EDISON

Oryzon Genomics

R&D results

Interim data from Phase IIa ETHERAL AD study

Pharma & biotech

On 15 July 2019, Oryzon presented interim data from the Phase IIa ETHERAL trial at the Alzheimer's Association International Conference (AAIC 2019) in Los Angeles. A randomised, double-blind, three-arm study is enrolling mild- to moderate Alzheimer's disease (AD) patients to investigate vafidemstat, an LSD1/MAOB inhibitor. The interim analysis of the blinded data from the first 104 patients (out of 125 in European centres plus 30 more patients in the US) showed the drug was safe and well tolerated. The trial remains blinded, so no conclusions on efficacy can be made at this point, but Oryzon's presentation included an initial assessment of certain functional parameters and some biomarker data. The placebo-controlled, 24-week treatment results from the European part of the trial are expected in H120. We maintain our valuation of €430m or €11.0/share.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/17	4.3	(4.6)	(0.14)	0.0	N/A	N/A
12/18	6.8	(3.7)	(0.03)	0.0	N/A	N/A
12/19e	6.1	(6.8)	(0.17)	0.0	N/A	N/A
12/20e	6.1	(6.8)	(0.17)	0.0	N/A	N/A

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

No clinically relevant safety concerns

Although the primary endpoint of the study is safety and tolerability, secondary endpoints include measures of cognition, function, behaviour and CSF biomarkers, which will provide insights into efficacy. At the time of the interim analysis 87.5% (91/104) patients had completed at least one month of treatment and no clinically relevant effects on platelets, neutrophils and other haematological parameters have been observed. 36 patients completed six month of treatment with no significant safety issues. This confirmed the data from the Phase I trial with healthy volunteers and is a significant reassurance given that any AD treatment would likely be a life-long intervention and that LSD1 is a key regulator of haematopoiesis.

Initial analysis of blinded patient data

Because the trial remains blinded, no conclusions on efficacy can be made yet, but the poster did describe disease progression in the first 33 patients, who completed 24 weeks of therapy. The researchers said that 'while some patients clearly progress, others maintain baseline values or even improve'. This was shown using selected functional scores (MMSE and CMAI) and the proinflammatory biomarker S100A9 (Exhibit 1). Only six patients showed a clear increase on S100A9 levels, whereas the other patients were stable or showed a significant decrease.

Valuation: €430m or €11.0/share

Our valuation remains €430m or €11.0/share and our forecasts are unchanged (Exhibit 3). The full results from the ETHERAL trial are the next catalyst in this indication and will prompt us to review our rNPV of the project. As a reminder, Oryzon recently presented interim data from the two cohorts of ADHD and borderline personality disorder patients from the Phase II REIMAGINE trial with vafidemstat, which showed improvements in aggression and agitation, as well as other core features of the diseases.

18 July 2019

Price	**€3.68**
Market cap	**€144m**
Net cash (€m) at end Q119	16.2
Shares in issue	39.1m
Free float	70%
Code	ORY
Primary exchange	Madrid Stock Exchange
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	6.1	(3.4)	(3.3)
Rel (local)	4.3	(0.7)	1.2
52-week high/low		€4.64	€2.08

Business description

Oryzon Genomics is a Spanish biotech focused on epigenetics. Iadademstat (Phase IIa) is being explored for acute leukaemias and SCLC; vafidemstat, its CNS product, is in Phase IIa trials in MS, AD and aggression. Newer asset ORY-3001 is being developed for certain orphan indications.

