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COMPANY NOTE | EQUITY RESEARCH | February 17, 2023

Healthcare: Biotechnology

Company Update
Estimates Changed

Oryzon Genomics SA | ORY.SM - €2.49 - MADRID | *Buy*

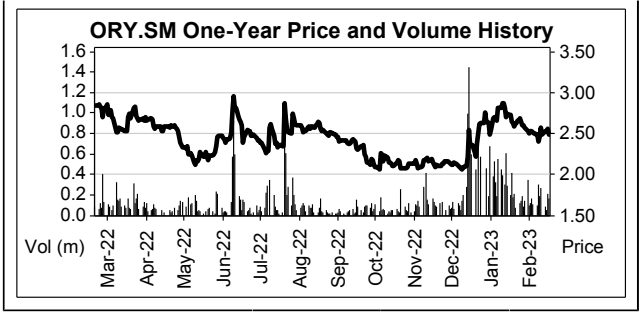
Stock Data	
52-Week Low - High	€1.98 - €3.06
Shares Out. (mil)	56.31
Mkt. Cap.(mil)	€140.22
3-Mo. Avg. Vol.	286,050
12-Mo.Price Target	€15.00
Cash (mil)	$22.7
Tot. Debt (mil)	$23.3

Revenue ($ millions)

Yr Dec	—2022—	—2023E—	—2024E—
		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	—2022—	—2023E—		—2024E—
		Curr	Prev	Curr
1Q	(0.03)A	(0.06)E	--	-
2Q	0.01A	(0.06)E	--	-
3Q	(0.01)A	(0.08)E	--	-
4Q	(0.05)A	(0.09)E	--	-
YEAR	(0.08)A	(0.29)E	(0.30)E	(0.60)E
P/E	NM	NM	NM	NM



ORY 4Q22: Four Trials Running, Four to Start, Funded Into 1H24 on Current Cash

ORY ended 4Q22 with $22.7M, enough cash to fund operations into 1H24, and ORY has access to additional convertible debt financing that it has not yet drawn down. ORY is enrolling patients into four trials, and expects to initiate four more, starting soon with the expected first patient into its FRIDA trial. ORY believes that the FRIDA trial, which is its central strategy, is iadademstat's fastest route to market. The SCLC basket, PORTICO, EVOLUTION, and schizophrenia pilot trials are enrolling.

Iadademstat

- **ALICE trial.** At ASH in 4Q22, ORY presented its final Phase 2 ALICE trial data, with the results showing that iadademstat plus azacitidine was safe and effective in elderly or unfit AML patients, 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.
- **FRIDA trial.** Regarding two iadademstat trials that have not yet enrolled any patients, ORY is done preparing its Phase 1b FRIDA trial in rel/ref AML with FLT3 mutations, which will test iadademstat plus gilteritinib in up to 45 patients. FRIDA has primary endpoints of safety, tolerability, and determining the RP2D, and secondary endpoints of efficacy (i.e., CR/CRh, DoR, MRD), and ORY will meet with the FDA to best plan development of this combination therapy. ORY believes that the FRIDA trial, which is its central strategy, is iadademstat's fastest route to market.
- **STELLAR trial.** ORY's Phase 1b/2 STELLAR trial in the U.S. in first-line SCLC is being designed, and it is a randomized, multi-center trial of iadademstat plus a checkpoint inhibitor in this setting that could potentially support accelerated approval.
- **SCLC basket trial.** ORY is also conducting a collaborative Phase 2 basket trial in the U.S. of iadademstat in combination with synergistic agents in platinum rel/ref SCLC and extrapulmonary high grade neuroendocrine tumors. The first patient was enrolled in January 2023.
- **Combination with immunotherapies.** ORY received approval by the EU intergovernmental organization EUREKA secretariat of funding for the BRAVE Project (Breaking immune Resistance of Advanced cancers by HERV-K Vaccination and Epigenetic modulation) under the Eurostars-3 program. ORY, ImProTher, and the University of Copenhagen will evaluate iadademstat in combination with various immunotherapies, including checkpoint inhibitors and/or oncological vaccines, in solid tumors. The two-year program starts in 2Q23, with a global budget of €1.4 million of which ORY will pay about half. *(text continued on page 2)*

