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COMPANY NOTE | EQUITY RESEARCH | October 27, 2023

Healthcare: Biotechnology

Company Update
Estimates Changed

Oryzon Genomics SA | ORY.SM - €2.00 - MADRID | *Buy*

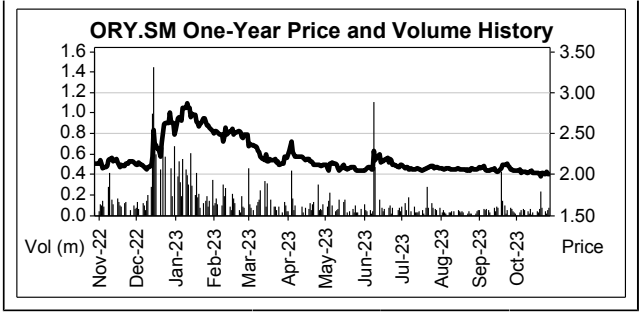
Stock Data	
52-Week Low - High	€1.86 - €2.93
Shares Out. (mil)	58.58
Mkt. Cap.(mil)	€117.16
3-Mo. Avg. Vol.	53,174
12-Mo.Price Target	€15.00
Cash (mil)	$8.8
Tot. Debt (mil)	€20.1

Rev ($M)

Yr Dec	—2022—	—2023E—	—2024E—
		Curr	Curr
1Q	0.0A	0.0A	0.0E
2Q	0.0A	0.0A	0.0E
3Q	0.0A	0.0A	0.0E
4Q	0.0A	0.0E	0.0E
YEAR	0.0A	0.0E	0.0E

EPS $

Yr Dec	—2022—	—2023E—		—2024E—	
		Curr	Prev	Curr	Prev
1Q	(0.03)A	(0.03)A	(0.03)A	(0.02)E	--
2Q	0.01A	0.02A	0.02A	(0.02)E	--
3Q	(0.01)A	(0.02)A	(0.06)E	(0.02)E	--
4Q	(0.05)A	(0.04)E	(0.06)E	(0.02)E	--
YEAR	(0.08)A	(0.07)E	(0.13)E	(0.09)E	(0.38)E
P/E	NM	NM	NM	NM	NM



ORY 3Q23: Four Trials Running, Two to Start, Funded Into 1H24

ORY ended 3Q23 with $8.8M, enough to fund operations into 1H24, and the company has access to additional convertible debt financing that it has not yet drawn down. ORY enrolled one trial (PORTICO), is enrolling three trials, and expects to initiate at least two more trials. ORY believes that the FRIDA trial, which is its central iadademstat strategy, is iadademstat's fastest route to market. The FRIDA, SCLC basket, and EVOLUTION trials are enrolling, with enrollment to start in 2024 for the STELLAR and HOPE trials.

Vafidemstat

- **PORTICO trial.** PORTICO, which is fully enrolled as of July at 210 patients, is a randomized Phase 2b trial in BPD patients at 15-20 centers in the U.S. and Europe, from which we expect topline results in 1Q24. Preliminary blinded aggregate safety data (data cutoff of May 23 involving data from 167 BPD patients) was reviewed by the trial's independent Data Monitoring Committee (DMC) on June 26. The DMC characterized the aggregate safety results as positive and recommended that the trial continue as planned. Earlier this month, ORY presented a poster at the European College of Neuropsychopharmacology Congress today that updated PORTICO's blinded safety results and involved 198 patients. PORTICO enrolled a real-world BPD population by allowing common comorbidities and concomitant medications that are typically exclusionary in BPD trials, as well as allowing patients to receive concomitant psychotherapy. In aggregate, the newer blinded safety data from 198 of the 210 enrolled patients demonstrates that vafidemstat is safe and well-tolerated, with a low 2% discontinuation rate due to treatment-emergent adverse events (TEAEs) and 0% discontinuation rate due to serious TEAEs. The only serious TEAE that was also deemed severe was fully resolved during the trial without dose interruption. The PORTICO screen failure rate was low (36.6%), versus the most recent BPD trial with brexpiprazole at 62%, and the PORTICO dropout rate was likewise lower (20.7% versus 26.3%). The PORTICO safety data thus far shows vafidemstat to be safe and well tolerated and aligns well with prior aggregated safety data from seven completed vafidemstat trials, in which about 400 patients and healthy volunteers have received vafidemstat. PORTICO's primary endpoints are reduction of aggression/agitation and overall BPD improvement. Top-line results will hopefully clearly inform the design of a pivotal trial in BPD.
- **EVOLUTION trial.** The Phase 2b EVOLUTION trial evaluating vafidemstat in schizophrenia continues to enroll patients in Spain and is looking to establish vafidemstat efficacy on negative symptoms and cognitive impairment in patients with schizophrenia. EVOLUTION is partially funded by the Spanish Ministry of Science. *(text continues on page 2)*

Intraday price: €2.03 at 3:45PM ET, 10/27/2023

- **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 patients. ORY is talking to regulatory agencies to refine the final design of HOPE, and should be filing an IND in 2024 in the U.S.

