ROTH Capital Partners

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COMPANY NOTE | EQUITY RESEARCH | December 12, 2022

Healthcare: Biotechnology **Company Update**

Oryzon Genomics SA | ORY.SM - €2.09 - MADRID | *Buy*

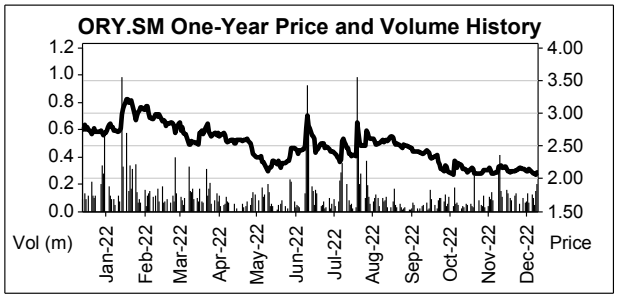
Stock Data	
52-Week Low - High	€1.98 - €3.35
Shares Out. (mil)	54.74
Mkt. Cap.(mil)	€114.41
3-Mo. Avg. Vol.	96,628
12-Mo.Price Target	€15.00
Cash (mil)	$27.1
Tot. Debt (mil)	$26.2

Revenue ($ millions)

Yr Dec	—2021—	—2022E—	—2023E—
		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	—2021—	—2022E—	—2023E—
		Curr	Curr
1Q	(0.04)A	(0.03)A	-
2Q	0.02A	0.01A	-
3Q	(0.03)A	(0.01)A	-
4Q	(0.04)A	(0.06)E	-
YEAR	(0.10)A	(0.10)E	(0.30)E
P/E	NM	NM	NM



ORY: Final Phase 2 Iadademstat Data at ASH Strongly Supports Future Development

Iadademstat plus azacitidine was safe and effective in ORY's AML trial, with no significant non-hematological toxicity observed. Responses were rapid, deep, and durable, with 86% of responders responding by two treatment cycles. Also, 36% of responders responded for ≥12 months and 30% for ≥18 months. The iadademstat RP2D is 90µg/m2/day, and we look forward to next trial results with iadademstat/chemotherapy, especially given that LSD1 target engagement consistently reaches >90%, resulting in a higher quality of response without significantly increasing toxicity.

- **Discontinuation details.** Of 36 AML patients treated, two had major protocol deviations and seven (three low dose, four high dose) died prior to their first assessment, resulting in 27 efficacy evaluable patients. At present 17 of the 27 evaluable patients are deceased and the remaining 10 are censored as of their last visit, with six known to be alive (three of whom are on compassionate use treatment) and the status of the other four, who were alive at their last visit, currently unknown.
- **Efficacy details.** Updated efficacy assessments for the 27 efficacy evaluable patients showed a CR rate of 33% (9/27), CRi rate of 19% (5/27), PR rate of 30% (8/27), SD rate of 15% (4/27), and PD rate of 4% (1/27), yielding a CR/CRi rate of 52% and an ORR of 81%. The median time to response for the 22 responders was 2.1 months, and the median duration of response was 8.8 months. Furthermore, 82% of the 11 of 14 CR or CRi patients (9/11) that were evaluated for MRD status were MRD negative, and 71% (10/14) of the total CR/CRi patient population was blood transfusion independent.
- **Mutational analysis.** Somatic mutational status at enrollment was also correlated with ORR, with 75% (6/8) TP53 mutants responding, 75% (6/8) TET2 mutants responding, 100% (7/7) RAS pathway mutants responding, 100% (6/6) DNM3TA mutants responding, 60% (3/5) SRF2 mutants responding, 100% NPM1 mutants responding, 100% (3/3) IDH1-2 mutants responding, 100% (3/3) FLT3-ITD mutants responding, 67% (2/3) ASXL1 mutants responding, 67% (2/3) CEBPA mutants responding, 67% (2/3) EZH2 mutants responding, and 33% (1/3) ETV6 mutants responding.
- **Iadademstat dose analysis.** Median OS for all 27 evaluable patents was 11.1 months, with the 60µg/m2/day dose group (n=13) at 8.1 months and the 90µg/m2/day dose group (n=14) at 12.3 months. Response rate analysis by dose yielded a 39% CR/CRi rate and 85% ORR for the lower dose, and a 65% CR/CRi rate and 79% ORR for the higher dose. Also, most of the patients with deeper responses achieved higher median iadademstat C trough levels in the 90µg/m2/day cohort, as well as higher LSD1 target engagement. Although all grade AE frequency statistically trended toward the higher dose group, that difference was not statistically different (p=0.0667). *(text continued on page 2)*

- **Bottom line.** Iadademstat plus azacitidine was safe and effective for newly diagnosed unfit/elderly AML patients, with no significant non-hematological toxicity observed. Patient responses were rapid, deep, and durable, with 86% of responders responding by two treatment cycles. Also, 36% of responders responded for ≥12 months and 30% for ≥18 months. ORY selected 90µg/m2/day as the RP2D of iadademstat in combination with standard dose azacitidine, and we look forward to the next trial results employing that regimen, especially given that LSD1 target engagement consistently reaches >90%, resulting in a higher quality of response without significantly increasing toxicity. In addition to the median OS results above, we note that 42% of patients were alive at 18 months, and that responses were seen across a broad range of AML mutations, including FLT3 and TP53 mutations, and with monocytic AML subtypes, all of which is known to correlate with a poor prognosis when only treating with standard therapy.

