ROTH Capital Partners

Jonathan Aschoff, Ph.D., (646) 616-2795
jaschoff@roth.com

Sales (800) 933-6830, **Trading** (800) 933-6820

COMPANY NOTE | EQUITY RESEARCH | July 22, 2022

Healthcare: Biotechnology

Company Update
Estimates Changed

Oryzon Genomics SA | ORY.SM - €2.56 - MADRID | *Buy*

Stock Data	
52-Week Low - High	€2.04 - €3.70
Shares Out. (mil)	53.96
Mkt. Cap.(mil)	€137.88
3-Mo. Avg. Vol.	145,788
12-Mo.Price Target	€15.00
Cash (mil)	$31.6
Tot. Debt (mil)	$25.5

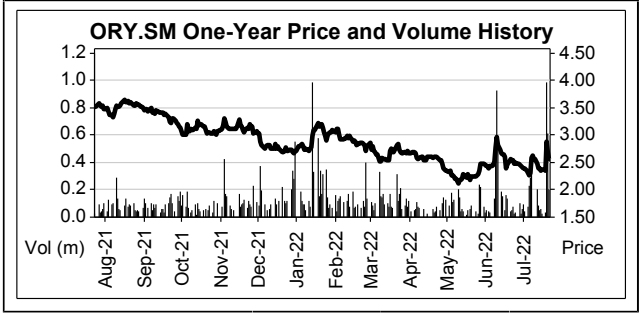
Cash (mil): Pro forma cash of about $31.6M includes 8M euros raised since 1Q22 via convertible debt, which also raises debt by 8M euros to about $25.5M.

Revenue ($ millions)

Yr Dec	—2021—	—2022E—	—2023E—
		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	—2021—	—2022E—		—2023E—	
		Curr	Prev	Curr	Prev
1Q	(0.04)A	(0.03)A	(0.03)A	-	-
2Q	0.02A	0.01A	(0.06)E	-	-
3Q	(0.03)A	(0.05)E	(0.05)E	-	-
4Q	(0.04)A	(0.05)E	(0.06)E	-	-
YEAR	(0.10)A	(0.14)E	(0.20)E	(0.34)E	(0.39)E
P/E	NM	NM	NM	NM	NM



ORY 2Q22: Clinical Pipeline Substantially Ramping Up, Well Funded for Two Years

ORY ended 2Q22 with pro forma cash of $31.6M, which should be enough for 18 months, but with access to an additional €12M in convertible debt that can fund operations through 1H24. ORY is conducting three trials, and expects to initiate four more, starting this year with the expected initiation of its first Kabuki Syndrome trial. The results of ongoing pilot studies to characterize patients with specific mutations to inform subsequent precision psychiatry clinical trials with vafidemstat are expected to conclude in 2022.

- **Iadademstat.** ORY entered into a Cooperative Research and Development Agreement (CRADA) with the NCI, pursuant to which ORY and the NCI will collaborate to develop iadademstat further in clinical trials in solid and hematological malignancies. Iadademstat will now be developed in new indications and in combination with other agents such as investigational and marketed immuno-oncology and molecularly-targeted agents. The CRADA increases iadademstat's chances of clinical success in mid-stage clinical trials and its recognition by potential future commercial partners, in our view. At last month's EHA annual meeting, ORY presented updated (42 month) results from its Phase 2 ALICE trial (n=36) evaluating 60 or 90ug/m2/day iadademstat plus 75mg/m2 azacitidine combination therapy in elderly/unfit AML patients. The EHA poster is an update from the 4Q21 ASH poster that involves the same number of patients, and highlights include one additional CR, for an ORR of 81%, up from an ORR of 78% at ASH. Also, 12 of the 14 CR/CRi patients (86%; all 7 CRs and 5 of 7 CRi) became transfusion independent, nine of the 14 (64%) had durable responses lasting more than six months, and the drug was well tolerated even in this fragile population. We believe that these robust results contributed to the establishing ORY's recent CRADA, and we look forward to an ALICE trial update at ASH in 4Q22. ORY is preparing to start its Phase 1b FRIDA trial in rel/ref AML with FLT3 mutations, which will test iadademstat plus gilteritinib in up to 45 patients and which should begin patient recruitment in 3Q22. FRIDA has primary endpoints of safety, tolerability, and determining the RP2D, and secondary endpoints of efficacy (i.e., CR/CRh, DoR, MRD). ORY's Phase 1b/2 STELLAR trial in first-line SCLC is being designed and is expected to start in 2H22 in the U.S. STELLAR is a randomized, multi-center trial of iadademstat plus a checkpoint inhibitor in this setting that could potentially support accelerated approval. ORY is also preparing a Phase 1b/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.
- **Vafidemstat.** 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. PORTICO has a pre-defined interim analysis to adjust the sample size in case of excessive variability around the endpoints or an unexpectedly *(text continued on page 2)*

- *(text continued from page 1)* high placebo rate. ORY is also enrolling its Phase 2b EVOLUTION trial in schizophrenia patients in Spain. Primary EVOLUTION endpoints include the drug's impact on negative symptoms and cognitive impairment in schizophrenics. 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, which should start in 2H22 in the U.S. and possibly in Europe as well, and could potentially support accelerated approval, if successful. ORY is also conducting a preclinical collaboration on KS with Kennedy Krieger Institute and Johns Hopkins University to evaluate the molecular effects of LSD1 inhibition with vafidemstat in KS patient samples. KS is an autosomal dominant/X-linked disorder that affects multiple organ systems including neuro, immune, auditory and cardiac systems. Most molecularly confirmed cases of KS have loss-of-function variants in KMT2D (aka MLL2) gene, catalyzes the addition of methyl groups to lysine 4 of histone 3, which are marks associated with open chromatin, thus regulating the expression of critical target genes, and opening up the door to treatment with a LSD1 inhibitor like vafidemstat.