Next events

Autism spectrum disorder results from the Phase II REIMAGINE trial	9 September 2019
First readout from Phase IIa CLEPSIDRA with iadademstat in SCLC	Q319
Aggression in AD results from the vafidemstat's Phase II REIMAGINE	December 2019
Readouts from Phase II trials with vafidemstat in AD and MS	H219/ H120

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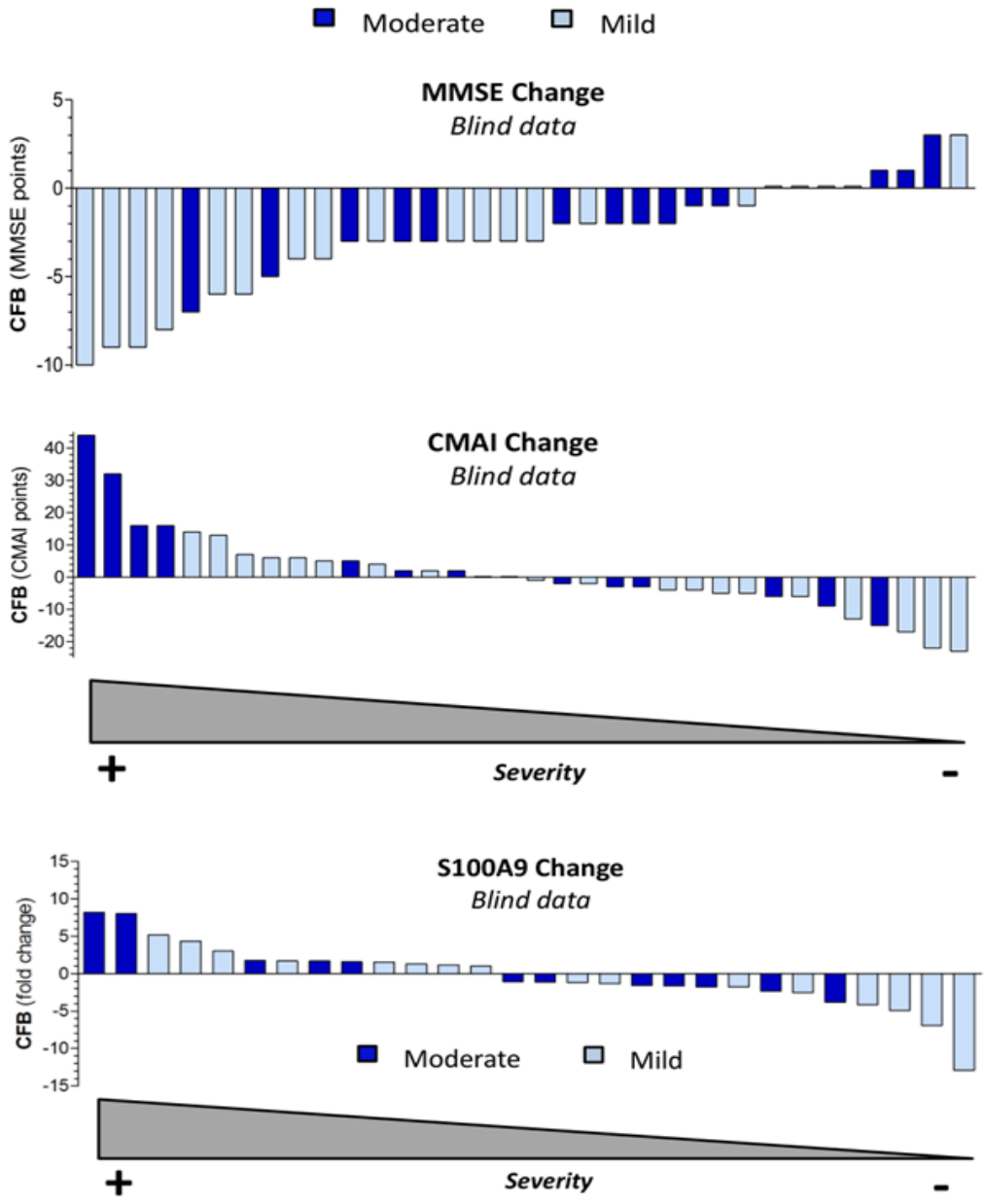
Edison profile page

