

Oryzon Genomics

R&D results

Positive signals from first ALICE trial dataset

On 14 June 2019, Oryzon presented dose-finding data from the Phase II ALICE trial at the 24th Congress of the European Hematology Association (EHA-2019) in Amsterdam. The single-arm, open-label study enrolled newly diagnosed, elderly acute myeloid leukaemia (AML) patients and investigated iadademstat in combination with standard of care chemotherapy drug azacitidine. In addition to dose finding data, initial efficacy was also investigated. Overall, findings in this trial confirm the data seen in the first-in-man Phase I study Oryzon completed in late 2016 and support further investigation of an azacitidine/iadademstat combination in the second efficacy part of the ALICE trial.

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.

Dose-finding data set from Phase II ALICE trial

In this part of the study, which included six AML patients, the combination of iadademstat with azacitidine demonstrated a good safety profile and the recommended dose of 90 µg/m² was established. This was the initially selected dose, therefore only six patients were needed. Iadademstat produced a clear differentiation effect in leukaemic blasts, ie turn them into normal blood cells (Exhibit 1). 80% of objective responses were observed in five evaluable patients (Exhibit 2). Of these, 75% (3/5) were complete remissions with incomplete haematologic recovery (CRI), while 25% (1/5) were partial remissions. Interestingly, the observed clinical responses appeared rapidly with a median time of 1.5 months.

Our take

Although the study was small and the focus was on establishing the recommended dose, the efficacy findings can be interpreted as showing potential. Notably, impaired differentiation of the leukaemic blasts is at the core of the pathophysiology of the disease. Iadademstat's ability to induce the differentiation of blasts demonstrates it does what it was designed for. We note that reported overall response rates (ORR) in AML patients treated with azacitidine monotherapy are 25–32% depending on age ([Seymour et al, 2016](#)). A recently published article ([DiNardo et al, 2019](#)) described a clinical trial (n=145) where AML patients received venetoclax plus azacitidine or decitabine (both chemical analogs of cytidine) and the ORR was 67%. Venetoclax is a novel anticancer drug being developed by AbbVie/Genentech and the ORR of 67% compares well with the initial 80% rate observed in Oryzon's trial. The second part of the ALICE trial should provide more insight in this regard.

Valuation: €430m or €11.0/share

Our valuation remains €430m or €11.0/share and our forecasts are unchanged. The full results from the ALICE trial is the next catalyst in this indication and will prompt us to review our rNPV of the project including the success probability and other target populations as Oryzon indicated that one of the goals of the trial is to understand the broader application of iadademstat in other leukaemias.

Pharma & biotech

18 June 2019

Price €3.47

Market cap €136m

Net cash (€m) at end Q418 16.1

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 (18.2) (5.8) 8.8

Rel (local) (16.9) (3.7) 17.4

52-week high/low €5.03 €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

Preliminary readouts from Phase II trials with vafidemstat in AD and MS H219/ H120

Analysts

Jonas Peculius +44 (0)20 3077 5728

Alice Nettleton +44 (0)20 3077 5700

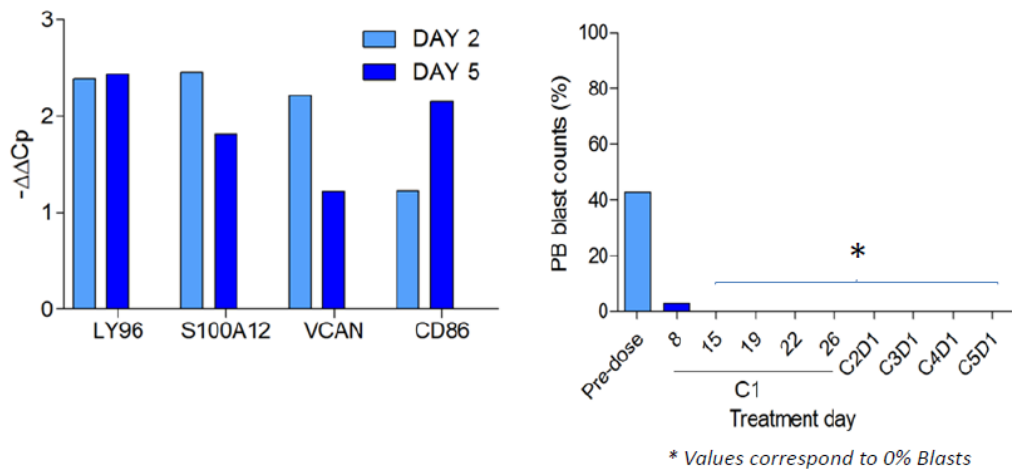
healthcare@edisongroup.com
[Edison profile page](#)

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Next steps

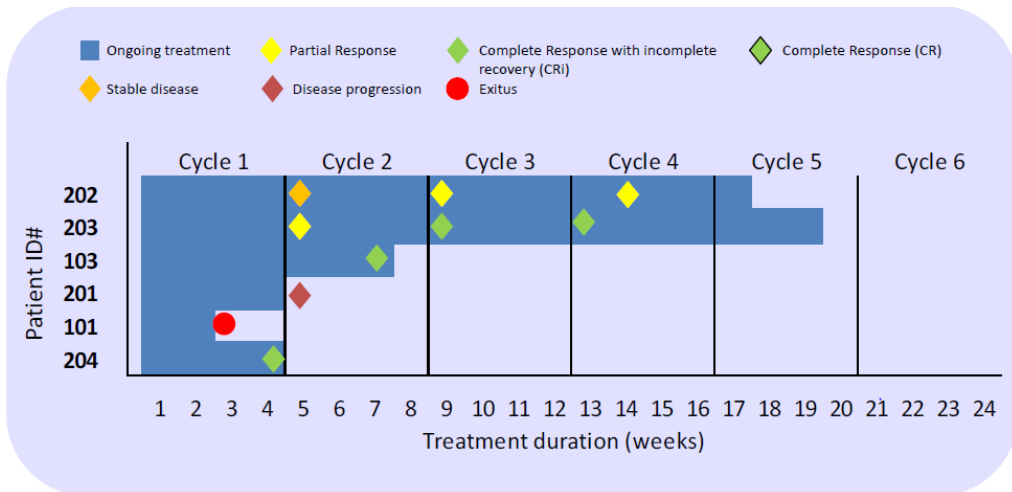
The second part of the ALICE study will enrol up to 18 more patients and focus on the effectiveness of the drug combination. The next set of data should be presented at the ASH meeting in Orlando in December 2019. Iadademstat, as a selective LSD1 inhibitor, has been shown to be effective in preclinical models, including combinations with azacitidine. In addition, Oryzon has already completed a Phase I first-in-man trial, where iadademstat was given as a monotherapy, and demonstrated preliminary [antileukaemic activity](#) (reviewed in detail in our [initiation report](#)).

Exhibit 1: Peripheral blast differentiation (data from patient #203)



Source: Oryzon, [EHA-2019 conference](#)

Exhibit 2: Preliminary efficacy results



Source: Oryzon, [EHA-2019 conference](#)

Exhibit 3: Oryzon rNPV valuation

Product	Indication	Launch	Peak sales (US\$m)	Value (€m)	Probability of success (%)	rNPV (€m)	NPV/share (€/share)
ladademstat (ORY-1001)	AML	2023	927	284.1	15%	56.3	1.4
ladademstat (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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Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
1,185 Avenue of the Americas
3rd Floor, New York, NY 10036
United States of America

Sydney +61 (0)2 8249 8342
Level 4, Office 1205
95 Pitt Street, Sydney
NSW 2000, Australia