EDISON

Oryzon Genomics

R&D results

Maturing ALICE trial dataset continues to impress

Pharma & biotech

On 9 December 2019, Oryzon presented more data from the Phase II ALICE trial at the 61st ASH annual meeting in Orlando, Florida. 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. Six of the eight evaluable patients (75%) achieved objective (OR) responses, which was in line with the first results reported in June 2019. For comparison, OR rates are 25–32% in AML patients treated with azacitidine monotherapy. Our valuation is €437m or €9.5/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)	(0.16)	0.0	N/A	N/A
12/20e	6.1	(6.8)	(0.15)	0.0	N/A	N/A

Note: *Normalised, excluding amortisation of acquired intangibles and exceptional items.

Second, positive batch of data from Ph II ALICE trial

ORs were assessed by bone marrow (BM) aspirate. Of the 13 enrolled patients, eight had at least one bone marrow aspirate, and therefore were evaluable. Three patients died before their first BM evaluation and two were just starting treatment. Six of the eight evaluable patients (75%) achieved ORs: two complete responses (CRs), three complete responses with incomplete haematologic recovery (CRi) and one partial response (PR). As a reminder, in the first set of data published in June 2019, the OR rate was 80% in five evaluable patients (3/5 CRi and 1/5 PR). Given the small sample size, an outcome in just one patient can significantly influence the results. In addition, the trial is not complete yet. However, the OR rates have been consistent so far within the 75–80% range and compare very favourably with the classical chemotherapy, but also with venetoclax. The latter is a novel drug approved for front-line AML treatment in November 2018. Venetoclax (AbbVie/Genentech) plus azacitidine or decitabine achieved an OR rate of 67%.

Next steps

The second part of the ALICE study will enrol 18 patients, so these results will be expanded in coming months with additional patients and longer follow-up times. Oryzon also indicated that even though the results are not final yet, the existing evidence 'may warrant further trials with this combination therapy in a confirmatory study setting'. Oryzon will obviously need to complete the ALICE trial before designing a confirmative study. However, the statement, which was part of the poster presentation, seems confident.

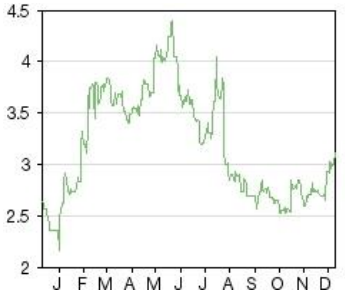
Valuation: €437m or €9.5/share

Our valuation is €437m or €9.5/share (versus €430m or €11.0/share) after a technical adjustment to include a private placement in July 2019. The full results from the ALICE trial (expected next year) will be a substantial catalyst for the share price, as Oryzon indicated that one of the goals of the trial is to understand the broader application of iadademstat in other leukaemias, with another haematological indication a possible next step.

10 December 2019

Price	**€3.11**
Market cap	**€142m**
Net cash (€m) at end-Q319	25.9
Shares in issue	45.8m
Free float	70%
Code	ORY
Primary exchange	Madrid Stock Exchange
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	15.0	11.7	9.1
Rel (local)	15.5	7.6	2.8
52-week high/low	€4.40		€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

Vafidemstat Phase IIa REIMAGINE-AD data from the AD patients	H120
Vafidemstat Phase IIa ETHERAL EU 6m interim trial results	H120
Updated data from iadademstat Phase IIa CLEPSIDRA in SCLC	2020
Updated data from iadademstat Phase IIa ALICE in AML 2020	2020