Vafidemstat

- **PORTICO trial.** Active patient recruitment is ongoing in the randomized, 156-patient Phase 2b PORTICO trial in BPD patients at 15-20 centers in the U.S. and Europe. PORTICO's primary endpoints are reduction of aggression/ agitation and overall BPD improvement. ORY presented initial blinded safety data from the first 43 PORTICO patients at the European Conference on Mental Health in September. In short, no serious or severe adverse reactions were reported, with 41 mostly mild adverse reactions reported in 12 patients (blinded, so unknown if vafidemstat or placebo), and with no reactions leading to treatment discontinuation or patient withdrawal. PORTICO has a pre-defined interim analysis in 1Q23 on the first 90 patients that have concluded at least 2/3 of the trial. The analysis exists to adjust the sample size in case of excessive variability around the endpoints or an unexpectedly high placebo rate.
- **EVOLUTION trial.** The Phase 2b EVOLUTION trial evaluating vafidemstat in schizophrenia continues to enroll patients and is looking to establish vafidemstat efficacy on negative symptoms and cognitive impairment in patients with schizophrenia.
- **HOPE trial.** ORY is working with KOLs to finalize the design of HOPE, a randomized, double-blind, placebo-controlled, 50-60 patient Phase 1/2 personalized medicine trial with vafidemstat in Kabuki Syndrome (KS) patients. ORY is talking to regulatory agencies to refine the final design of HOPE, and should be filing an IND in 2023 in the U.S. and possibly filing to start enrolling in Europe as well.
- **Schizophrenia pilot trials.** ORY's precision medicine programs in psychiatric disease are progressing, with collaborations in autism at the Seaver Autism Center for Research and Treatment at the Icahn School of Medicine at Mount Sinai Hospital and the Institute of Medical and Molecular Genetics (INGEMM) at Hospital Universitario La Paz, as well as in schizophrenia with Columbia University. Pilot studies to characterize patients with specific mutations to inform subsequent precision psychiatry trial design with vafidemstat are ongoing with no timing guidance yet for release of results.

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 $1.04 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	2021A	1Q22	2Q22	3Q22	4Q22	2022A	1Q23E	2Q23E	3Q23E	4Q23E	2023E	2024E
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	15,118	4,228	4,166	4,274	5,033	17,701	5,184	5,340	5,500	5,665	21,688	27,110
G&A	4,502	2,993	3,176	3,484	5,529	1,343	1,520	659	1,249	4,771	1,261	1,274	1,287	1,300	5,122	11,269
Total operating expenses	**10,865**	**11,482**	**15,823**	**17,075**	**20,647**	**5,571**	**5,686**	**4,933**	**6,282**	**22,472**	**6,445**	**6,614**	**6,787**	**6,964**	**26,810**	**38,379**
Operating income	**(10,845)**	**(11,482)**	**(15,823)**	**(17,075)**	**(20,647)**	**(5,571)**	**(5,686)**	**(4,933)**	**(6,282)**	**(22,472)**	**(6,445)**	**(6,614)**	**(6,787)**	**(6,964)**	**(26,810)**	**(38,379)**
Other income (net)	5,659	8,143	11,522	11,805	12,510	3,826	3,894	4,248	4,693	16,661	3,000	3,000	2,000	2,000	10,000	
Net income (pretax)	**(5,186)**	**(3,339)**	**(4,301)**	**(5,269)**	**(8,137)**	**(1,745)**	**(1,792)**	**(685)**	**(1,589)**	**(5,811)**	**(3,445)**	**(3,614)**	**(4,787)**	**(4,964)**	**(16,810)**	**(38,379)**
Net financial & tax	1,047	(1,991)	(187)	(1,098)	(2,760)	67	(2,139)	(67)	863	(1,276)	(250)	(250)	(250)	(250)	(1,000)	(1,100)
Net income	**(6,233)**	**(1,348)**	**(4,114)**	**(4,171)**	**(5,377)**	**(1,812)**	**347**	**(618)**	**(2,452)**	**(4,535)**	**(3,195)**	**(3,364)**	**(4,537)**	**(4,714)**	**(15,810)**	**(37,279)**
EPS basic	**(0.20)**	**(0.04)**	**(0.10)**	**(0.08)**	**(0.10)**	**(0.03)**	**0.01**	**(0.01)**	**(0.05)**	**(0.08)**	**(0.06)**	**(0.06)**	**(0.08)**	**(0.09)**	**(0.29)**	**(0.60)**
EPS diluted	**(0.20)**	**(0.04)**	**(0.10)**	**(0.08)**	**(0.10)**	**(0.03)**	**0.01**	**(0.01)**	**(0.05)**	**(0.08)**	**(0.06)**	**(0.06)**	**(0.08)**	**(0.09)**	**(0.29)**	**(0.60)**
Basic shares outstanding	31,711	34,638	41,589	49,235	52,762	52,762	52,762	53,609	54,284	53,354	54,338	54,393	54,447	54,502	54,420	62,583
Diluted shares outstanding	31,711	34,638	41,565	49,235	52,762	52,762	52,762	53,609	54,284	53,354	54,338	54,393	54,447	54,502	54,420	62,583

