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COMPANY NOTE | EQUITY RESEARCH | July 25, 2023

Healthcare: Biotechnology

Company Update
Estimates Changed

Oryzon Genomics SA | ORY.SM - €2.10 - MADRID | *Buy*

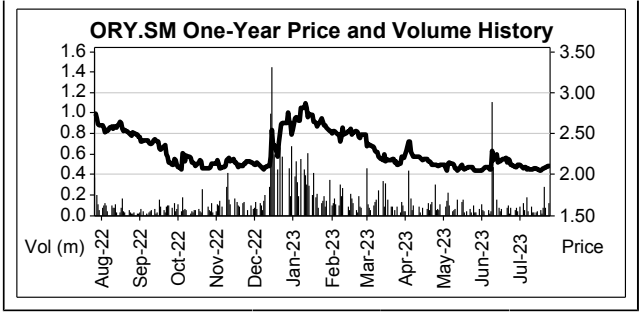
Stock Data	
52-Week Low - High	€1.98 - €2.93
Shares Out. (mil)	57.85
Mkt. Cap.(mil)	€121.49
3-Mo. Avg. Vol.	101,358
12-Mo.Price Target	€15.00
Cash (mil)	$14.6
Tot. Debt (mil)	€20.1

Rev ($M)

Yr Dec	—2022—	—2023E—	—2024E—
		Curr	Curr
1Q	0.0A	0.0A	-
2Q	0.0A	0.0A	-
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	Prev
1Q	(0.03)A	(0.03)A	(0.03)A	-	-
2Q	0.01A	0.02A	(0.05)E	-	-
3Q	(0.01)A	(0.06)E	(0.07)E	-	-
4Q	(0.05)A	(0.06)E	(0.07)E	-	-
YEAR	(0.08)A	(0.13)E	(0.22)E	(0.38)E	(0.46)E
P/E	NM	NM	NM	NM	NM



ORY 2Q23: Four Trials Running, Two to Start, Funded Into 1H24 With Current Cash

ORY ended 2Q23 with $14.6M, enough to fund operations into 1H24, as per our projections, 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 at least two more. ORY believes that the FRIDA trial, which is its central strategy, is iadademstat's fastest route to market. The FRIDA, SCLC basket, PORTICO, and EVOLUTION trials are enrolling, with enrollment to start by 2024 in the STELLAR and HOPE trials.

Vafidemstat

- **PORTICO trial.** Active patient recruitment is ongoing in the randomized, 188-patient Phase 2b PORTICO trial in BPD patients at 15-20 centers in the U.S. and Europe, and enrollment should be complete in 3Q23, thus allowing for preliminary results in late 2023/early 2024. Recent 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 PORTICO trial continue as planned to its ultimate enrollment of 188 patients. More specifically about the blinded safety results, no treatment-related serious adverse events or deaths were observed. A total of 306 adverse events among 98 patients treated either with vafidemstat or placebo were reported, with most of the events being mild (216) or moderate (78), and only 12 events reported as severe among in nine patients, which led to six treatment discontinuations or patient withdrawals. Overall, the PORTICO safety data thus far showing vafidemstat to be safe and well tolerated aligns well with prior aggregated safety data from seven completed vafidemstat trials, in which almost 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.
- **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 2023 in the U.S. and possibly filing to start enrolling in Europe as well.
- **Psychiatric pilot trials.** ORY's precision medicine programs in psychiatric disease are progressing, with collaborations *(text continued on page 2)*

- *(text continued from page 1)* 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.

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.
- **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 March, 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.

