ROTH Capital Partners

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COMPANY NOTE | EQUITY RESEARCH | April 18, 2022

Healthcare: Biotechnology **Company Update**

Oryzon Genomics SA | ORY.SM - €2.59 - MADRID | *Buy*

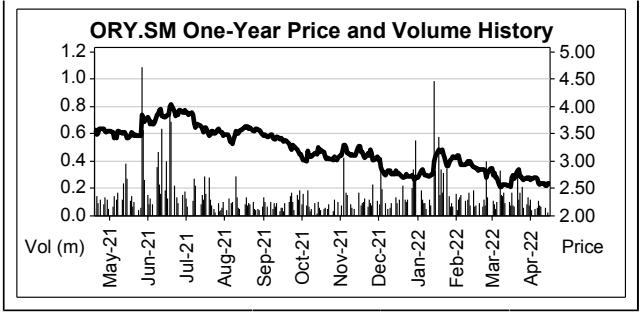
Stock Data	
52-Week Low - High	€2.43 - €4.10
Shares Out. (mil)	53.06
Mkt. Cap.(mil)	€137.43
3-Mo. Avg. Vol.	133,187
12-Mo.Price Target	€15.00
Cash (mil)	$32.5
Tot. Debt (mil)	$17.0

Revenue ($ millions)

Yr Dec	—2021—	—2022E—	—2023E—
		Curr	Curr
1Q	0.0A	0.0E	-
2Q	0.0A	0.0E	-
3Q	0.0A	0.0E	-
4Q	0.0A	0.0E	-
YEAR	0.0A	0.0E	0.0E

EPS $

Yr Dec	—2021—	—2022E—	—2023E—
		Curr	Curr
1Q	(0.04)A	(0.05)E	-
2Q	0.02A	(0.05)E	-
3Q	(0.03)A	(0.05)E	-
4Q	(0.04)A	(0.06)E	-
YEAR	(0.10)A	(0.21)E	(0.40)E
P/E	NM	NM	NM



ORY: AACR Poster Makes Case for LSD1 Inhibition & ICI Combo Therapy in SCLC

An AACR poster described a rationale for combination therapy with an LSD1 inhibitor and an immune checkpoint inhibitor in patients with SCLC. LSD1 inhibition was shown to restore expression of MHC-I protein and MHC-I-mediated antigen processing and presentation in SCLC cell lines, thereby restoring the utility of checkpoint inhibition in mouse models of SCLC. Regarding ORY's AML program, a paper was recently published supporting evaluation of dual FLT3 and LSD1 inhibition in AML patients with FLT3-mutated disease.

- At AACR, there was a poster presented by MSKCC (abstract 1370) describing how inhibiting LSD1 rescued the ability of SCLC cell lines to present antigens in the context of MHC-I. The authors inhibited LSD1 with iadademstat and RNA interference and saw a strong correlation between LSD1 inhibition and expression of MHC-I protein and MHC-I-mediated antigen processing and presentation. LSD1 inhibition also enabled MHC-I-restricted T cell-mediated cytolysis when the SCLC cells were engineered to express NY-ESO1 and co-cultured with pre-activated NYESO1-specific CD8+ T cells. The authors then conducted *in vivo* experiments in which SCLC cells were engrafted into syngenic mice. The mice were then treated with iadademstat and an anti-PD-L1 immune checkpoint inhibitor, or just iadademstat alone. The combination therapy was found to resensitize SCLC tumors to anti-PD-L1 therapy that were previously resistant to anti-PD-L1 therapy, whereas anti-PD-L1 therapy alone did not impede tumor growth. The results demonstrate that LSD1 is a negative regulator of MHC-I, given that LSD1 inhibition restores expression of MHC-I protein and MHC-I-mediated antigen processing and presentation. It would therefore make sense to clinically evaluate the combination of an LSD1 inhibitor such as iadademstat with immune checkpoint inhibitors in SCLC, especially since SCLC tumors are known to exhibit low or absent MHC-I expression.

- Unrelated to AACR, a recent publication showed that LSD1 inhibition augments the effect FLT3 kinase inhibition in most of the 66 FLT3-mutant primary AML cell isolates evaluated, resulting in synergistic cell death. The combination therapy activated a pro-differentiative epigenetic and transcriptional program while also suppressing the activity of MYC target genes, largely through suppression of MYC-bound promoters and the activation of PU.1-bound enhancers. STAT5 was determined to be a putative regulator of MYC gene expression, and FLT3 inhibition resulted in a loss of STAT5 binding at the MYC blood super-enhancer and a loss of super-enhancer activation. LSD1 inhibition prevented the removal of repressive H3K9me1 marks at MYC target genes, resulting in suppression of MYC expression. These results support evaluation of dual FLT3 and LSD1 inhibition in AML patients with FLT3-mutated disease.

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 4x multiple of our projected 2030 operating income of $1.42 billion. We arrive at this valuation by projecting future revenue from vafidemstat in borderline personality disorder and Kabuki syndrome, as well as iadademstat in AML and SCLC.