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 $1.17 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	1Q22A	2Q22A	3Q22A	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	4,228	4,166	4,274	4,573	17,241	21,551
G&A	4,502	2,993	3,176	3,484	1,302	1,200	1,070	1,957	5,529	1,343	1,520	659	1,384	4,906	6,378
Total operating expenses	**10,865**	**11,482**	**15,823**	**17,075**	**5,580**	**4,128**	**5,052**	**5,887**	**20,647**	**5,571**	**5,686**	**4,933**	**5,957**	**22,147**	**27,929**
Operating income	**(10,845)**	**(11,482)**	**(15,823)**	**(17,075)**	**(5,580)**	**(4,128)**	**(5,052)**	**(5,887)**	**(20,647)**	**(5,571)**	**(5,686)**	**(4,933)**	**(5,957)**	**(22,147)**	**(27,929)**
Other income (net)	5,659	8,143	11,522	11,805	3,536	2,256	3,252	3,466	12,510	3,826	3,894	4,248	3,000	14,968	6,000
Net income (pretax)	**(5,186)**	**(3,339)**	**(4,301)**	**(5,269)**	**(2,044)**	**(1,872)**	**(1,800)**	**(2,421)**	**(8,137)**	**(1,745)**	**(1,792)**	**(685)**	**(2,957)**	**(7,179)**	**(21,929)**
Net financial & tax	1,047	(1,991)	(187)	(1,098)	89	(2,823)	36	(62)	(2,760)	67	(2,139)	(67)	50	(2,089)	(2,298)
Net income	**(6,233)**	**(1,348)**	**(4,114)**	**(4,171)**	**(2,133)**	**951**	**(1,836)**	**(2,359)**	**(5,377)**	**(1,812)**	**347**	**(618)**	**(3,007)**	**(5,090)**	**(19,631)**
EPS basic	**(0.20)**	**(0.04)**	**(0.10)**	**(0.08)**	**(0.04)**	**0.02**	**(0.03)**	**(0.04)**	**(0.10)**	**(0.03)**	**0.01**	**(0.01)**	**(0.06)**	**(0.10)**	**(0.30)**
EPS diluted	**(0.20)**	**(0.04)**	**(0.10)**	**(0.08)**	**(0.04)**	**0.02**	**(0.03)**	**(0.04)**	**(0.10)**	**(0.03)**	**0.01**	**(0.01)**	**(0.06)**	**(0.10)**	**(0.30)**
Basic shares outstanding	31,711	34,638	41,589	49,235	52,762	52,762	52,762	52,762	52,762	52,762	52,762	53,609	53,662	53,199	64,395
Diluted shares outstanding	31,711	34,638	41,565	49,235	52,762	52,762	52,762	52,762	52,762	52,762	52,762	53,609	53,662	53,199	64,395

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

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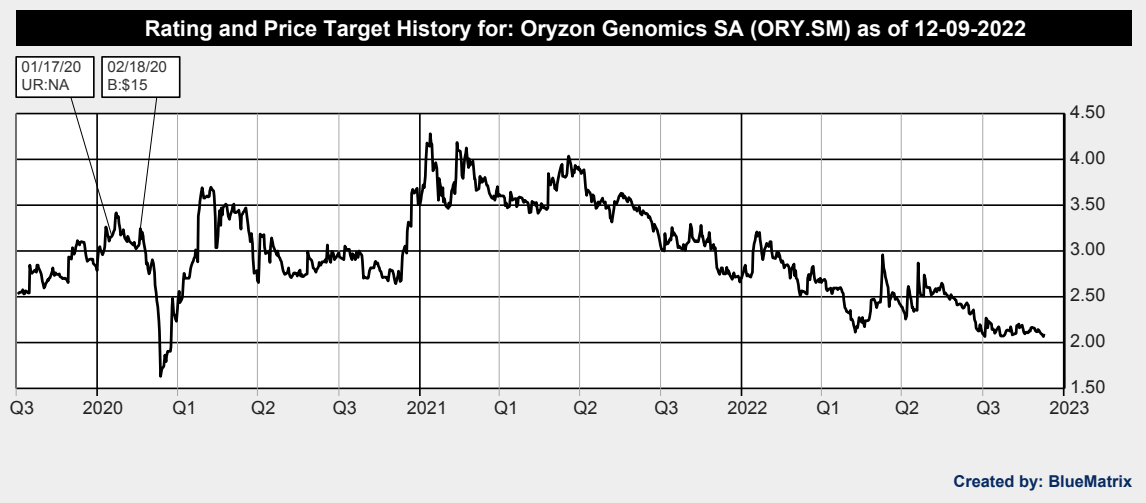
Disclosures:

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 12/12/22	
Rating	**Count**	**Percent**	**Count**	**Percent**
Buy [B]	**302**	**79.47**	**208**	**68.87**
Neutral [N]	**49**	**12.89**	**25**	**51.02**
Sell [S]	**3**	**0.79**	**2**	**66.67**
Under Review [UR]	**26**	**6.84**	**14**	**53.85**

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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