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 $1.33 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)

Jonathan Aschoff, Ph.D. (646) 616-2795
jaschoff@roth.com

	2017A	2018A	2019A	2020A	1Q21	2Q21	3Q21	4Q21	2021A	1Q22A	2Q22A	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	4,228	4,166	4,458	4,770	17,621	22,908
G&A	4,502	2,993	3,176	3,484	1,302	1,200	1,070	1,957	5,529	1,343	1,520	1,566	1,613	6,041	7,854
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**	**6,023**	**6,382**	**23,662**	**30,761**
Operating income	**(10,845)**	**(11,482)**	**(15,823)**	**(17,075)**	**(5,580)**	**(4,128)**	**(5,052)**	**(5,887)**	**(20,647)**	**(5,571)**	**(5,686)**	**(6,023)**	**(6,382)**	**(23,662)**	**(30,761)**
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	3,000	3,000	13,720	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)**	**(3,023)**	**(3,382)**	**(9,942)**	**(24,761)**
Net financial & tax	1,047	(1,991)	(187)	(1,098)	89	(2,823)	36	(62)	(2,760)	67	(2,139)	50	50	(1,972)	(2,169)
Net income	**(6,233)**	**(1,348)**	**(4,114)**	**(4,171)**	**(2,133)**	**951**	**(1,836)**	**(2,359)**	**(5,377)**	**(1,812)**	**347**	**(3,073)**	**(3,432)**	**(7,970)**	**(22,592)**
EPS basic	**(0.20)**	**(0.04)**	**(0.10)**	**(0.08)**	**(0.04)**	**0.02**	**(0.03)**	**(0.04)**	**(0.10)**	**(0.03)**	**0.01**	**(0.05)**	**(0.05)**	**(0.14)**	**(0.34)**
EPS diluted	**(0.20)**	**(0.04)**	**(0.10)**	**(0.08)**	**(0.04)**	**0.02**	**(0.03)**	**(0.04)**	**(0.10)**	**(0.03)**	**0.01**	**(0.05)**	**(0.05)**	**(0.14)**	**(0.34)**
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	63,314	63,377	58,054	66,546
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	63,314	63,377	58,054	66,546

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

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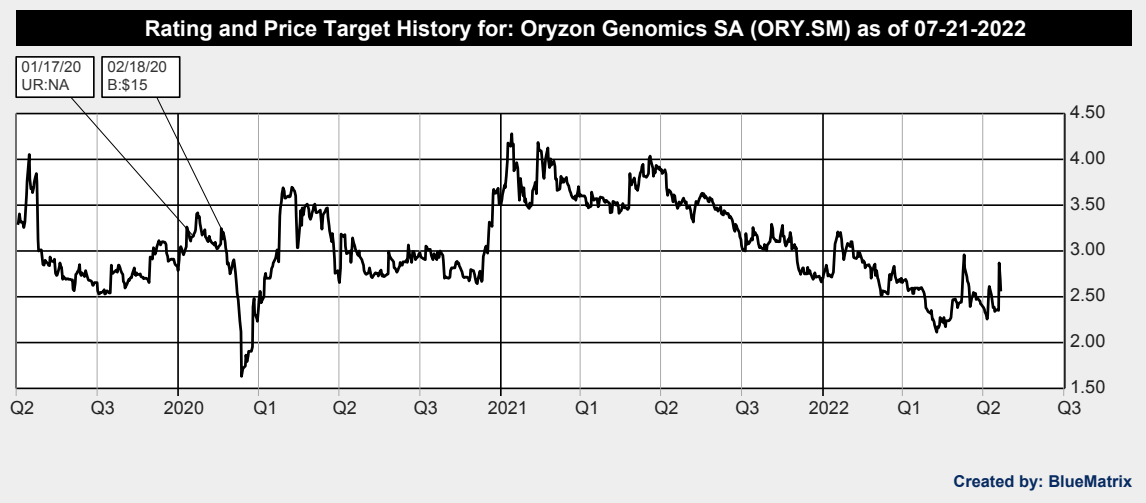
Disclosures:

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 07/22/22	
Rating	**Count**	**Percent**	**Count**	**Percent**
Buy [B]	**350**	**84.75**	**224**	**64.00**
Neutral [N]	**50**	**12.11**	**30**	**60.00**
Sell [S]	**2**	**0.48**	**1**	**50.00**
Under Review [UR]	**11**	**2.66**	**6**	**54.55**

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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