EDISON

Oryzon Genomics

Q122 update

Key milestones and extended cash runway

Pharma and biotech

Oryzon is progressing with its lead assets, iadademstat and vafidemstat, in the clinic. The ALICE study continues to generate positive readouts in acute myeloid leukaemia (AML) with initiation of Phase Ib FRIDA in second line planned for H222. In borderline personality disorder (BPD) Oryzon is expecting interim readouts this year and is filing an investigational new drug (IND) application to initiate the Phase Ib study in Kabuki syndrome. We believe positive readouts in the AML and BPD setting could serve as important catalysts in 2022. With a gross cash position of €25.2m at end-March 2022, we estimate Oryzon has a cash runway through into Q225. We value Oryzon at €802m, or €15.1/share, from €739m, or €13.9/share.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/20	9.5	(4.8)	(0.07)	0.0	N/A	N/A
12/21	10.6	(7.2)	(0.09)	0.0	N/A	N/A
12/22e	9.9	(7.0)	(0.10)	0.0	N/A	N/A
12/23e	10.0	(7.3)	(0.10)	0.0	N/A	N/A

Note: *PBT is reported, EPS is fully diluted

Positive regulatory milestones so far

Oryzon has so far had a positive year, with CY H122 bringing favourable news for the progression of iadademstat. An IND was approved by the FDA in March, allowing indication expansion into second-line relapsed/refractory AML patients and initiation of the Phase Ib FRIDA study. This was followed by orphan drug designation for treatment of small-cell lung cancer (SCLC), adding to its previous designation in AML, and Oryzon intends to file an IND application to initiate Phase Ib of the STELLAR trial in SCLC in 2022.

Extended cash runway to FY25

At end Q122, Oryzon had a gross cash position of €25.2m. We note that it has debt obligations of €4.3m in FY22 and €5.2m in FY23. Oryzon recently announced that it has entered into a €20m convertible bond financing agreement. We estimate that the current annual burn rate of around €13–15m (c €15m cash burn rate in FY21), excluding debt obligations and assuming execution of all convertible notes, will provide a cash runway into Q225 (Q324 if outstanding debts are repaid). This will capitalise the company past key inflection points from the ALICE, PORTICO and FRIDA studies. The company is also set to receive additional financing (€1.87m) in the form of a non-refundable grant to fund FRIDA.

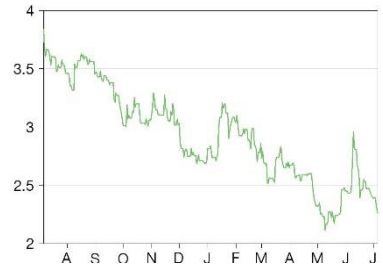
Valuation: €802m or €15.1/share

We value Oryzon at €802m or €15.1/share, based on a risk-adjusted NPV analysis using a 12.5% discount rate and H122e net cash of c €2.9m. We have rolled our model forward and updated our exchange rate assumption to $1.05/€ (from $1.14/€), which had a c 5% upside effect on our rNPV. We have revised our FY22 estimates, but our underlying long-term assumptions remain unchanged (for details see our Outlook note).

6 July 2022

Price	**€2.26**
Market cap	**€120m**
	US$1.05/€
Net cash (€m) at end-December 2021	11.1
Shares in issue	53.1m
Free float	80%
Code	ORY
Primary exchange	Madrid Stock Exchange
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(7.0)	(15.4)	(42.0)
Rel (local)	1.9	(8.3)	(34.8)
52-week high/low		€3.84	€2.11

Business description

Oryzon Genomics is a Spanish biotech focused on epigenetics. Iadademstat is being explored for acute leukaemias and SCLC. Vafidemstat, its CNS asset, has completed several Phase IIa trials and a Phase IIb trial in borderline personality disorder is now the lead study, but Oryzon is rapidly expanding its CNS R&D pipeline.