Analyst

Jonas Peciulis +44 (0)20 3077 5728

healthcare@edisongroup.com

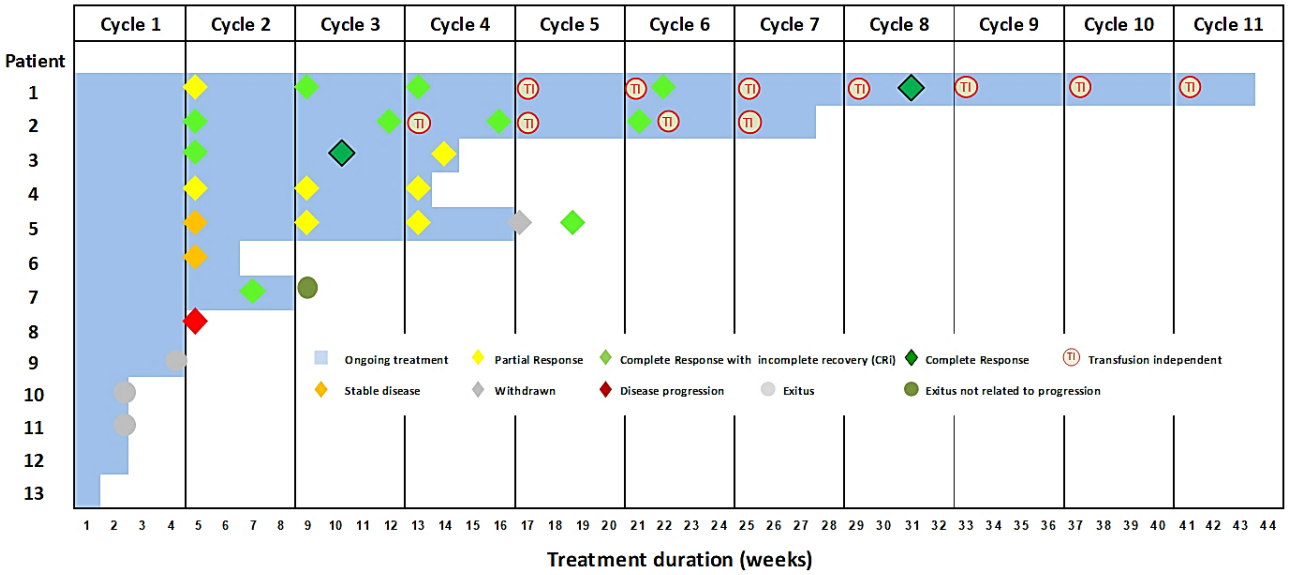
Edison profile page

Phase IIa ALICE data from Part 2

The single-arm, open-label study is enrolling newly diagnosed, elderly acute myeloid leukaemia (AML) patients and is investigating iadademstat in combination with standard of care chemotherapy drug azacitidine. Oryzon intends to enrol 18 patients in the ongoing Part 2 (expansion cohort) of the ALICE trial. At the time of writing the ASH poster, 13 patients have been enrolled in ALICE. The main endpoints include:

- Dose finding data,
- PK/PD evaluation (including a set of six blood biomarkers), and
- Initial efficacy (OR measured by bone marrow aspirate).

Exhibit 1: Patients enrolled in the Phase IIa ALICE trial



Source: C Buesa et al. Iadademstat Shows Efficacy in Elderly AML Patients in Combination with Azacitidine. ALICE Trial. Poster presentation at ASH 2019.

Safety/tolerability

Overall, the authors of the ASH poster concluded that the combination of iadademstat and azacitidine shows a good safety profile in elderly AML patients. In Part 1 (dose finding), the recommended dose of 90µg/m^2 was established. Later, the dose was lowered to 60µg/m^2 by the safety monitoring committee (SMC). This decision was made after one patient withdrew consent after experiencing severe fatigue and another patient died due to an intracranial haemorrhage. Oryzon did not see any clinically relevant non-haematological adverse events.

LSD1 inhibitor class drugs are known to have haematological sides effects at higher doses, however, these are usually predictable and manageable. We note that a clear drug-side effect relationship is not always straightforward to prove. For example, intracranial haemorrhage (haemorrhagic stroke) can have many causes, especially in such elderly, highly ill patients. So, the decision to lower the dose could serve as a precaution. The tolerability of the drug will improve at the lower dose and, more importantly, Oryzon believes this will not come at the expense of efficacy, as existing PK/PD data show that a 60µg/m^2/d level is also able to saturate LSD1 target engagement with a clear biomarker effect.

Putting Iadademstat efficacy results in perspective

OR rates 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 (Venclexta, AbbVie/Genentech) is a novel anticancer drug approved (accelerated approval) by the FDA for frontline treatment of AML in combination with azacitidine or decitabine or low-dose cytarabine. Iadademstat's initial 75–80% OR rate is much higher than the historical response rates with classic chemotherapy and compares well with Venetoclax's OR of 67%.

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 2: 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-2019e)				23.0	100%	23.0	0.5
Valuation				**2,186.6**		**436.6**	**9.5**

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 3: 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)	(6,186)	(6,314)
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	34.6	42.5	45.8
EPS - normalised (€)	(0.14)	(0.03)	(0.16)	(0.15)
EPS - reported (€)	(0.16)	(0.03)	(0.16)	(0.15)
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	36,488	23,856
Stocks	7	135	71	103
Debtors	857	971	914	943
Cash	34,950	34,320	35,264	22,572
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	58,345	51,550
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	20,000	0
Other*	653	(6,576)	(5,534)	(5,726)
Dividends	0	0	0	0
Net Cash Flow	12,728	4,538	6,945	(12,692)
Opening net debt/(cash)	1,172	(11,555)	(16,093)	(23,038)
HP finance leases initiated	0	0	0	0
Other	0	0	0	0
Closing net debt/(cash)	(11,555)	(16,093)	(23,038)	(10,345)

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

General disclaimer and copyright

This report has been commissioned by Oryzon Genomics and prepared and issued by Edison, in consideration of a fee payable by Oryzon Genomics. Edison Investment Research standard fees are £49,500 pa for the production and broad dissemination of a detailed note (Outlook) following by regular (typically quarterly) update notes. Fees are paid upfront in cash without recourse. Edison may seek additional fees for the provision of roadshows and related IR services for the client but does not get remunerated for any investment banking services. We never take payment in stock, options or warrants for any of our services.