Next steps

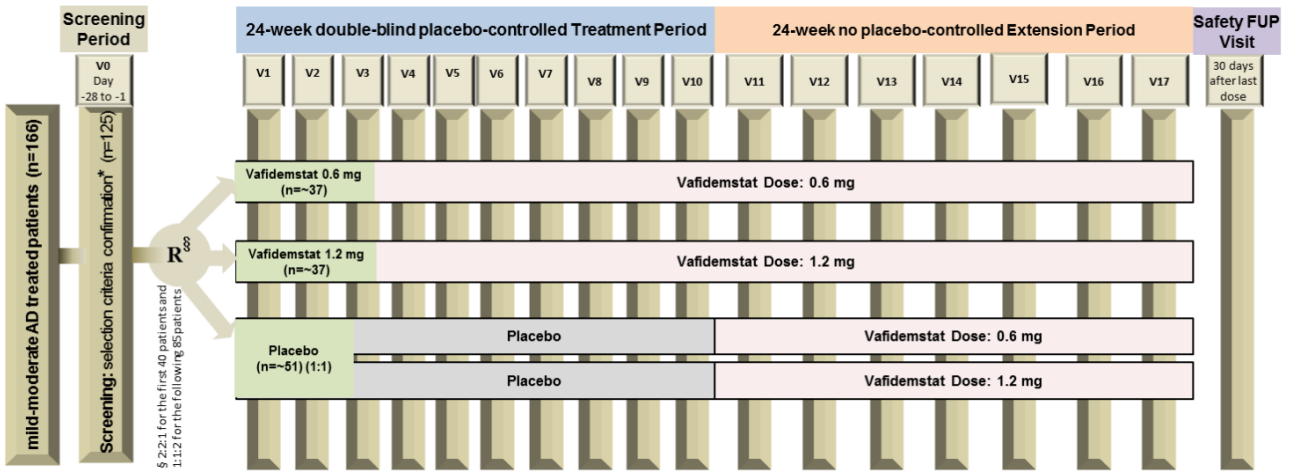
By mid-June, 75% of patients were enrolled to the ETHERAL trial (total n = 104). This suggests the last patient may be recruited by end of July 2019. ETHERAL-US (n = 30) is also enrolling after the FDA approved the initial new drug application IND in early 2019. The patients are randomised into three arms (placebo, low dose, high dose) using an adaptive design. The first 24 weeks are placebo-controlled, following which the placebo patients are randomised into vafidemstat therapy (low dose or high dose) so that all patients receive treatment (ie no placebo control, Exhibit 2) for another 24 weeks. Oryzon plans to report the placebo-controlled results (ie from the first 24 weeks) from the European part of the trial in H120. The full results including the extension period and the US data should be reported later in 2020.

Exhibit 1: Functional score and biomarker evolution in blinded data analysis



Source: Bullock et al, AAIC 2019, Oryzon. Note: MMSE = mini-mental state examination; CMAI = Cohen-Mansfield agitation inventory.

Exhibit 2: Phase IIa ETHERAL AD study design



Source: Oryzon. Note: FUP = follow up; V = visit; R = randomisation.

Exhibit 3: Oryzon rNPV valuation

Product	Indication	Launch	Peak sales (US$m)	Value (€m)	Probability of success (%)	rNPV (€m)	NPV/share (€/share)
Iadademstat (ORY-1001)	AML	2023	927	284.1	15%	56.3	1.4
Iadademstat (ORY-1001)	SCLC	2026	571	137.6	8%	25.2	0.6
Vafidemstat (ORY-2001)	AD	2026	4,510	1,018.3	15%	160.5	4.1
Vafidemstat (ORY-2001)	MS	2027	1,940	446.6	20%	105.8	2.7
Vafidemstat (ORY-2001)	BPD	2027	1,290	277.0	20%	65.7	1.7
Net cash (end-2018)				16.1	100%	16.1	0.4
Valuation				**2,179.6**		**429.6**	**11.0**

Source: Edison Investment Research. Note: AML = acute myeloid leukaemia; SCLC = small cell lung cancer; AD = Alzheimer's disease; MS = multiple sclerosis; BPD = borderline personality disorder.