Next events

Phase II PORTICO interim data	H222
Phase II ALICE final readout	H222

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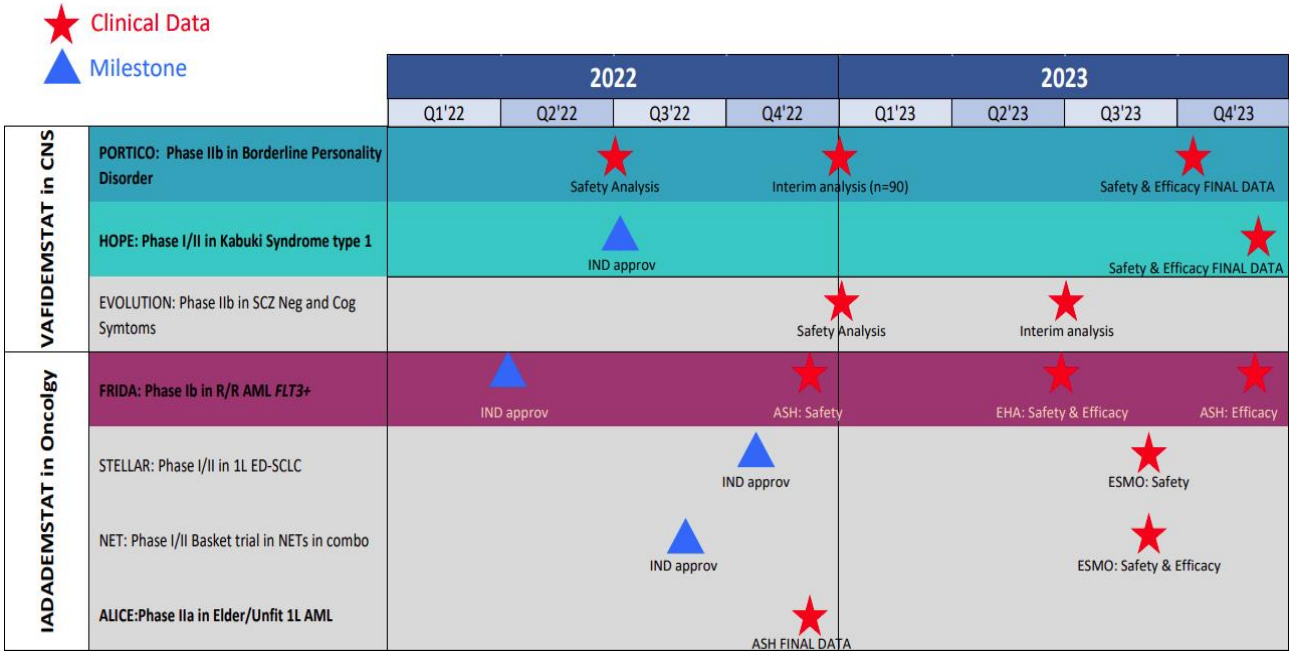
Edison profile page

A catalyst-rich H222 expected

Signs of things to come for iadademstat

Oryzon Genomics specialises in epigenetic therapeutics, its primary assets focusing on inhibition of the Lysine specific demethylase 1 (LSD1) epigenetic target. LSD1 is a gene expression regulator, overexpression of which has been demonstrated in a variety of cancers and deregulation of activity associated with various neuronal physiological disorders. With LSD1 contributing to broad, dynamic gene regulation Oryzon views this as a prime target for small molecule inhibition across multiple indications in oncology and central nervous system (CNS) diseases with high unmet need (Exhibit 1). In AML Oryzon is investigating combination therapies of iadademstat with standard-of-care chemotherapy drug azacitidine in ALICE and with FDA-approved FLT3 inhibitor gilteritinib in FRIDA. The STELLAR trial is in preparation and intends to evaluate iadademstat in combination with an immune checkpoint inhibitor (ICI).

Exhibit 1: Oryzons' clinical development schedule



Source: Oryzon corporate presentation

In H222 we expect several catalysts from' Oryzon's development pipeline. The final results of the proof-of-concept ALICE trial in first-line AML are expected to be presented at the American Society of Hematology (ASH) Annual Meeting and Exposition 2022 in December. The open-label 48-month study has continued to show positive safety and efficacy data, with the latest round of readouts demonstrating objective responses (OR) in 81% of patients (cf azacitidine monotherapy, OR c 30%). Responses were observed in all patients with an FLT3 mutation, providing further encouragement for the FRIDA study, which aims to target this AML subpopulation and is now the primary target population Oryzon is seeking to develop iadademstat for. Approximately 50% of patients relapse after first line AML treatment and 30% possess an FLT3 mutation. Initial safety data from this trial, expected at end-2022, will be important. Oryzon also intends to seek approval for initiation of the STELLAR trial in SCLC this year, with the study potentially supporting an application for accelerated approval in this indication, provided sufficiently positive data.