Factors that could impede shares of ORY.SM from achieving our price target include vafidemstat and iadademstat failing to generate statistically significant clinical results. Also, regulatory agencies could fail to approve these drugs even if pivotal clinical trials 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 the European leader in epigenetics. Oryzon has one of the strongest portfolios in the field, with two LSD1 inhibitors, iadademstat and vafidemstat, in Phase II clinical trials, and other pipeline assets directed against other epigenetic targets. In addition, Oryzon has a strong platform for biomarker identification and target validation for a variety of malignant and neurological diseases.

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

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	2017A	2018A	2019A	2020A	1Q21	2Q21	3Q21	4Q21	2021A	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	3,930	15,118	4,127	4,333	4,549	4,777	17,786	23,121
G&A	4,502	2,993	3,176	3,484	1,302	1,200	1,070	1,957	5,529	1,566	1,581	1,597	1,613	6,357	8,264
Total operating expenses	**10,865**	**11,482**	**15,823**	**17,075**	**5,580**	**4,128**	**5,052**	**5,887**	**20,647**	**5,692**	**5,914**	**6,147**	**6,390**	**24,143**	**31,386**
Operating income	**(10,845)**	**(11,482)**	**(15,823)**	**(17,075)**	**(5,580)**	**(4,128)**	**(5,052)**	**(5,887)**	**(20,647)**	**(5,692)**	**(5,914)**	**(6,147)**	**(6,390)**	**(24,143)**	**(31,386)**
Other income (net)	5,659	8,143	11,522	11,805	3,536	2,256	3,252	3,466	12,510	3,000	3,000	3,000	3,000	12,000	6,000
Net income (pretax)	**(5,186)**	**(3,339)**	**(4,301)**	**(5,269)**	**(2,044)**	**(1,872)**	**(1,800)**	**(2,421)**	**(8,137)**	**(2,692)**	**(2,914)**	**(3,147)**	**(3,390)**	**(12,143)**	**(25,386)**
Net financial & tax	1,047	(1,991)	(187)	(1,098)	89	(2,823)	36	(62)	(2,760)	50	50	50	50	200	220
Net income	**(6,233)**	**(1,348)**	**(4,114)**	**(4,171)**	**(2,133)**	**951**	**(1,836)**	**(2,359)**	**(5,377)**	**(2,742)**	**(2,964)**	**(3,197)**	**(3,440)**	**(12,343)**	**(25,606)**
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)**	**(0.40)**
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)**	**(0.40)**
Basic shares outstanding	31,711	34,638	41,589	49,235	52,762	52,762	52,762	52,762	52,762	55,400	60,386	60,446	60,506	59,184	63,532
Diluted shares outstanding	31,711	34,638	41,565	49,235	52,762	52,762	52,762	52,762	52,762	55,400	60,386	60,446	60,506	59,184	63,532

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

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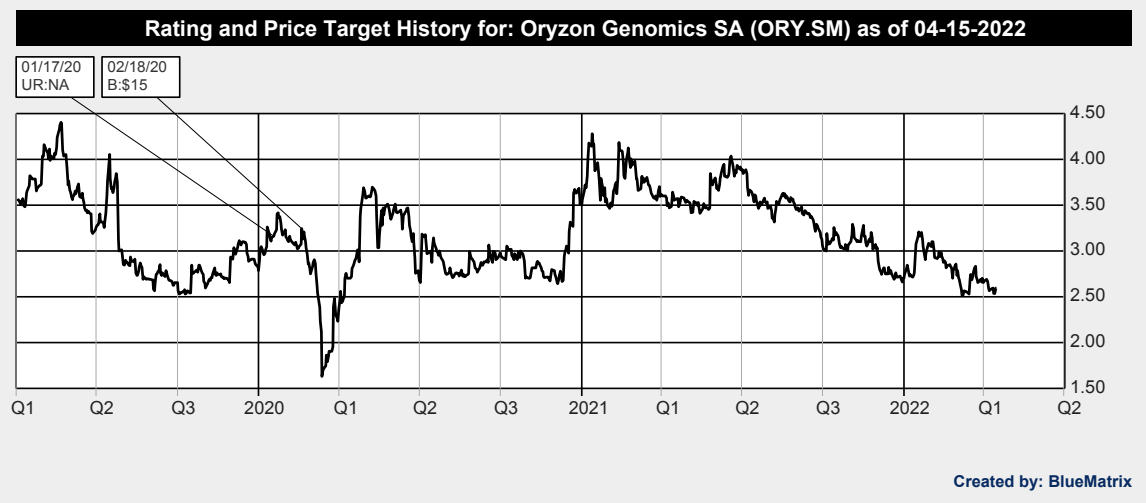
Disclosures:

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 04/18/22	
Rating	**Count**	**Percent**	**Count**	**Percent**
Buy [B]	**347**	**82.03**	**230**	**66.28**
Neutral [N]	**48**	**11.35**	**28**	**58.33**
Sell [S]	**2**	**0.47**	**1**	**50.00**
Under Review [UR]	**26**	**6.15**	**17**	**65.38**

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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