EDISON

Oryzon Genomics

New data further back MS indication

Q416 results and R&D update

Pharma & biotech

Oryzon has two assets, ORY-1001 and ORY-2001, in the clinical stage of development, with ORY-3001 being investigated for oncology indications in the preclinical stage. While the most advanced, ORY-1001, is now in Roche's hands, Oryzon has been making progress with the newer programmes. Data from the Phase I trial with ORY-2001 for Alzheimer's disease (AD) will be announced by end March 2017 and fresh preclinical data from ORY-2001 studies support its potential in a second indication, multiple sclerosis (MS). We make minor adjustments to our valuation, increasing it slightly to €266m.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/15	7.2	(0.1)	(0.01)	0.0	N/A	N/A
12/16	5.0	(4.7)	(0.17)	0.0	N/A	N/A
12/17e	4.2	(6.1)	(0.21)	0.0	N/A	N/A
12/18e	4.5	(6.8)	(0.24)	0.0	N/A	N/A

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

Financials: FY16 EBIT matches our estimate

Oryzon's FY16 results released on 24 February 2016 showed full year revenues at €735k (our estimate was €915k), consisting of a reimbursement payment from Roche and the recognition of deferred income. In addition, the company recorded €4.3m in income to account for the capitalisation of development costs, higher than our expected €3.9m. FY16 R&D costs of €5.2m were slightly ahead of our estimate of €4.8m, while personnel expenses of €2.5m were spot on. Adding other operating costs, Oryzon's operating loss was €4.6m, close to our expectation of €4.7m.

R&D pipeline progress

Roche, Oryzon's partner for ORY-1001, has initiated its first clinical Phase I trial in small cell lung cancer with the first patient dosed in January 2017. Roche took over the development of the asset after Oryzon presented positive Phase I/IIa data in December 2016. The next catalyst for Oryzon is a data readout from Phase I with its second lead candidate, ORY-2001. Oryzon announced that it will present the findings during the presentation on 31 March 2017 at the 13th International Conference on Alzheimer's and Parkinson's Diseases in Vienna, Austria. ORY-2001 is selective dual LSD1-MAOB inhibitor and the first-in-man clinical trial with 88 healthy volunteers sought to assess safety, the PK/PD profile and a potential biomarker for the drug. Subject to favourable data, ORY-2001 could move to Phase II in H217 to be investigated in AD patients for the first time, while other neurodegenerative diseases may also be added with fresh preclinical data supporting MS.

Valuation: Slightly upped to €266m or €9.3/share

We value Oryzon at €266m or €9.3/share, slightly up from €250m or €8.8/share previously. The main changes include the revision of our forecasts following FY16 results and rolling our model forward, while we keep our valuation assumptions unchanged. The next catalyst is Phase I data; however, we also look forward to any new details about ORY-3001, which is approaching clinical testing.

13 March 2017

Price	**€4.18**
Market cap	**€119m**
Net cash (€m) at end Q416 (including term deposits)	4.3
Shares in issue	28.5m
Free float	30%
Code	ORY
Primary exchange	Madrid Stock Exchange
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(4.5)	(10.5)	27.0
Rel (local)	(10.5)	(18.0)	11.3
52-week high/low		€5.1	€2.6

Business description

Oryzon Genomics is a Spanish biotechnology company focused on developing novel epigenetic compounds. Lead compound ORY-1001 is partnered with Roche, which is responsible for further development in acute leukaemia and SCLC. ORY-2001 has potential for Alzheimer's disease and has entered Phase I. ORY-3001 is a new preclinical asset.

Next events

ORY-2001 Phase I results	H117
News from Roche on ORY-1001 in AML	2017

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Edison profile page

Fresh preclinical ORY-2001 data for MS

Initially, ORY-2001 demonstrated efficacy in preclinical dementia models and AD was therefore selected as a primary indication. However, following the insights from biomarker analysis showing ORY-2001's down-regulating effect on neuroinflammatory genes, including S100A9, Oryzon investigated ORY-2001 in an experimental autoimmune encephalomyelitis (EAE) mice model, a widely used proxy for MS, which has been shown to up-regulated S100A9. First preclinical data from this study supporting ORY-2001 for MS were announced in September 2016 and discussed in our previous report. We subsequently included the indication in our valuation.

