ROTH Capital Partners

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COMPANY NOTE | EQUITY RESEARCH | April 03, 2020

Healthcare: Biotechnology

Oryzon Genomics SA | ORY.SM - €2.56 - MADRID | *Buy*

Company Update

Estimates Changed

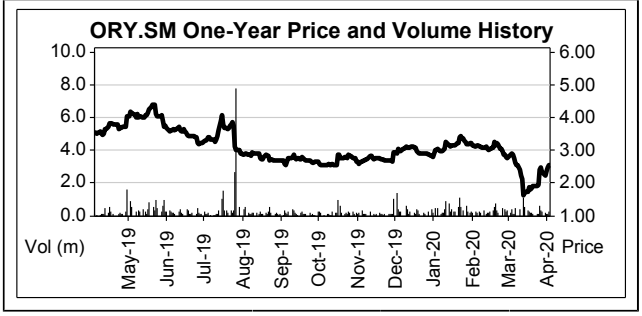
Stock Data	
52-Week Low - High	€1.48 - €4.47
Shares Out. (mil)	45.79
Mkt. Cap.(mil)	€116.99
3-Mo. Avg. Vol.	332,362
12-Mo.Price Target	€15.00
Cash (mil)	$39.6
Tot. Debt (mil)	$13.2

EPS $

Yr Dec	—2019—	—2020E—		—2021E—	
		Curr	Prev	Curr	Prev
1Q	(0.04)A	(0.10)E	(0.12)E	-	-
2Q	(0.02)A	(0.10)E	(0.12)E	-	-
3Q	(0.02)A	(0.11)E	(0.12)E	-	-
4Q	(0.02)A	(0.11)E	(0.13)E	-	-
YEAR	(0.10)A	(0.42)E	(0.49)E	(0.51)E	(0.60)E
P/E	NM	NM	NM	NM	NM

Revenue ($ millions)

Yr Dec	—2019—	—2020E—	—2021E—
		Curr	Curr
1Q	0.0A	0.0E	0.0E
2Q	0.0A	0.0E	0.0E
3Q	0.0A	0.0E	0.0E
4Q	0.0A	0.0E	0.0E
YEAR	0.0A	0.0E	0.0E



ORY.SM: Positive Vafidemstat Data in Alzheimer's Disease Presented at AAT-AD/PD

ORY released preliminary results from its Phase 2a trials in AD (REIMAGINE-AD and ETHERAL). The analyses demonstrate vafidemstat's ability to statistically control agitation and aggression in AD patients, and impact biomarkers of neuroinflammation, but thus far there is no meaningful improvement in cognition. To be fair, the trials are not powered to demonstrate a cognitive benefit at six months, but nonetheless investors are always closely watching cognitive endpoints in AD. We look forward to subsequent analyses of more mature datasets.

- ORY released preliminary results from its Phase 2a trials in AD (REIMAGINE-AD in moderate-to-severe AD and ETHERAL in mild-to-moderate AD). The analyses clearly demonstrate the ability of vafidemstat to statistically control agitation and aggression in AD patients, as well as impact biomarkers of neuroinflammation, but thus far there is no statistically significant improvement in cognition. To be fair, the trials are not powered to demonstrate a cognitive benefit at six months, but nonetheless investors are always closely watching cognitive endpoints in AD.
- In REIMAGINE-AD, we highlight the reduction of aggression as per Clinical Global Impression of Improvement (CGI-I) scale ($p<0.05$), the reduction of aggression as per Cohen-Mansfield Agitation Inventory (CMAI) scale ($p<0.05$), the reduction of aggression as per Neuropsychiatric Inventory (NPI) 4-item Agitation/Aggression subscale ($p<0.05$ for both severity x frequency and emotional distress), the global improvement on the NPI total score ($p<0.05$ for both severity x frequency and emotional distress), and the global improvement on the caregiver burden as measured by the Zarit Caregiver Burden Interview (ZBI) scale ($p<0.05$). We also note vafidemstat's highly favorable safety profile, which comes in handy particularly when considering that AD might best be treated with combination therapy and that the population in general is elderly and chronically treated and therefore safety is crucial.
- In ETHERAL, preliminary six-month results from 96 patients who completed six months of therapy showed that vafidemstat was safe and well tolerated, with significant reduction in YKL40, a CSF biomarker of inflammation for drug versus placebo ($p=0.007$ for all patients). Preliminary analysis of ADAS-Cog showed no significant differences between groups, thereby supporting ORY's decision to conduct the next AD trials specifically using endpoints of agitation-aggression, especially given the positive results in ASD, BPD, and ADHD. We look forward to full six-month ETHERAL trial data at the AAIC-2020 conference in early 3Q20.
- With $39.6 million in cash, ORY has enough cash to fund its operations through 2021, and especially in these troubled times, cash is king.