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 $992 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	1Q22	2Q22	3Q22	4Q22	2022A	1Q23A	2Q23A	3Q23E	4Q23E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
Global iadademstat revenue																	25,778	99,451	209,468	313,934	372,470	389,751
Global vafidemstat revenue																	98,463	342,237	520,351	615,106	684,577	721,921
Collaboration revenue	20																					
Total revenue	**20**																**124,241**	**441,689**	**729,819**	**929,040**	**1,057,047**	**1,111,672**
Cost of revenue																-	5,420	17,066	34,941	48,990	59,606	64,604
R&D	6,363	8,489	12,647	13,591	15,118	4,228	4,166	4,274	5,033	17,701	4,372	4,264	4,477	4,701	17,814	21,377	25,653	28,218	29,629	29,925	30,224	30,526
G&A	4,502	2,993	3,176	3,484	5,529	1,343	1,520	659	1,249	4,771	1,223	1,096	1,107	1,118	4,544	6,816	12,269	18,403	20,243	22,268	23,381	24,550
Total operating expenses	**10,865**	**11,482**	**15,823**	**17,075**	**20,647**	**5,571**	**5,686**	**4,933**	**6,282**	**22,472**	**5,595**	**5,360**	**5,584**	**5,819**	**22,358**	**28,193**	**43,341**	**63,687**	**84,813**	**101,183**	**113,211**	**119,680**
Operating income	**(10,845)**	**(11,482)**	**(15,823)**	**(17,075)**	**(20,647)**	**(5,571)**	**(5,686)**	**(4,933)**	**(6,282)**	**(22,472)**	**(5,595)**	**(5,360)**	**(5,584)**	**(5,819)**	**(22,358)**	**(28,193)**	**80,899**	**378,001**	**645,006**	**827,857**	**943,836**	**991,991**
Other income (net)	5,659	8,143	11,522	11,805	12,510	3,826	3,894	4,248	4,693	16,661	4,215	4,054	2,000	2,000	12,269							
Net income (pretax)	**(5,186)**	**(3,339)**	**(4,301)**	**(5,269)**	**(8,137)**	**(1,745)**	**(1,792)**	**(685)**	**(1,589)**	**(5,811)**	**(1,380)**	**(1,306)**	**(3,584)**	**(3,819)**	**(10,089)**	**(28,193)**	**80,899**	**378,001**	**645,006**	**827,857**	**943,836**	**991,991**
Net financial & tax	1,047	(1,991)	(187)	(1,098)	(2,760)	67	(2,139)	(67)	863	(1,276)	392	(2,459)	(250)	(250)	(2,567)	(2,824)	(3,106)	94,500	161,251	206,964	235,959	247,998
Net income	**(6,233)**	**(1,348)**	**(4,114)**	**(4,171)**	**(5,377)**	**(1,812)**	**347**	**(618)**	**(2,452)**	**(4,535)**	**(1,772)**	**1,153**	**(3,334)**	**(3,569)**	**(7,522)**	**(25,369)**	**84,005**	**283,501**	**483,754**	**620,893**	**707,877**	**743,994**
EPS basic	**(0.20)**	**(0.04)**	**(0.10)**	**(0.08)**	**(0.10)**	**(0.03)**	**0.01**	**(0.01)**	**(0.05)**	**(0.08)**	**(0.03)**	**0.02**	**(0.06)**	**(0.06)**	**(0.13)**	**(0.38)**	**1.20**	**3.85**	**6.26**	**7.65**	**8.30**	**8.31**
EPS diluted	**(0.20)**	**(0.04)**	**(0.10)**	**(0.08)**	**(0.10)**	**(0.03)**	**0.01**	**(0.01)**	**(0.05)**	**(0.08)**	**(0.03)**	**0.02**	**(0.06)**	**(0.06)**	**(0.13)**	**(0.38)**	**1.00**	**3.23**	**5.29**	**6.52**	**7.13**	**7.18**
Basic shares outstanding	31,711	34,638	41,589	49,235	52,762	52,762	52,762	53,609	54,284	53,354	56,190	57,339	57,397	57,454	57,095	66,801	70,141	73,649	77,331	81,198	85,257	89,520
Diluted shares outstanding	31,711	34,638	41,565	49,235	52,762	52,762	52,762	53,609	54,284	53,354	56,190	57,339	57,397	57,454	57,095	66,801	84,179	87,686	91,368	95,235	99,295	103,557

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

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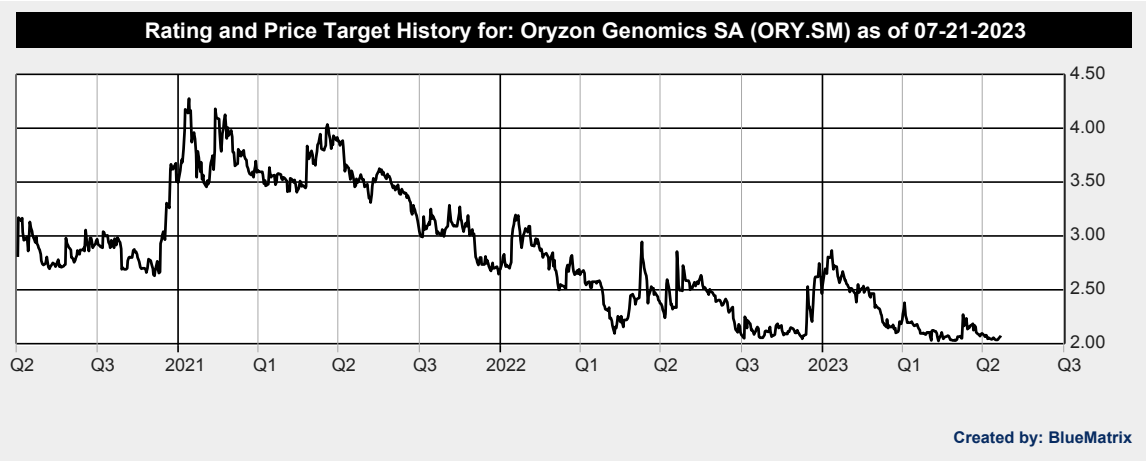
Disclosures:

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 07/24/23	
Rating	**Count**	**Percent**	**Count**	**Percent**
Buy [B]	**378**	**76.06**	**225**	**59.52**
Neutral [N]	**96**	**19.32**	**31**	**32.29**
Sell [S]	**3**	**0.60**	**0**	**0**
Under Review [UR]	**19**	**3.82**	**4**	**21.05**

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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.

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