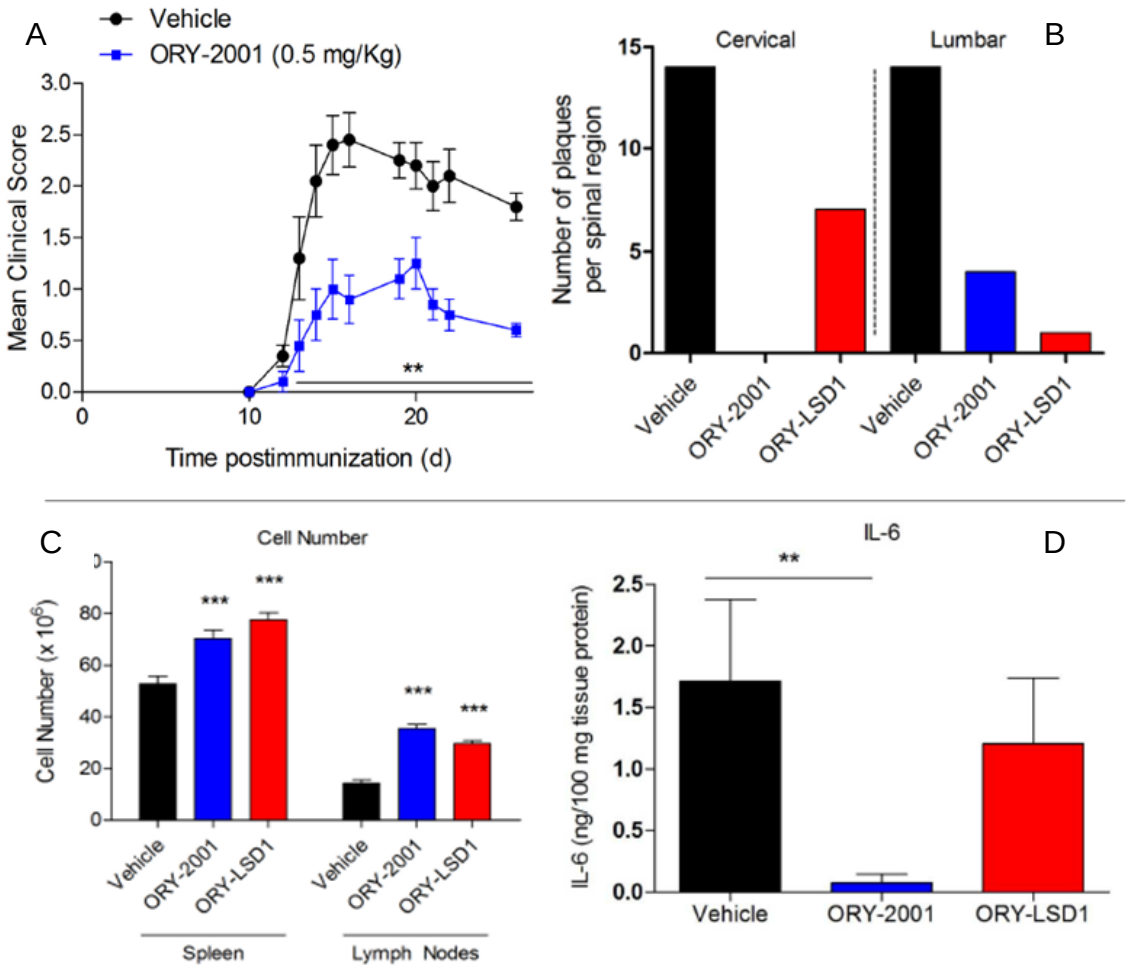
The new set of data was presented at the second annual conference of the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) in Orlando, Florida, in February 2017 and expands on the insights presented in September 2016. During the study mice were injected with a specific peptide, which triggered an autoimmune reaction and the production of antibodies against the myelin sheet protecting the motor neurons. A gradual demyelination (destruction of the neurons' protective sheet) leads to the development of different degrees of paralysis, mimicking the natural course of MS. The study included a vehicle (sham) and two controlled arms: EAE mice treated with ORY-2001 (dual LSD1-MAO-B inhibitor) and ORY-LSD1 (proprietary selective LSD1 inhibitor). Key findings include:

- When administered from the onset of the first symptoms, ORY-2001 provided an effective and long-lasting protection in terms of survival and mobility, therefore decreasing the development of EAE (Exhibit 1A). This was observed even at very low doses of ORY-2001 (0.05mg/kg; up to 3mg/kg safely tested).
- The histopathological analysis two weeks after the first symptoms showed a substantially lower number of demyelination plaques in the lumbar and cervical regions of ORY-2001-treated animals (Exhibit 1B).
- Treatment with ORY-2001 and ORY-LSD1 resulted in a significant increase in the number of immune cells retained in the spleen and lymph nodes of treated animals, suggesting a reduced egress of lymphocytes from immune tissues (egress is usually associated with an inflammatory response) (Exhibit 1C).
- Treatment with ORY-2001 also caused a reduction of various pro-inflammatory cytokines such as IL-6 and IL-1beta and chemokines such as IP-10 and MCP-1, which are involved in inflammation leading to the destruction of motor neurons in MS.

Cumulatively, these findings indicate that ORY-2001 shows an ability to counteract a number of pathophysiological processes associated with MS and that the dual inhibition of LSD1-MAOB (ORY-2001's mechanism of action) appears to be more efficacious in this context than LSD1 inhibition alone.

MS is an autoimmune disease that attacks and destroys neurons in the central nervous system to variable degrees and causes significant physical disability. The hallmark of MS is episodic relapses that occur months or years apart and affect various anatomic locations. Around 400,000 people are diagnosed with MS in the US each year and around 85% of those have a relapsing-remitting course of the disease, which is in contrast to the progressive type when symptoms gradually get worse over time rather than appearing as relapses (source: Multiple Sclerosis, Medscape). We discussed the MS market potential including the competitive landscape in more detail in our previous report.

Exhibit 1: Effects of the treatment with ORY-2001 in EAE mice model



Source: T. Maes et al. ORY-2001 Reduces Lymphocyte Egress and Demyelination in Experimental Autoimmune Encephalomyelitis and Highlights the Epigenetic Axis in Multiple Sclerosis. Presented at the second annual conference of ACTRIMS, February 2017. Note: Clinical score reflects the extent of the paralysis – 0 = no signs; 5.0 = hind and foreleg paralysis.

Valuation

We value Oryzon at €266m or €9.3/share, slightly up from €250m or €8.8/share previously. The main changes include the revision of our estimates to reflect higher R&D costs and rolling our model forward. We have not made any significant changes to our valuation assumptions, which are included in more detail for all projects in our previous reports. We are still not including ORY-3001 in our rNPV calculations, although Oryzon is clearly making progress, with the latest update being the indication that this asset may be ready for Phase I in H217. We will revisit ORY-3001 when more details are announced, eg the exact indications that the project will include and potential timelines.

Exhibit 2: Oryzon rNPV valuation

Product	Indication	Launch	Peak sales* (US$m)	Value (€m)	Probability (%)	rNPV (€m)	NPV/share (€/share)
ORY-1001	AML	2022	900	259.0	20%	60.0	2.1
ORY-1001	SCLC	2025	635	121.8	12%	21.8	0.8
ORY-2001	AD	2026	4,510	813.0	12%	99.7	3.5
ORY-2001	MS	2026	1,940	359.5	20%	80.1	2.8
Net cash (end-2016)				4.3	100%	4.3	0.2
Valuation				1,557.6		265.8	9.3

Source: Edison Investment Research. Note: *Peak sales are rounded to the nearest US$10m, shown in US$. SCLC = small cell lung cancer; AML = acute myeloid leukaemia; AD = Alzheimer's disease; MS = multiple sclerosis. Net cash includes term deposits.

