EDISON

Oryzon Genomics

Q318 company update

Ramping up R&D activity; catalysts in 2019

Pharma & biotech

The €13m (gross) private placement announced on 30 October 2018 will support Oryzon's expanding R&D programme with a total of five clinical trials now underway. Two new Phase IIa trials with iadademstat (formerly ORY-1001) are starting in acute myeloid leukaemia (AML) (ALICE trial) and small cell lung cancer (SCLC) (CLEPSIDRA trial). Results from another two Phase IIa studies with vafidemstat (formerly ORY-2001) in Alzheimer's disease (AD) patients (ETHERAL) and multiple sclerosis (MS) patients (SATEEN) are due to report results in H219. Before that, interim results from the innovative design 'basket trial' with vafidemstat in aggression control in various neuropsychiatric conditions are due in H119. Our valuation is €342m or €8.7 per share (vs €328m or €9.6 per share).

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/16	5.0	(4.7)	(0.17)	0.0	N/A	N/A
12/17	4.3	(4.6)	(0.14)	0.0	N/A	N/A
12/18e	7.0	(5.6)	(0.09)	0.0	N/A	N/A
12/19e	6.3	(7.3)	(0.19)	0.0	N/A	N/A

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

REIMAGINE trial to test holistic vafidemstat effects

Oryzon successfully initiated a further Phase IIa trial with vafidemstat, a dual LSD1/MAOB inhibitor, in aggression. The innovative trial design (basket trial) has been borrowed from drug development in oncology and will include patients with Lewy body dementia, AD, autism spectrum disorder, borderline personality disorder and attention deficit hyperactivity disorder. Aggression is often seen in a variety of neurodegenerative and neuropsychiatric conditions and vafidemstat has demonstrated holistic effects in this regard in preclinical models (more detailed overview in our recent outlook report). Oryzon hopes that testing it in different conditions will allow it to pin down a more precise psychiatric setting where the drug could be useful. Preliminary results are expected in H119.

Two new trials with iadademstat about to start

Oryzon has received authorisation from the regulatory authorities to initiate two Phase IIa studies with iadademstat, a specific LSD1 inhibitor. The Phase IIa ALICE study will recruit elderly AML patients (n=36) who will receive ORY-1001 in combination with standard of care, azacitidine. The other Phase IIa CLEPSIDRA trial will recruit relapsed SCLC patients (n=36) who will receive iadademstat in combination with platinum-etoposide chemotherapy. Interim results from both studies are expected in 2019. We have reviewed key data on iadademstat in our outlook report, including an article recently published in Cell, where a team at the Harvard Medical School described the findings that inhibiting LSD1 could lead to the activation of immune response and overcomes resistance to anti-PD-1 therapy.

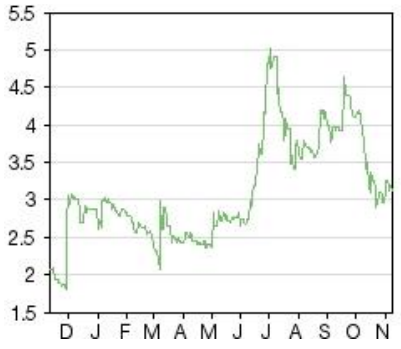
Valuation: €342m or €8.7 per share

At €342m our valuation is marginally higher on an absolute basis and slightly lower on a per-share basis at €8.7/share (from €328m or €9.6/share) due to the share issue and rolling our model forward. Near-term catalysts will be multiple preliminary readouts from the Phase IIa studies in 2019.

9 November 2018

Price	**€3.13**
Market cap	**€122m**
	US$1.16/€
Net cash (€m) at end Q318 (including share issue in October 2018)	16.3
Shares in issue	39.1m
Free float	65%
Code	ORY
Primary exchange	Madrid Stock Exchange
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(19.1)	(16.0)	43.8
Rel (local)	(19.0)	(10.8)	60.3
52-week high/low		€5.0	€1.8

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

Preliminary readouts from Phase IIa studies with vafidemstat and iadademstat	H119

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Two Phase IIa readouts are key short-term catalysts

The two ongoing lead trials are the Phase IIa ETHERAL and SATEEN studies testing vafidemstat in AD and MS patients respectively.

- ETHERAL trial (n=150) is a randomised, double-blind, placebo-controlled, 24-week study with ORY-2001 in mild-to-moderate AD patients.
- A randomised, double-blind, placebo-controlled, 36-week SATEEN study (n=24) will evaluate vafidemstat in patients with relapsing-remitting MS and secondary progressive MS.