Iadademstat

- **FRIDA trial.** ORY continues to enroll patients in its Phase 1b FRIDA trial in rel/ref AML with FLT3 mutations, which will evaluate iadademstat plus gilteritinib in up to 45 patients in the U.S. at up to 15 centers. 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, if FRIDA is successful. ORY believes that the FRIDA trial, which is its central strategy, is iadademstat's fastest route to market. ORY presented a poster at ASCO 2023 describing FRIDA 's design and reporting that the first dose escalation cohort was completed with no DLTs yet observed. Since ASCO, ORY has started dosing the second FRIDA dose cohort.
- **SCLC basket trial.** ORY is also conducting a collaborative Phase 2 basket trial in the U.S. of iadademstat in combination with synergistic agents, such as paclitaxel, in platinum rel/ref SCLC and extrapulmonary high grade neuroendocrine tumors. The first patient was enrolled in January 2023 and enrollment continues. The trial is being conducted in collaboration with Fox Chase Cancer Center, which will test iadademstat in combination with different therapies in trials funded by ORY.
- **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.

HDAC-6 program

- In 1Q23, ORY announced that it selected ORY-4001, a selective HDAC-6 inhibitor, as its drug candidate to bring into the clinic for neurological diseases such as Charcot-Marie-Tooth (CMT) and ALS, among others. HDAC-6 inhibitors are believed to be potentially effective treatments for CMT, ALS, and other neurological disorders lacking effective treatments. Last year, ORY and the CMT Research Foundation agreed to explore ORY's HDAC-6 inhibitors, and ORY-4001 was selected due to the positive preclinical results generated under this collaboration. ORY-4001 is highly selective against other HDAC classes, resulting in a favorable safety profile that avoids hematoxicity, as well as being strongly anti-inflammatory *in vivo*. ORY-4001 has shown multiple positive responses in a validated CMT1A peripheral neuropathy *in vivo* model which reliably recapitulates many of the symptoms of CMT in humans, and it will now enter into IND enabling studies. CMT is a progressive, degenerative peripheral nerve disease affecting 150k U.S. patients and over 3M globally. CMT is caused by a variety of genetic mutations, with CMT1A mutation causing the disease in about half of the patients.
- In June, ORY orally presented encouraging preclinical results for ORY-4001 at the 2023 Peripheral Nerve Society annual meeting, showing the drug to reverse disease progression symptoms in a murine model of CMT. The current results have inclined ORY to start IND enabling studies for ORY-4001.
- In September, animal model data in CMT was presented at the Third Annual Global CMT Research Convention. ORY-4001 reversed disease progression symptoms in a CMT mouse model that reliably recapitulates many human symptoms, improving myelination and restoring axon integrity in the sciatic nerve, and improving compound muscle action potential and nerve conduction by contrast to untreated animals.

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 $869 million. 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 and the European leader in epigenetics, with a strong focus on personalized medicine in CNS disorders and oncology. Oryzon's team is composed of highly qualified professionals from the pharma industry located in Barcelona, Boston, NYC and San Diego. Oryzon has an advanced clinical portfolio with two LSD1 inhibitors, vafidemstat in CNS and iadademstat in oncology, in several Phase II clinical trials. The company has 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. For more information, visit www.oryzon.com