Exhibit 4: Financial summary

€000s	2017	2018	2019e	2020e
Year end 31 December	Local GAAP	Local GAAP	Local GAAP	Local GAAP
PROFIT & LOSS				
Revenue	4,317	6,781	6,119	6,137
Cost of Sales	0	0	0	0
Gross Profit	4,317	6,781	6,119	6,137
Research and development	(5,306)	(7,412)	(9,454)	(9,560)
EBITDA	(3,498)	(2,766)	(6,046)	(6,175)
Operating Profit (before amort. and except.)	(3,660)	(2,905)	(3,660)	(2,905)
Intangible Amortisation	(664)	(7)	(8)	(9)
Exceptionals	0	(4)	0	0
Other	0	0	0	0
Operating Profit	(4,324)	(2,916)	(6,194)	(6,324)
Exceptionals	0	0	0	0
Net Interest	(928)	(796)	(586)	(471)
Profit Before Tax (norm)	(4,588)	(3,701)	(6,771)	(6,786)
Profit Before Tax (reported)	(5,252)	(3,712)	(6,780)	(6,795)
Tax	55	2,535	0	0
Profit After Tax (norm)	(4,533)	(1,166)	(6,771)	(6,786)
Profit After Tax (reported)	(5,197)	(1,177)	(6,780)	(6,795)
Average Number of Shares Outstanding (m)	31.7	31.7	34.6	39.1
EPS - normalised (€)	(0.14)	(0.03)	(0.17)	(0.17)
EPS - reported (€)	(0.16)	(0.03)	(0.17)	(0.17)
Dividend per share (€)	0.0	0.0	0.0	0.0
Gross Margin (%)	100.0	100.0	100.0	100.0
EBITDA Margin (%)	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A
BALANCE SHEET				
Fixed Assets	24,914	31,786	37,758	43,807
Intangible Assets	22,458	29,330	35,441	41,569
Tangible Assets	638	665	526	447
Investments	1,818	1,791	1,791	1,791
Current Assets	36,130	35,664	16,488	3,856
Stocks	7	135	71	103
Debtors	857	971	914	943
Cash	34,950	34,320	15,264	2,572
Other	316	239	239	239
Current Liabilities	(8,696)	(10,441)	(4,017)	(4,229)
Creditors	(1,343)	(2,192)	(1,767)	(1,979)
Short term borrowings	(7,354)	(8,249)	(2,249)	(2,249)
Long Term Liabilities	(17,915)	(11,884)	(11,884)	(11,884)
Long term borrowings	(16,041)	(9,977)	(9,977)	(9,977)
Other long term liabilities	(1,874)	(1,907)	(1,907)	(1,907)
Net Assets	34,432	45,125	38,345	31,550
CASH FLOW				
Operating Cash Flow	(4,281)	(2,799)	(6,936)	(6,495)
Net Interest	(426)	2,133	(586)	(471)
Tax	0	0	0	0
Capex	(105)	(170)	0	0
Acquisitions/disposals	0	0	0	0
Financing	16,887	11,949	0	0
Other*	653	(6,576)	(5,534)	(5,726)
Dividends	0	0	0	0
Net Cash Flow	12,728	4,538	(13,055)	(12,692)
Opening net debt/(cash)	1,172	(11,555)	(16,093)	(3,038)
HP finance leases initiated	0	0	0	0
Other	0	0	0	0
Closing net debt/(cash)	(11,555)	(16,093)	(3,038)	9,655

Source: Edison Investment Research, Oryzon Genomics accounts. Note: Oryzon reports in Spanish GAAP. *Includes cash outflows related to development costs that were capitalised.

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