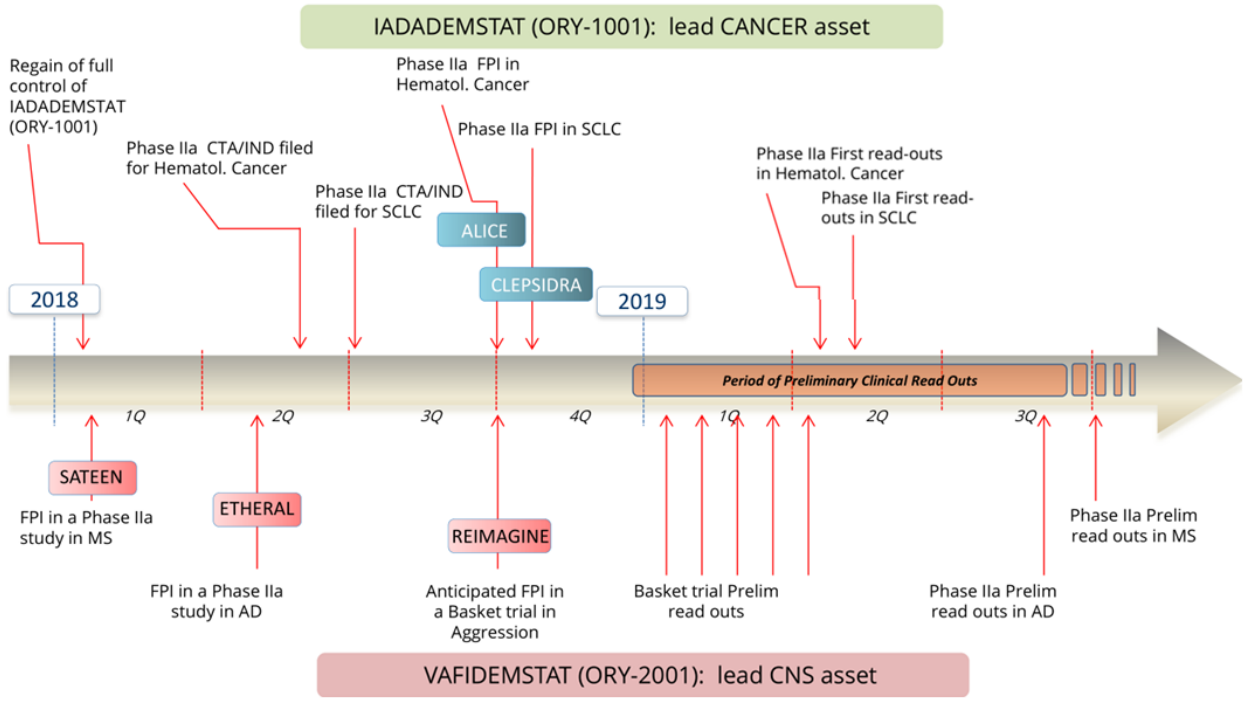
The readouts from these trials are expected in H219 and will provide the first insights into the clinical efficacy of the drug.

Exhibit 1: R&D pipeline

Product	Indication and stage	Mechanism of action	Notes
Iadademstat (ORY-1001)	■ **AML**, Phase IIa ALICE trial in combination with azacitidine ■ **SCLC**, Phase IIa CLEPSIDRA trial in combination with platinum-etoposide	Small molecule LSD1 inhibitor - LSD1 is a histone eraser enzyme that removes methyl groups	■ Oryzon reported supportive Phase I/IIa data in acute leukaemia at the ASH conference in December 2016. ■ Two new Phase IIa trials are about to start enrolling patients in AML (ALICE) and SCLC (CLEPSIDRA). **First readouts from both trials expected in Q219.**
Vafidemstat (ORY-2001)	■ **AD**, Phase IIa ETHERAL trial, monotherapy ■ **MS**, Phase II SATEEN trial, monotherapy ■ **Aggression**, Phase IIa REIMAGINE trial, monotherapy	Small molecule LSD1 and MAOB inhibitor	■ Reported Phase I safety and PK/PD data from healthy volunteers on 31 March 2017 at the ADPD conference. ■ Oryzon initiated clinical trials in MS (SATEEN) and AD (ETHERAL). **Preliminary readouts expected in H219.** ■ Basket trial REIMAGINE in aggression in several neuropsychiatric disorders initiated. **Preliminary readout expected Q119.**
ORY-3001	■ Undisclosed non-oncological diseases	Small molecule LSD1 inhibitor	Initial positive preclinical data published in sickle cell disease, but further development not disclosed yet. Successfully completed regulatory toxicology.

Source: Edison Investment Research, Oryzon Genomics

Exhibit 2: Expected 2018–2019 newsflow



Source: Oryzon Genomics

Financials and valuation

According to Oryzon's Q318 report, R&D costs were €1.7m, compared with €1.3m in Q317. We expect R&D costs to increase somewhat in Q418 and FY19 due to the initiation of two new Phase IIa studies, so our estimates remain unchanged (FY18 and FY19 R&D costs of €8.5m and €9.5m respectively). SG&A costs for Q318 were €0.7m, compared with €0.9m in Q317, in line with our expectations.