REIMAGINE-AD trial

REIMAGINE-AD is a Phase 2a trial designed to measure vafidemstat's potential in agitation-aggression in moderate-to-severe AD, recent results from which were presented at the AAT-AD/PD annual meeting. REIMAGINE-AD enrolled 12 patients and treated them for two, four, or six months with vafidemstat (1.2mg), and results after six months of treatment were reported. Vafidemstat was found to be safe and well tolerated, and it delivered a significant statistical clinical improvement in these various clinical assessment scales:

- Reduction of aggression as per Clinical Global Impression of Improvement (CGI-I) scale ($p<0.05$)
- Reduction of aggression as per Cohen-Mansfield Agitation Inventory (CMAI) scale ($p<0.05$)
- Reduction of aggression as per Neuropsychiatric Inventory (NPI) 4-item Agitation/Aggression subscale ($p<0.05$ for both severity x frequency and emotional distress)
- Global improvement on the NPI total score ($p<0.05$ for both severity x frequency and emotional distress)
- Global improvement on the caregiver burden as measured by the Zarit Caregiver Burden Interview (ZBI) scale ($p<0.05$)
- Memory/cognitive capabilities as per MMSE (in 11 patients completing 2 months of treatment) ($p<0.05$ at early time point only)

ORY noted that behavioral improvements for these older patients needed a greater treatment duration than previously reported in younger psychiatric patients in the original REIMAGINE trial. More specifically regarding the MMSE endpoint in 11 patients (one patient withdrew consent during the first two months) during the first two months, seven patients improved in MMSE, three had with stable scores, and one patient worsened. Only five (two improved, three worsened) of the 11 patients had an assessment at six months, which had a clear negative impact on the six-month p-value. Unfortunately the MMSE benefit was short-lived, being present at two months but lost at the four and six month time points for the group as a whole, despite being maintained for two of the four moderate AD patients at months four and six, which has convinced physicians to extend treatment in these two patients to 12 months. Also, there was no benefit to Clinical Global Impression of Severity (CGI-S) at six months either. While we had hoped for a demonstrable cognitive benefit to be shown in this setting, we note that six months is a relatively short time frame within which to show a cognitive benefit, and that vafidemstat can reduce agitation and aggression in moderate-to-severe AD within this time frame; we see no reason why the drug, especially with its unique mechanism of action in AD and thus the likely absence of overlapping toxicity, cannot be given in combination with one that has a more positive impact on cognition, especially given the severity of disease examined in this trial. Vafidemstat delivered compelling results across the board in the original REIMAGINE trial in ASD, BPD, and ADHD, and we are impressed with statistical significance on several distinct endpoints relating to the clear unmet need of agitation and aggression in AD. In our view, these preliminary results clearly show that vafidemstat reduces agitation and aggression in AD patients, and improves caregiver burden, and we believe that that alone is a clinically meaningful contribution.

ETHERAL trial

ETHERAL is a randomized, double-blind, three-arm, 24-week, placebo-controlled Phase 2a trial having a subsequent 24-week extension period (in which all patients receive either 0.6mg or 1.2mg vafidemstat daily) to best evaluate vafidemstat mild-to-moderate AD, an earlier AD setting than REIMAGINE-AD. Although primary endpoints are safety and tolerability, we are more interested in the secondary endpoints of cognition, function and behavior, given the trial's duration, and the trial is also measuring novel CSF biomarkers related to inflammation and neuronal damage, a very hot area of focus in this setting. Pharmacokinetic analysis statistically showed that vafidemstat acted as a selective LSD1 inhibitor ($p<0.001$ for all comparisons). Preliminary six-month results from 96 (of the 117-patients enrolled in the European cohort) patients who completed six months of therapy showed that vafidemstat was safe and well tolerated (no surprise), with seven patients reporting severe TEAEs (four placebo, two taking low dose vafidemstat, and one taking high dose vafidemstat), and a highly favorable distribution of adverse events overall. There was a significant reduction in YKL40, a CSF biomarker of inflammation for drug versus placebo ($p=0.007$ for all patients), primarily driven by moderate AD patients, as one would expect given the observation of increasing inflammation as AD progresses. There were also improvements in the levels of neurogranin (a synaptic damage biomarker) and NFL, but these differences were nonstatistical trends for the overall trial. Preliminary analysis of the gold standard ADAS-Cog clinical endpoint showed no significant differences between groups, thereby supporting ORY's decision to conduct the next AD trials specifically using endpoints of agitation-aggression, especially given the positive results in aggression and agitation endpoints from the ASD, BPD, and ADHD cohorts of the REIMAGINE trial, and the reality that improvement in these areas is clinically meaningful. Unexpected placebo group performance was observed and will require further analysis as to its contribution to the cognitive outcome. We look forward to more mature six-month ETHERAL trial data at the AAIC-2020 conference in early 3Q20.