Source: SEC filings, company press releases, and ROTH MKM

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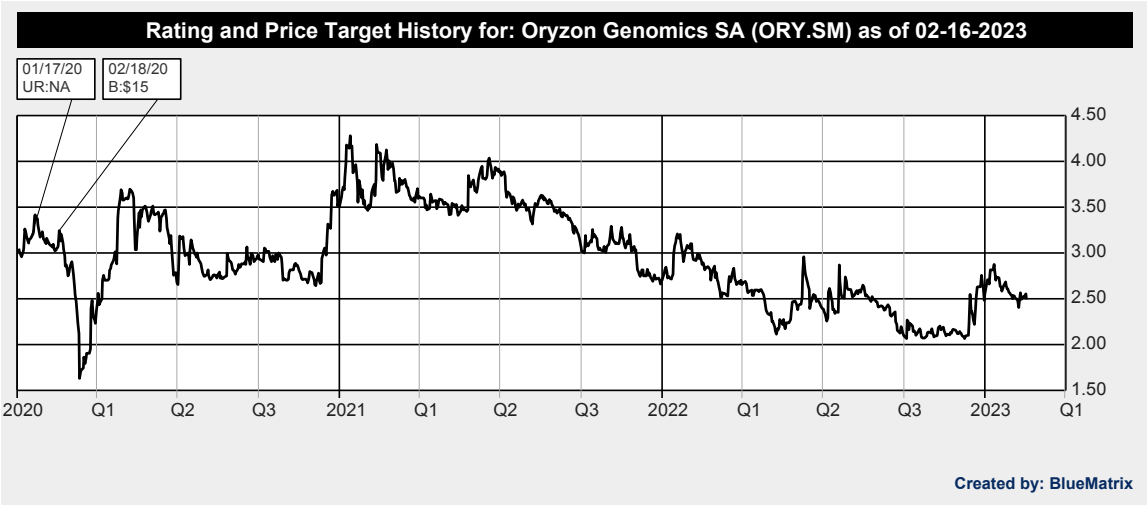
Disclosures:

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 02/17/23	
Rating	**Count**	**Percent**	**Count**	**Percent**
Buy [B]	**371**	**73.32**	**215**	**57.95**
Neutral [N]	**94**	**18.58**	**26**	**27.66**
Sell [S]	**4**	**0.79**	**1**	**25.00**
Under Review [UR]	**21**	**4.15**	**9**	**42.86**
[]	**0**	**0.00**	**0**	**0**

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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