The private placement transaction closed on 31 October 2018 and raised gross proceeds of €13m at €2.62 per share (12% discount to average of the closing price over the previous three days). The reported Q318 cash position was €22.5m. Considering this cash position, the private placement (post-period) and total debt (€18.4m) bring the estimated net cash to €16.3m. Our model suggests this should be sufficient well into H220.

Our valuation is higher on an absolute basis at €342m and slightly lower on a per-share basis at €8.7 per share (from €328m or €9.6 per share) due to the share issue and rolling our model forward. As Oryzon is on track to develop its assets in all the indications we include in our valuation, we leave our assumptions unchanged. Near-term catalysts will be multiple preliminary readouts from Phase IIa studies in 2019 (Exhibit 1).

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	271.7	15	49.7	1.3
Iadademstat (ORY-1001)	SCLC	2026	571	132.9	8	23.0	0.6
Vafidemstat (ORY-2001)	AD	2026	4,510	991.6	15	153.5	3.9
Vafidemstat (ORY-2001)	MS	2027	1,940	438.8	20	104.1	2.7
Net cash (est. end-2018 + share issue)				11.6	100	11.6	0.3
Valuation				**1,846.6**		**341.9**	**8.7**

Source: Edison Investment Research

Exhibit 4: Financial summary

€000s	2016	2017	2018e	2019e
December	Local GAAP	Local GAAP	Local GAAP	Local GAAP
PROFIT & LOSS				
Revenue	5,009	4,317	7,034	6,301
Cost of Sales	0	0	0	0
Gross Profit	5,009	4,317	7,034	6,301
Research and development	(5,210)	(5,306)	(8,502)	(9,454)
EBITDA	(3,721)	(3,498)	(4,678)	(6,350)
Operating Profit (before amort. and except.)	(3,879)	(3,660)	(3,879)	(3,660)
Intangible Amortisation	(695)	(664)	(767)	(887)
Exceptionals	(4)	0	0	0
Other	0	0	0	0
Operating Profit	(4,578)	(4,324)	(5,556)	(7,348)
Exceptionals	(58)	0	0	0
Net Interest	(844)	(928)	(793)	(802)
Profit Before Tax (norm)	(4,724)	(4,588)	(5,582)	(7,263)
Profit Before Tax (reported)	(5,480)	(5,252)	(6,349)	(8,150)
Tax	32	55	2,200	0
Profit After Tax (norm)	(4,692)	(4,533)	(3,382)	(7,263)
Profit After Tax (reported)	(5,448)	(5,197)	(4,149)	(8,150)
Average Number of Shares Outstanding (m)	27.6	27.6	31.7	36.6
EPS - normalised (c)	(0.17)	(0.14)	(0.09)	(0.19)
EPS - reported (EUR)	(0.20)	(0.16)	(0.11)	(0.21)
Dividend per share (c)	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	21,269	24,914	31,070	36,373
Intangible Assets	18,810	22,458	28,725	34,139
Tangible Assets	696	638	527	417
Investments	1,763	1,818	1,818	1,818
Current Assets	28,475	36,130	33,640	13,993
Stocks	8	7	150	79
Debtors	978	857	3,500	2,178
Cash	22,028	34,950	29,990	11,736
Other	5,461	316	0	0
Current Liabilities	(7,597)	(8,696)	(10,084)	(3,890)
Creditors	(2,119)	(1,343)	(1,731)	(1,537)
Short term borrowings	(5,477)	(7,354)	(8,354)	(2,354)
Long Term Liabilities	(19,419)	(17,915)	(11,992)	(11,992)
Long term borrowings	(17,723)	(16,041)	(10,041)	(10,041)
Other long term liabilities	(1,696)	(1,874)	(1,951)	(1,951)
Net Assets	22,729	34,432	42,633	34,483
CASH FLOW				
Operating Cash Flow	(4,536)	(4,281)	(7,792)	(5,953)
Net Interest	(471)	(426)	(793)	(802)
Tax	0	0	2,200	0
Capex	(28)	(105)	0	0
Acquisitions/disposals	0	0	0	0
Financing	287	16,887	12,350	0
Other*	(6,819)	653	(5,925)	(5,499)
Dividends	0	0	0	0
Net Cash Flow	(11,567)	12,728	40	(12,254)
Opening net debt/(cash)	(10,395)	1,172	(11,555)	(11,595)
HP finance leases initiated	0	0	0	0
Other	0	0	(0)	0
Closing net debt/(cash)	1,172	(11,555)	(11,595)	659

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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