ROTH Capital Partners

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COMPANY NOTE | EQUITY RESEARCH | November 15, 2021

Healthcare: Biotechnology **Company Update**

Oryzon Genomics SA | ORY.SM - €3.10 - MADRID | *Buy*

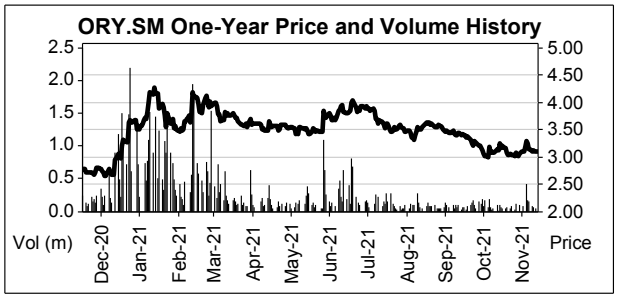
Stock Data	
52-Week Low - High	€2.61 - €4.40
Shares Out. (mil)	53.06
Mkt. Cap.(mil)	€164.49
3-Mo. Avg. Vol.	86,444
12-Mo.Price Target	€15.00
Cash (mil)	$35.8
Tot. Debt (mil)	$14.9

Revenue ($ millions)

Yr Dec	—2020—	—2021E—	—2022E—
		Curr	Curr
1Q	0.0A	0.0A	-
2Q	0.0A	0.0A	-
3Q	0.0A	0.0A	-
4Q	0.0A	0.0E	-
YEAR	0.0A	0.0E	0.0E

EPS $

Yr Dec	—2020—	—2021E—	—2022E—
		Curr	Curr
1Q	(0.03)A	(0.04)A	(0.05)E
2Q	0.00A	0.02A	(0.05)E
3Q	(0.02)A	(0.03)A	(0.05)E
4Q	(0.03)A	(0.04)E	(0.06)E
YEAR	(0.08)A	(0.10)E	(0.21)E
P/E	NM	NM	NM



ORY: In Vitro LSD1 Inhibitor Comparison Shows Differentiation of Iadademstat

ORY published a peer-reviewed article comparing *in vitro* results obtained with 10 LSD1 inhibitors (citation) and found that iadademstat, its LSD1 inhibitor that is currently in the clinic for AML and SCLC, had certain superior properties. There were substantial differences in potency and selectivity among LSD1 inhibitors evaluated, with iadademstat being the most potent. The preclinical work also showed that LSD1 inhibitors used as research tools have very low activity and selectivity, and thus are likely not optimally clinically predictive.

- Lysine-specific demethylase 1 (LSD1) is integrated in several chromatin modifying multiprotein complexes such that it can demethylate lysines on certain histone and nonhistone proteins to either repress or activate gene expression, depending upon the circumstances. Given the overexpression of LSD1 in many cancers, LSD1 inhibitors, like ORY's iadademstat, are in clinical development in a broad array of cancers. The current paper describes the results of *in vitro* assays comparing 10 LSD1 inhibitors, five research tool compounds and five clinical-stage drug candidates. The clinical compounds include CC-90011 (pulrodemstat), GSK-2879552, IMG-7289 (bomedemstat), SP-2577 (seclidemstat), and iadademstat. The publication attempts to characterize *in vitro*, under the same experimental conditions, the entire small molecule LSD1 inhibitor class in oncology.
- Iadademstat was shown to be differentiated from the 10 compounds on several parameters, including LDS1 IC_{50}, selectivity versus LSD2 inhibition, efficacy against various AML cell lines (i.e., cell viability, percent LSD1 engagement, CD11b expression (cell differentiation marker), and interaction with GFI1 peptide) and efficacy against the NCI-H510A SCLC cell line (cell viability, percent LSD1 engagement, GRP expression (an established SCLC marker), and INSM1:LSD1 interaction (a well-established driver of SCLC)).
- This side by side characterizing of the entire LSD1 inhibitor compound class (research tools and clinical stage oncology candidates) finally allows for the comparison of potency, selectivity, and cellular activity among these related compounds. In general, the potency ranking of catalytic inhibition paralleled LSD1 target engagement and consequently the capacity to disrupt the SNAG-domain/LSD1 protein-protein interaction (higher disruption means higher anticancer potency). Regulation of cell differentiation markers (i.e., induction of CD11b in AML cell lines and repression of GRP in the NCI-H510A SCLC cell line) also paralleled anticancer effects. Iadademstat and research tool OG-668 were found to be the most potent irreversible inhibitors in all *in vitro* assays performed, as OG-668 is known to be a robust *in vitro* research tool. Clinical stage compounds GSK-2879552 and bomedemstat are notably less potent than iadademstat (e.g., GSK-2879552 and bomedemstat are 491-fold and 174-fold less active than iadademstat in the *(text continued on page 2)*

(ORY traded intraday at €3.12 at 1:16PM GMT+1)

- *(text continued from page 1)* LSD1 HTRF assay (measures IC_{50}), respectively, and 849-fold and 345-fold less active in AML viability assays, respectively), in line with their lower LSD1 target engagement. The experiments demonstrate OG-668 to be the preferred *in vitro* research tool and iadademstat to be the most potent clinical stage candidate.