VALUATION

Our 12-month price target of €15, is based on a DCF analysis using a 40% discount rate that is applied to all cash flows and the terminal value, which is based on a 5x multiple of our projected 2030 operating income of $1.4 billion. We arrive at this valuation by only projecting future revenue from vafidemstat in AD and iadademstat in AML. We view our valuation to be conservative given that it excludes revenue from vafidemstat in ASD, BPD, and ADHD, and from iadademstat in SCLC. Commercial success outside of the two financially modeled indications would serve as upside to our valuation. We believe that ORY.SM has prudently selected areas of unmet need and therefore market demand.

Factors that could impede shares of ORY.SM from achieving our price target include vafidemstat and iadademstat failing to generate statistically significant Phase 3 results in AD and AML, respectively. Also, regulatory agencies could fail to approve these drugs even if both Phase 3 programs are statistical successes, due to the agency viewing the results as not clinically meaningful. Loss of key management personnel could also impede achieving our price target, as could smaller than projected commercial opportunity due to changes in market size, competitive landscape, and drug pricing and reimbursement.

RISKS

- Clinical risk. ORY.SM's clinical staged products could fail to deliver statistically significant results in late-stage clinical trials, substantially reducing the value of ORY.SM's product candidates and therefore our target price.
- Regulatory risk. Even if successful in the clinic, ORY.SM's products could fail to be approved by domestic and/or foreign regulatory bodies, which would reduce ORY.SM's value and therefore our target price.
- Financing risk. ORY.SM will need additional capital to fund its operations, and such financing may not occur or it could be substantially dilutive to existing investors.
- Competitive risk. For any future approved ORY.SM products, they may not be well adopted in a competitive marketplace, which would adversely affect ORY.SM's value and therefore our target price.
- High stock price volatility. This issue is common among small-cap biotechnology companies with relatively low trading volumes.

COMPANY DESCRIPTION

Founded in 2000 in Barcelona, Spain, Oryzon (ISIN Code: ES0167733015) is a clinical stage biopharmaceutical company considered as a European champion in epigenetics. Oryzon has one of the strongest portfolios in the field. Oryzon's LSD1 program has rendered clinical stage vafidemstat and iadademstat. In addition, Oryzon has ongoing programs for developing inhibitors against other epigenetic targets. Oryzon has a strong technological platform for biomarker identification and performs biomarker and target validation for a variety of malignant and neurodegenerative diseases. Oryzon has offices in Spain and the United States

Oryzon Genomics SA
Income Statement
Fiscal Year ends December
(in 000, except per share items)

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	2017A	2018A	1Q19	2Q19	3Q19	4Q19	2019A	1Q20E	2Q20E	3Q20E	4Q20E	2020E	2021E
Global iadademstat revenue													
Global vafidemstat revenue													
Collaboration revenue	20												
Total revenue	**20**												
Cost of revenue													
R&D	6,363	8,489	2,610	3,022	3,462	3,553	12,647	3,731	4,104	4,309	4,524	16,668	22,501
G&A	4,502	2,993	876	1,042	742	516	3,176	697	704	711	718	2,828	2,970
Total operating expenses	**10,865**	**11,482**	**3,486**	**4,064**	**4,204**	**4,069**	**15,823**	**4,427**	**4,807**	**5,020**	**5,242**	**19,496**	**25,471**
Operating income	**(10,845)**	**(11,482)**	**(3,486)**	**(4,064)**	**(4,204)**	**(4,069)**	**(15,823)**	**(4,427)**	**(4,807)**	**(5,020)**	**(5,242)**	**(19,496)**	**(25,471)**
Other income (net)	5,659	8,143	2,497	2,516	3,208	3,301	11,522					-	
Net income (pretax)	**(5,186)**	**(3,339)**	**(989)**	**(1,548)**	**(996)**	**(768)**	**(4,301)**	**(4,427)**	**(4,807)**	**(5,020)**	**(5,242)**	**(19,496)**	**(25,471)**
Net financial & tax	1,047	(1,991)	368	(924)	73	296							
Net income	**(6,233)**	**(1,348)**	**(1,357)**	**(624)**	**(1,069)**	**(1,064)**	**(4,301)**	**(4,427)**	**(4,807)**	**(5,020)**	**(5,242)**	**(19,496)**	**(25,471)**
EPS basic	**(0.20)**	**(0.04)**	**(0.04)**	**(0.02)**	**(0.02)**	**(0.02)**	**(0.10)**	**(0.10)**	**(0.10)**	**(0.11)**	**(0.11)**	**(0.42)**	**(0.51)**
EPS diluted	**(0.20)**	**(0.04)**	**(0.04)**	**(0.02)**	**(0.02)**	**(0.02)**	**(0.10)**	**(0.10)**	**(0.10)**	**(0.11)**	**(0.11)**	**(0.42)**	**(0.51)**
Basic shares outstanding	31,711	34,638	38,455	38,638	43,677	45,489	41,589	45,943	46,403	46,867	47,336	46,637	49,702
Diluted shares outstanding	31,711	34,638	38,455	38,638	43,677	45,489	41,565	45,943	46,403	46,867	47,336	46,637	49,702