Vafidemstat in the clinic and targeting rare diseases

In CNS, vafidemstat is being explored as a monotherapy treatment for the regulation of neuronal physiological processes. The Phase IIb PORTICO double-blind study intends to enrol c 156 patients in Europe and the United States, to evaluate vafidemstat in its lead indication for the treatment of BPD. The trial has two primary endpoints: to demonstrate reduction of aggression and overall clinical BPD improvement. Interim top-line readouts (90 patients) are expected by end of 2022, which will guide the subsequent development strategy.

Safety data are expected to be presented from the double-blind Phase IIb EVOLUTION trial, to assess vafidemstat for the treatment of schizophrenia in patients currently being treated with antipsychotic therapy, at end-2022. The trial will recruit up to 100 patients, with efficacy assessed through the primary endpoints of a reduction in both negative and cognitive schizophrenia symptoms.

The Phase I/II HOPE study represents Oryzon's first efforts to develop drugs for rare conditions. Kabuki syndrome is a rare disorder that affects multiple systems, including neurological, immune, auditory and cardiac systems. In 2021 Oryzon received a $1m grant to support efforts in the clinical development of Kabuki syndrome. The company is hoping to receive IND approval for initiation of the safety/dosing trial in H222 with first patient enrolment (FPI) by end-2022. Positive results from the study could support an application for accelerated approval in the EU/US.

Valuation

We value Oryzon at €802m or €15.1/share, based on a risk adjusted NPV analysis using a 12.5% discount rate and H122e net cash of c €2.9m. Our underlying long-term assumptions remain unchanged, and we roll our model forward in time. We have also updated our FX assumptions to $1.05/€ (from $1.14/€), which had a c 5% upside effect. Our model includes five rNPV projects (Exhibit 2, for more details details see our Outlook note).

Exhibit 2: Valuation of Oryzon

Product	Indication	Launch	Peak sales ($m)	Value (€m)	Probability	rNPV (€m)	NPV/share (€/share)
Iadademstat	2L AML	2026	500	722.5	30%	211.2	4.0
Iadademstat	1L SCLC	2026	730	763.7	25%	185.0	3.5
Vafidemstat	BPD	2027	1,610	1,193.5	20%	228.6	4.3
Vafidemstat	Schizophrenia, negative symptoms	2027	700	600.3	15%	82.4	1.6
Vafidemstat	Aggression in AD	2028	900	640.2	15%	91.6	1.7
Estimate Net Cash end H122e				2.9	100%	2.9	0.2
Valuation				**3,931.2**		**801.7**	**15.1**

Source: Edison Investment Research

Financials

Oryzon's total operational spending in FY21 was €17.6m, a higher spend than that of FY20 of €13.9m. Research and development expenditure was c €13.0m in FY21 compared with €11.1m in FY20 with Oryzon stepping up pre-clinical and clinical activities and general and administrative expenses of c €4.5m up from c €2.8m. This additional spend was linked to professional services related to evaluation, study and legal preparation related to a potential stock market quotation for Oryzon on the US market (Nasdaq). Oryzon improved their working capital position in FY21, reducing net cash loss from operations by c €1.2m (€3.6m in FY21 vs €4.8m in FY20). We estimate a net cash loss of c €16.3m in FY22 and €15.6m in FY23, in line with current spending in operations and increased R&D activity. We expect 2022 and 2023 free cash flow losses to increase

to €16.3m and decline slightly to €12.4m, respectively, with the timing of clinical trials. These reflect fairly consistent capital expenditure of €10m annually.

At end Q122 Oryzon had a gross cash position of €25.2m with a quarterly cash burn rate of c €3.5m, in line with our estimations. We also note that the company had both short-term debt (€4.3m) and long-term debt obligations (€13.3m) with principal repayments of €4.3m in FY22 and €5.2m FY23. The company has also announced that it has entered into a convertible bonds financing agreement with a Swiss institutional investor, Nice & Green, to raise up to €20m over 30 months. The raise will help capitalise the company past key inflection points from ongoing clinical trials in FY22, FY23 and fund clinical development into H124. The financing agreement consists of four tranches, including an initial tranche of €8m, followed by three optional future tranches of €4m each, to be executed at Oryzon's request, subject to customary conditions.

While we had not anticipated any immediate funding requirement for Oryzon, the decision may have been triggered by the relatively favourable terms the company has been able to secure, particularly in light of the tight capital market situation. The convertible bonds have no warrants attached, come with zero interest rate and have a maturity of 24 months. The conversion price will be 95% of the average closing daily volume-weighted average price but will not exceed a 9.99% discount to the closing price preceding the conversion date. Oryzon also holds the right to redeem any or all notes at 3% interest. Oryzon ended Q122 with a gross cash balance of €25.2m and, assuming all €20m worth of convertible notes are executed, we expect pro forma cash (€45.2m) to extend the runway into Q225 (or Q324 incorporating the upcoming debt repayments, €4.3m in FY22 and €5.2m in FY23).