VALUATION

Our 12-month price target of €15, is based on a DCF analysis using a 35% discount rate that is applied to all cash flows and the terminal value, which is based on a 4x multiple of our projected 2030 operating income of $915 million. We arrive at this valuation by only projecting future revenue from vafidemstat in borderline personality disorder and iadademstat in AML and SCLC. We view our valuation to be conservative given that it excludes revenue from vafidemstat in ASD, AD, and ADHD. Commercial success outside the three 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	2019A	2020A	1Q21A	2Q21A	3Q21A	4Q21E	2021E	1Q22E	2Q22E	3Q22E	4Q22E	2022E	2023E
Global iadademstat revenue															
Global vafidemstat revenue															
Collaboration revenue	20														
Total revenue	**20**														
Cost of revenue															
R&D	6,363	8,489	12,647	13,591	4,278	2,928	3,982	4,380	15,568	4,599	4,829	5,071	5,324	19,823	25,770
G&A	4,502	2,993	3,176	3,484	1,302	1,200	1,070	1,081	4,653	1,092	1,102	1,113	1,125	4,432	7,978
Total operating expenses	**10,865**	**11,482**	**15,823**	**17,075**	**5,580**	**4,128**	**5,052**	**5,461**	**20,221**	**5,691**	**5,932**	**6,184**	**6,449**	**24,255**	**33,748**
Operating income	**(10,845)**	**(11,482)**	**(15,823)**	**(17,075)**	**(5,580)**	**(4,128)**	**(5,052)**	**(5,461)**	**(20,221)**	**(5,691)**	**(5,932)**	**(6,184)**	**(6,449)**	**(24,255)**	**(33,748)**
Other income (net)	5,659	8,143	11,522	11,805	3,536	2,256	3,252	3,000	12,044	3,000	3,000	3,000	3,000	12,000	
Net income (pretax)	**(5,186)**	**(3,339)**	**(4,301)**	**(5,269)**	**(2,044)**	**(1,872)**	**(1,800)**	**(2,461)**	**(8,177)**	**(2,691)**	**(2,932)**	**(3,184)**	**(3,449)**	**(12,255)**	**(33,748)**
Net financial & tax	1,047	(1,991)	(187)	(1,098)	89	(2,823)	36	50	(2,648)	50	50	50	50	200	
Net income	**(6,233)**	**(1,348)**	**(4,114)**	**(4,171)**	**(2,133)**	**951**	**(1,836)**	**(2,511)**	**(5,529)**	**(2,741)**	**(2,982)**	**(3,234)**	**(3,499)**	**(12,455)**	**(33,748)**
EPS basic	**(0.20)**	**(0.04)**	**(0.10)**	**(0.08)**	**(0.04)**	**0.02**	**(0.03)**	**(0.04)**	**(0.10)**	**(0.05)**	**(0.05)**	**(0.05)**	**(0.06)**	**(0.21)**	**(0.54)**
EPS diluted	**(0.20)**	**(0.04)**	**(0.10)**	**(0.08)**	**(0.04)**	**0.02**	**(0.03)**	**(0.04)**	**(0.10)**	**(0.05)**	**(0.05)**	**(0.05)**	**(0.06)**	**(0.21)**	**(0.54)**
Basic shares outstanding	31,711	34,638	41,589	49,235	52,762	52,762	52,762	59,093	54,344	59,152	59,211	59,270	59,330	59,241	62,296
Diluted shares outstanding	31,711	34,638	41,565	49,235	52,762	52,762	52,762	59,093	54,344	59,152	59,211	59,270	59,330	59,241	62,296

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

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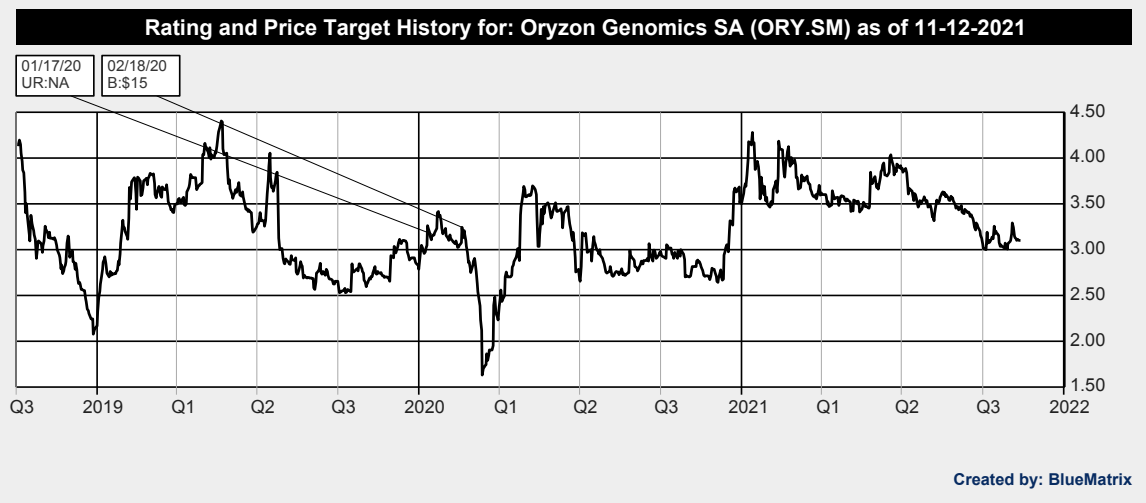
Disclosures:



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 11/15/21	
Rating	**Count**	**Percent**	**Count**	**Percent**
Buy [B]	**324**	**78.64**	**220**	**67.90**
Neutral [N]	**49**	**11.89**	**28**	**57.14**
Sell [S]	**1**	**0.24**	**0**	**0**
Under Review [UR]	**38**	**9.22**	**25**	**65.79**

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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