Accuracy of content: All information used in the publication of this report has been compiled from publicly available sources that are believed to be reliable, however we do not guarantee the accuracy or completeness of this report and have not sought for this information to be independently verified. Opinions contained in this report represent those of the research department of Edison at the time of publication. Forward-looking information or statements in this report contain information that is based on assumptions, forecasts of future results, estimates of amounts not yet determinable, and therefore involve known and unknown risks, uncertainties and other factors which may cause the actual results, performance or achievements of their subject matter to be materially different from current expectations.

Exclusion of Liability: To the fullest extent allowed by law, Edison shall not be liable for any direct, indirect or consequential losses, loss of profits, damages, costs or expenses incurred or suffered by you arising out or in connection with the access to, use of or reliance on any information contained on this note.

No personalised advice: The information that we provide should not be construed in any manner whatsoever as, personalised advice. Also, the information provided by us should not be construed by any subscriber or prospective subscriber as Edison's solicitation to effect, or attempt to effect, any transaction in a security. The securities described in the report may not be eligible for sale in all jurisdictions or to certain categories of investors.

Investment in securities mentioned: Edison has a restrictive policy relating to personal dealing and conflicts of interest. Edison Group does not conduct any investment business and, accordingly, does not itself hold any positions in the securities mentioned in this report. However, the respective directors, officers, employees and contractors of Edison may have a position in any or related securities mentioned in this report, subject to Edison's policies on personal dealing and conflicts of interest.

Australia

Edison Investment Research Pty Ltd (Edison AU) is the Australian subsidiary of Edison. Edison AU is a Corporate Authorised Representative (1252501) of Crown Wealth Group Pty Ltd who holds an Australian Financial Services Licence (Number: 494274). This research is issued in Australia by Edison AU and any access to it, is intended only for "wholesale clients" within the meaning of the Corporations Act 2001 of Australia. Any advice given by Edison AU is general advice only and does not take into account your personal circumstances, needs or objectives. You should, before acting on this advice, consider the appropriateness of the advice, having regard to your objectives, financial situation and needs. If our advice relates to the acquisition, or possible acquisition, of a particular financial product you should read any relevant Product Disclosure Statement or like instrument.

New Zealand

The research in this document is intended for New Zealand resident professional financial advisers or brokers (for use in their roles as financial advisers or brokers) and habitual investors who are "wholesale clients" for the purpose of the Financial Advisers Act 2008 (FAA) (as described in sections 5(c) (1)(a), (b) and (c) of the FAA). This is not a solicitation or inducement to buy, sell, subscribe, or underwrite any securities mentioned or in the topic of this document. For the purpose of the FAA, the content of this report is of a general nature, is intended as a source of general information only and is not intended to constitute a recommendation or opinion in relation to acquiring or disposing (including refraining from acquiring or disposing) of securities. The distribution of this document is not a "personalised service" and, to the extent that it contains any financial advice, is intended only as a "class service" provided by Edison within the meaning of the FAA (i.e. without taking into account the particular financial situation or goals of any person). As such, it should not be relied upon in making an investment decision.

United Kingdom

This document is prepared and provided by Edison for information purposes only and should not be construed as an offer or solicitation for investment in any securities mentioned or in the topic of this document. A marketing communication under FCA Rules, this document has not been prepared in accordance with the legal requirements designed to promote the independence of investment research and is not subject to any prohibition on dealing ahead of the dissemination of investment research.

This Communication is being distributed in the United Kingdom and is directed only at (i) persons having professional experience in matters relating to investments, i.e. investment professionals within the meaning of Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "FPO") (ii) high net-worth companies, unincorporated associations or other bodies within the meaning of Article 49 of the FPO and (iii) persons to whom it is otherwise lawful to distribute it. The investment or investment activity to which this document relates is available only to such persons. It is not intended that this document be distributed or passed on, directly or indirectly, to any other class of persons and in any event and under no circumstances should persons of any other description rely on or act upon the contents of this document.

This Communication is being supplied to you solely for your information and may not be reproduced by, further distributed to or published in whole or in part by, any other person.

United States

Edison relies upon the "publishers' exclusion" from the definition of investment adviser under Section 202(a)(11) of the Investment Advisers Act of 1940 and corresponding state securities laws. This report is a bona fide publication of general and regular circulation offering impersonal investment-related advice, not tailored to a specific investment portfolio or the needs of current and/or prospective subscribers. As such, Edison does not offer or provide personal advice and the research provided is for informational purposes only. No mention of a particular security in this report constitutes a recommendation to buy, sell or hold that or any security, or that any particular security, portfolio of securities, transaction or investment strategy is suitable for any specific person.

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