In our models, we project that Oryzon will launch its first product into the market in FY26. Based on the current annual cash burn projections (c €14m), we estimate that it will be required to raise an additional c €30m to continue to fund operations up to this point.

Exhibit 3: Financial summary

€'000s	2019	2020	2021	2022e	2023e
December	Local GAAP	Local GAAP	Local GAAP	Local GAAP	Local GAAP
PROFIT & LOSS					
Revenue	10,278	9,521	10,615	9,857	9,998
Cost of Sales	0	0	0	0	0
Gross Profit	10,278	9,521	10,615	9,857	9,998
Research and development	(11,322)	(11,075)	(13,023)	(12,049)	(12,536)
EBITDA	(3,679)	(4,148)	(6,867)	(6,811)	(7,152)
Operating Profit (before amort. and except.)	(3,820)	(4,293)	(7,011)	(6,964)	(7,310)
Intangible Amortisation	(9)	0	0	0	0
Exceptionals	(11)	0	0	0	0
Other	0	0	0	0	0
Operating Profit	(3,839)	(4,293)	(7,011)	(6,964)	(7,310)
Exceptionals	0	0	0	0	0
Net Interest	(737)	(484)	(169)	0	0
Profit Before Tax (norm)	(4,557)	(4,777)	(7,180)	(6,964)	(7,310)
Profit Before Tax (reported)	(4,576)	(4,777)	(7,180)	(6,964)	(7,310)
Tax	892	1,379	2,493	1,508	2,000
Profit After Tax (norm)	(3,666)	(3,398)	(4,687)	(5,456)	(5,310)
Profit After Tax (reported)	(3,685)	(3,398)	(4,687)	(5,456)	(5,310)
Average Number of Shares Outstanding (m)	41.6	49.2	53.1	53.1	53.1
EPS - normalised (€)	(0.09)	(0.07)	(0.09)	(0.10)	(0.10)
EPS - reported (€)	(0.09)	(0.07)	(0.09)	(0.10)	(0.10)
Dividend per share (€)	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	100.0	100.0	100.0	100.0	100.0
EBITDA Margin (%)	N/A	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A	N/A
BALANCE SHEET					
Fixed Assets	42,357	51,729	62,778	72,658	82,674
Intangible Assets	39,938	49,216	60,254	70,112	80,110
Tangible Assets	631	644	682	705	722
Investments	1,788	1,869	1,842	1,842	1,842
Current Assets	37,738	42,377	32,606	23,645	8,399
Stocks	289	317	104	104	104
Debtors	2,071	2,351	3,645	2,998	3,321
Cash	35,111	39,605	28,725	20,410	4,841
Other	267	105	132	132	132
Current Liabilities	(10,546)	(7,693)	(8,671)	(7,046)	(7,125)
Creditors	(4,000)	(2,839)	(4,365)	(2,740)	(2,819)
Short term borrowings	(6,547)	(4,854)	(4,306)	(4,306)	(4,306)
Long Term Liabilities	(8,420)	(10,483)	(15,451)	(23,451)	(23,451)
Long term borrowings	(6,699)	(8,680)	(13,354)	(21,354)	(21,354)
Other long term liabilities	(1,721)	(1,803)	(2,097)	(2,097)	(2,097)
Net Assets	61,129	75,931	71,262	65,807	60,497
CASH FLOW					
Operating Cash Flow	(3,610)	(5,432)	(4,673)	(7,789)	(7,396)
Net Interest	(324)	(247)	(253)	0	0
Tax	0	862	1,299	1,508	2,000
Capex*	(10,031)	(9,159)	(11,246)	(10,033)	(10,173)
Acquisitions/disposals	0	0	0	0	0
Financing	18,374	18,181	0	0	0
Dividends	0	0	0	0	0
Net Cash Flow	4,409	4,205	(14,873)	(16,314)	(15,569)
Opening net debt/(cash)	(16,093)	(21,866)	(26,071)	(11,065)	5,249
HP finance leases initiated	0	0	0	0	0
Other	1,364	0	(132)	0	0
Closing net debt/(cash)	(21,866)	(26,071)	(11,065)	5,249	20,818

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

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