Source: SEC filings, company press releases, and ROTH Capital Partners

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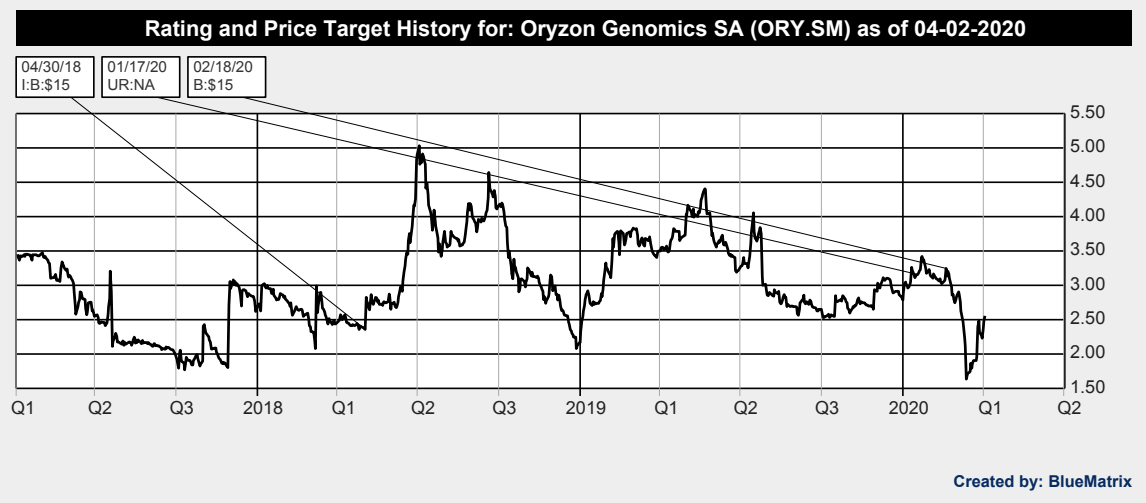
Disclosures:

Shares of Oryzon Genomics SA may be subject to the Securities and Exchange Commission's Penny Stock Rules, which may set forth sales practice requirements for certain low-priced securities.



Each box on the Rating and Price Target History chart above represents a date on which an analyst made a change to a rating or price target, except for the first box, which may only represent the first note written during the past three years. **Distribution Ratings/IB Services** shows the number of companies in each rating category from which Roth or an affiliate received compensation for investment banking services in the past 12 month.

Distribution of IB Services Firmwide

			IB Serv./Past 12 Mos. as of 04/03/20	
Rating	**Count**	**Percent**	**Count**	**Percent**
Buy [B]	**260**	**74.07**	**150**	**57.69**
Neutral [N]	**60**	**17.09**	**28**	**46.67**
Sell [S]	**3**	**0.85**	**1**	**33.33**
Under Review [UR]	**27**	**7.69**	**12**	**44.44**

Our rating system attempts to incorporate industry, company and/or overall market risk and volatility. Consequently, at any given point in time, our investment rating on a stock and its implied price movement may not correspond to the stated 12-month price target.

Ratings System Definitions - ROTH employs a rating system based on the following:

Buy: A rating, which at the time it is instituted and or reiterated, that indicates an expectation of a total return of at least 10% over the next 12 months.

Neutral: A rating, which at the time it is instituted and or reiterated, that indicates an expectation of a total return between negative 10% and 10% over the next 12 months.

Sell: A rating, which at the time it is instituted and or reiterated, that indicates an expectation that the price will depreciate by more than 10% over the next 12 months.

Under Review [UR]: A rating, which at the time it is instituted and or reiterated, indicates the temporary removal of the prior rating, price target and estimates for the security. Prior rating, price target and estimates should no longer be relied upon for UR-rated securities.

Not Covered [NC]: ROTH does not publish research or have an opinion about this security.

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