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

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	2017A	2018A	2019A	2020A	2021A	2022A	1Q23A	2Q23A	3Q23A	4Q23E	2023E	1Q24E	2Q24E	3Q24E	4Q24E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
Global iadademstat revenue																	7,653	61,183	122,988	181,436	214,468	224,938
Global vafidemstat revenue																	98,463	342,237	520,351	615,106	684,577	721,921
Collaboration revenue	20																					
Total revenue	**20**																**106,116**	**403,421**	**643,339**	**796,542**	**899,045**	**946,858**
Cost of revenue																	2,701	11,709	22,833	31,765	39,065	43,178
R&D	6,363	8,489	12,647	13,591	15,118	17,701	4,372	4,264	3,821	3,859	16,316	3,898	3,937	3,976	4,016	15,827	18,992	20,891	21,936	22,155	22,377	22,600
G&A	4,502	2,993	3,176	3,484	5,529	4,771	1,223	1,096	674	809	3,802	817	825	833	842	3,317	5,970	8,956	9,851	10,836	11,378	11,947
Total operating expenses	**10,865**	**11,482**	**15,823**	**17,075**	**20,647**	**22,472**	**5,595**	**5,360**	**4,495**	**4,668**	**20,118**	**4,715**	**4,762**	**4,809**	**4,858**	**19,144**	**27,664**	**41,555**	**54,620**	**64,757**	**72,820**	**77,725**
Operating income	**(10,845)**	**(11,482)**	**(15,823)**	**(17,075)**	**(20,647)**	**(22,472)**	**(5,595)**	**(5,360)**	**(4,495)**	**(4,668)**	**(20,118)**	**(4,715)**	**(4,762)**	**(4,809)**	**(4,858)**	**(19,144)**	**78,452**	**361,865**	**588,719**	**731,786**	**826,224**	**869,133**
Other income (net)	5,659	8,143	11,522	11,805	12,510	16,661	4,215	4,054	3,669	2,000	13,938	3,000	3,000	3,000	3,000	12,000						
Net income (pretax)	**(5,186)**	**(3,339)**	**(4,301)**	**(5,269)**	**(8,137)**	**(5,811)**	**(1,380)**	**(1,306)**	**(826)**	**(2,668)**	**(6,180)**	**(1,715)**	**(1,762)**	**(1,809)**	**(1,858)**	**(7,144)**	**78,452**	**361,865**	**588,719**	**731,786**	**826,224**	**869,133**
Net financial & tax	1,047	(1,991)	(187)	(1,098)	(2,760)	(1,276)	392	(2,459)	300	(250)	(2,017)	(250)	(250)	(250)	(250)	(1,000)	-	90,466	147,180	182,946	206,556	217,283
Net income	**(6,233)**	**(1,348)**	**(4,114)**	**(4,171)**	**(5,377)**	**(4,535)**	**(1,772)**	**1,153**	**(1,126)**	**(2,418)**	**(4,163)**	**(1,465)**	**(1,512)**	**(1,559)**	**(1,608)**	**(6,144)**	**78,452**	**271,399**	**441,539**	**548,839**	**619,668**	**651,850**
EPS basic	**(0.20)**	**(0.04)**	**(0.10)**	**(0.08)**	**(0.10)**	**(0.08)**	**(0.03)**	**0.02**	**(0.02)**	**(0.04)**	**(0.07)**	**(0.02)**	**(0.02)**	**(0.02)**	**(0.02)**	**(0.09)**	**1.10**	**3.63**	**5.63**	**6.66**	**7.17**	**7.18**
EPS diluted	**(0.20)**	**(0.04)**	**(0.10)**	**(0.08)**	**(0.10)**	**(0.08)**	**(0.03)**	**0.02**	**(0.02)**	**(0.04)**	**(0.07)**	**(0.02)**	**(0.02)**	**(0.02)**	**(0.02)**	**(0.09)**	**0.92**	**3.06**	**4.78**	**5.69**	**6.17**	**6.22**
Basic shares outstanding	31,711	34,638	41,589	49,235	52,762	53,354	56,190	57,339	58,154	58,212	57,474	66,944	67,614	67,681	67,749	67,497	71,137	74,693	78,428	82,349	86,467	90,790
Diluted shares outstanding	31,711	34,638	41,565	49,235	52,762	53,354	56,190	57,339	58,154	58,212	57,474	66,944	67,614	67,681	67,749	67,497	85,174	88,731	92,465	96,387	100,504	104,827

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

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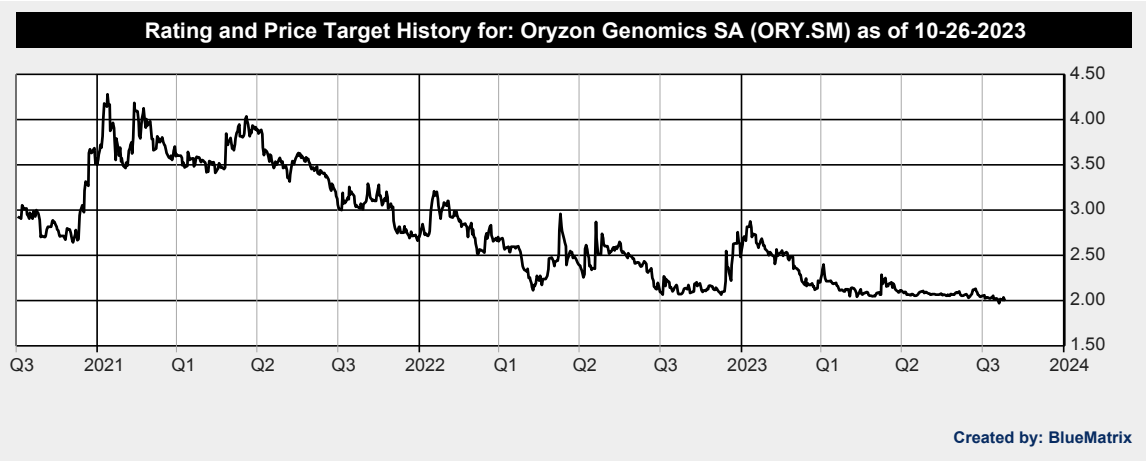
Disclosures:

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 10/27/23	
Rating	**Count**	**Percent**	**Count**	**Percent**
Buy [B]	**357**	**74.22**	**218**	**61.06**
Neutral [N]	**85**	**17.67**	**30**	**35.29**
Sell [S]	**2**	**0.42**	**1**	**50.00**
Under Review [UR]	**32**	**6.65**	**3**	**9.38**

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.

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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.

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