Financials

In FY16 Oryzon reported revenues of €735k (our estimate was €915k), which consisted of a reimbursement payment from Roche according to the R&D collaboration agreement (separate to the ORY-1001 licensing deal) and the recognition of deferred in income after a milestone payment of $4m from Roche in July 2015. In addition, the company recorded €4.3m income to account for the capitalisation of the development costs. Oryzon follows Spanish GAAP and research costs are expensed, while development costs can be capitalised by recognising income in the P&L statement. As this capitalisation level was above our expectations of €3.9m, we have therefore increased our forecasts.

Oryzon reported FY16 R&D costs of €5.2m, slightly ahead of our estimate of €4.8m, while personnel expenses of €2.5m were spot on. Adding other operating costs, Oryzon's operating loss was €4.6m, close to our expectation of €4.7m. We initially expected 2017 R&D costs to come in lower than 2016 after Roche took over the development of ORY-1001. However, in recent months Oryzon disclosed the third asset, ORY-3001, which is undergoing preclinical testing, and is ramping up the development of ORY-2001 in at least two indications currently, with potential to expand. We have therefore revised our 2017 R&D costs estimates upwards, which is the main change in our forecasts. This was offset by higher than expected capitalisation level, leading to a negligible effect on EPS in 2017 and a slight positive effect in 2018.

The 2016 year-end cash position was €27.3m (cash and term deposits classed as other current assets) and net cash of €4.3m (including term deposits); we expect cash to be at €14.4m by the end-2017. In total, during 2016 Oryzon managed to attract around €16m in new funding, assuming debt at attractive commercial terms. In addition, the company has a history of efficient use of available public grants, which could provide further non-dilutive financing (most recently it received a small public grant of $0.8m in December 2016).

Exhibit 3: Key changes to our financial forecasts

€m	2016			2017e			2018e
	Estimate	Actual	Change (%)	Old	New	Change (%)	New
Revenue	4.835	5.009	+4%	2.797	4.156	+49%	4.515
Gross profit	4.835	5.009	+4%	2.797	4.156	+49%	4.515
R&D costs	(4.783)	(5.210)	N/M	(3.774)	(5.274)	N/M	(6.041)
Operating profit (reported)	(4.715)	(4.578)	N/M	(6.281)	(5.783)	N/M	(6.682)
Profit before tax (reported)	(5.708)	(5.480)	N/M	(7.124)	(7.052)	N/M	(7.896)
Profit after tax (reported)	(5.312)	(5.448)	N/M	(7.124)	(7.052)	N/M	(7.896)
EPS reported (€)	(0.19)	(0.20)	N/M	(0.25)	(0.25)	N/M	(0.28)

