrol 40–50 patients, with updates expected through 2024.

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	(6.0)	(0.06)	0.0	N/A	N/A
12/24e	12.9	(4.2)	(0.03)	0.0	N/A	N/A
12/25e	33.7	15.5	0.29	0.0	7.2	N/A

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

Iadademstat is a small molecule, selective inhibitor of the enzyme LSD1, widely recognised as an important epigenetic target in cancer treatment. The Phase I/II CRADA trial (45–50 patients) sponsored by the NCI will include a Phase I dose-finding portion, followed by a Phase II randomised study. As previously communicated, interim data from this study will be used as an indicator to inform the design of the subsequent Phase Ib/II STELLAR trial. We believe that this strategy de-risks Oryzon's pipeline development plans, a key consideration given the tight market environment and an already busy pipeline with more advanced stage programmes ongoing.

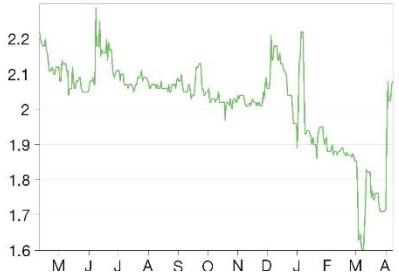
SCLC is a particularly aggressive form of neuroendocrine cancer, accounting for c 15% of all diagnosed lung cancer cases (annual incidence of c 200,000 cases worldwide). Nearly 70% of the patients are diagnosed with advanced/extensive disease. The five-year survival rate is below 7%, highlighting the need for novel, more effective treatments, in our view. While the approval of ICIs (atezolizumab and durvalumab, approved in 2019 and 2020, respectively) has improved outcomes for SCLC patients, efficacy has been modest (improvement in median overall survival of two to three months) over the standard etoposide-cisplatin chemotherapy treatment. Management plans to evaluate the combination of iadademstat with ICIs, aiming to demonstrate increased utility and benefit.

We expect interim data from the CRADA-MSKCC trial in 2024, supporting the IND application for the STELLAR trial, which we estimate will commence in 2025 (should data from this first study be positive). Based on our forecasts, we estimate Oryzon to be funded into 2025.

9 April 2024

Price	**€2.08**
Market cap	**€129m**
Net debt* (€m) at end-December 2023 *Excluding post-period debt-to-equity conversion	6.3
Shares in issue	62.0m
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 in borderline personality disorder (now the lead programme), and is in a Phase IIb trial in schizophrenia.

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