Source: Oryzon accounts, Edison Investment Research

Exhibit 4: Financial summary

EUR'000s	2013	2014	2015	2016	2017e	2018e
December	Local GAAP	Local GAAP	Local GAAP	Local GAAP	Local GAAP	Local GAAP
PROFIT & LOSS						
Revenue	2,360	15,536	7,185	5,009	4,156	4,515
Cost of Sales	0	0	0	0	0	0
Gross Profit	2,360	15,536	7,185	5,009	4,156	4,515
Research and development	(873)	(1,108)	(3,191)	(5,210)	(5,274)	(6,041)
EBITDA	(94)	11,659	688	(3,721)	(4,749)	(5,537)
Operating Profit (before amort. and except.)	(370)	11,398	448	(3,879)	(4,845)	(5,633)
Intangible Amortisation	(657)	(657)	(657)	(695)	(938)	(1,049)
Exceptionals	(186)	(4,617)	(24)	(4)	0	0
Other	0	0	0	0	0	0
Operating Profit	(1,213)	6,124	(233)	(4,578)	(5,783)	(6,682)
Exceptionals	0	667	(169)	(58)	0	0
Net Interest	(672)	(52)	(553)	(844)	(1,269)	(1,214)
Profit Before Tax (norm)	(1,042)	11,346	(105)	(4,724)	(6,115)	(6,847)
Profit Before Tax (reported)	(1,885)	6,739	(955)	(5,480)	(7,052)	(7,896)
Tax	89	(88)	(37)	32	0	0
Profit After Tax (norm)	(953)	11,258	(142)	(4,692)	(6,115)	(6,847)
Profit After Tax (reported)	(1,796)	6,651	(992)	(5,448)	(7,052)	(7,896)
Average Number of Shares Outstanding (m)	23.0	23.3	24.7	27.6	28.5	28.5
EPS - normalised (EUR)	(0.04)	0.48	(0.01)	(0.17)	(0.21)	(0.24)
EPS - (reported) (EUR)	(0.08)	0.29	(0.04)	(0.20)	(0.25)	(0.28)
Dividend per share (EUR)	0.0	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	100.0	100.0	100.0	100.0	100.0	100.0
EBITDA Margin (%)	N/A	75.0	9.6	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	73.4	6.2	N/A	N/A	N/A
BALANCE SHEET						
Fixed Assets	20,128	16,059	18,050	21,269	24,390	27,760
Intangible Assets	15,825	12,928	15,188	18,810	22,028	25,494
Tangible Assets	1,159	981	854	696	600	503
Investments	3,145	2,150	2,008	1,763	1,763	1,763
Current Assets	2,851	9,999	22,681	28,475	16,993	4,532
Stocks	2	9	4	8	6	7
Debtors	663	704	940	978	959	969
Cash	2,033	3,633	19,467	22,028	10,566	3,556
Other	153	5,654	2,270	5,461*	5,461*	0
Current Liabilities	(2,724)	(3,969)	(5,296)	(7,597)	(7,557)	(8,277)
Creditors	(1,005)	(1,299)	(2,401)	(2,119)	(2,080)	(2,100)
Short term borrowings	(1,719)	(2,670)	(2,895)	(5,477)	(5,477)	(6,177)
Long Term Liabilities	(11,251)	(8,196)	(7,841)	(19,419)	(19,419)	(18,719)
Long term borrowings	(9,117)	(6,420)	(6,177)	(17,723)	(17,723)	(17,023)
Other long term liabilities	(2,134)	(1,776)	(1,664)	(1,696)	(1,696)	(1,696)
Net Assets	9,004	13,893	27,594	22,729	14,406	5,296
CASH FLOW						
Operating Cash Flow	(113)	12,178	1,076	(4,536)	(6,036)	(6,742)
Net Interest	(672)	(52)	(553)	(471)	(1,269)	(1,214)
Tax	0	0	0	0	0	0
Capex	0	0	0	(28)	0	0
Acquisitions/disposals	(677)	798	0	0	0	0
Financing	0	0	14,725	287	0	0
Other	(161)	(9,579)	605	(6,819)**	(4,156)**	946
Dividends	0	0	0	0	0	0
Net Cash Flow	(1,623)	3,345	15,853	(11,567)	(11,462)	(7,010)
Opening net debt/(cash)	7,180	8,803	5,458	(10,395)	1,172	12,634
HP finance leases initiated	0	0	0	0	0	0
Other	0	0	0	0	0	(0)
Closing net debt/(cash)	8,803	5,458	(10,395)	1,172	12,634	19,644

Source: Source: Edison Investment Research, Oryzon Genomics accounts. Note: Oryzon reports in Spanish GAAP. *Term deposits classed as other current assets. **Includes cash outflows related to development costs that were capitalised.

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