ROTH Capital Partners

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COMPANY NOTE | EQUITY RESEARCH | March 21, 2022

Healthcare: Biotechnology **Company Update**

Oryzon Genomics SA | ORY.SM - €2.68 - MADRID | *Buy*

Stock Data	
52-Week Low - High	€2.43 - €4.10
Shares Out. (mil)	53.06
Mkt. Cap.(mil)	€142.21
3-Mo. Avg. Vol.	166,677
12-Mo.Price Target	€15.00
Cash (mil)	$35.8
Tot. Debt (mil)	$14.9

Revenue ($ millions)

Yr Dec	—2020—	—2021E—	—2022E—
		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	—2020—	—2021E—	—2022E—
		Curr	Curr
1Q	(0.03)A	(0.04)A	(0.05)E
2Q	0.00A	0.02A	(0.05)E
3Q	(0.02)A	(0.03)A	(0.05)E
4Q	(0.03)A	(0.05)E	(0.06)E
YEAR	(0.08)A	(0.10)E	(0.21)E
P/E	NM	NM	NM

ORY: FDA Clears IND for FRIDA Trial in FLT3mut+ Rel/Ref AML Patients

ORY received FDA notification that its iadademstat IND is approved for a Phase 1b trial, named FRIDA, in rel/ref AML carrying an FMS-like tyrosine kinase mutation called FLT3mut+, which accounts for about 30-40% of AML patients. FRIDA is an open-label, multi-center trial of iadademstat plus FLT3 inhibitor gilteritinib, with primary endpoints of safety and tolerability of the combination therapy, and to establish the therapy's recommended Phase 2 dose (RP2D). Iadademstat already generated positive AML results in combination with azacitidine.

- ORY received FDA notification that its iadademstat IND is approved for a Phase 1b trial, named FRIDA, in rel/ref AML carrying an FMS-like tyrosine kinase mutation called FLT3mut+, which accounts for about 30-40% of AML patients. FRIDA is an open-label, multi-center trial of iadademstat plus FLT3 inhibitor gilteritinib, with primary endpoints of safety and tolerability of the combination therapy, and to establish the therapy's recommended Phase 2 dose (RP2D). Secondary endpoints are efficacy oriented, and include rate of complete remission and complete remission with partial hematological recovery (CR/CRh), duration of responses, and assessing measurable residual disease. FRIDA will be conducted at 10 to 15 U.S. sites, and will enroll as many as 45 patients. A successful outcome will allow ORY to discuss with the FDA the best trial for further development. FRIDA represents ORY's new iadademstat development strategy in hemato-oncology and solid tumors, which will generally involve U.S. trials.
- Clinical results with iadademstat, a potent and selective LSD1 inhibitor, have already demonstrated that epigenetics is one of the underlying roots of leukemia and other cancers, and that LSD1 is a key drug target. Iadademstat has already been shown to have a favorable safety profile and to be capable of eliciting deep and prolonged responses in AML when given in combination with azacitidine. Iadademstat's preclinical synergy with FLT3 inhibitors makes FRIDA a rational trial to conduct.
- As a reminder of iadademstat's efficacy in elderly rel/ref AML populations that was reported at ASH in 4Q21, the drug delivered an ORR of 78% (21/27 evaluable), of which there was 62% (13/21) CR/CRi and 38% (8/21) PR in the ALICE trial. Six were CR and seven were CRi. We favorably compare this to the historical 28% ORR in this same population of AML treated with azacitidine monotherapy. We also note that among AML subgroups, both patients with M5b AML and all three patients with TP53-mutant AML achieved CR/CRi. Median time to response remains swift at two cycles of therapy (i.e., 55 days), and duration of response remains encouraging, with 77% (10/13) of the CR/CRi lasting more than six months (six lasting >one year; longest thus far at the October 15, ASH data cutoff was >1,000 days and ongoing), with the patient remaining transfusion independent and MRD-negative. The ALICE (*text continued on page 2)*

***(ORY recently traded at €2.82 at* 2:30 PM GMT+1)**

- *(text continued from page 1)* trial has determined that iadademstat should be dosed 90ug/m2/d in future trials when combined with azacitidine. Preliminary data indicates a direct correlation between quality of response and iadademstat exposure/LSD1 target engagement. The 90ug/m2/d dose more consistently achieved the exposure and LSD1 target engagement observed in CR/CRi patients than did the 60ug/m2/d dose that some ALICE patients received, and importantly did so without increasing toxicity. Looking only at patients receiving 90ug/m2/d of iadademstat, a 77% ORR and 80% CR/CRi rate was achieved. There were only two serious AEs reported as being probably related to the combination therapy treatment, one grade 3 differentiation syndrome and one fatal intracranial hemorrhage. The most frequent AE was platelet reduction, which was observed in 44% of patients, although grade 3 or lower thrombocytopenia was already present at baseline in 61% of patients. There were no other significant non-hematological toxicities or other organ-related toxicities observed, and we emphasize that ALICE enrolled a median patient age of 77 years.

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 $1.46 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. We view our valuation to be conservative given that it excludes revenue from vafidemstat in schizophrenia. We believe that ORY.SM has prudently selected areas of unmet need and therefore market demand.

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	1Q21A	2Q21A	3Q21A	4Q21E	2021E	1Q22E	2Q22E	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	4,380	15,568	4,599	4,829	5,071	5,324	19,823	25,770
G&A	4,502	2,993	3,176	3,484	1,302	1,200	1,070	1,081	4,653	1,092	1,102	1,113	1,125	4,432	5,762
Total operating expenses	**10,865**	**11,482**	**15,823**	**17,075**	**5,580**	**4,128**	**5,052**	**5,461**	**20,221**	**5,691**	**5,932**	**6,184**	**6,449**	**24,255**	**31,532**
Operating income	**(10,845)**	**(11,482)**	**(15,823)**	**(17,075)**	**(5,580)**	**(4,128)**	**(5,052)**	**(5,461)**	**(20,221)**	**(5,691)**	**(5,932)**	**(6,184)**	**(6,449)**	**(24,255)**	**(31,532)**
Other income (net)	5,659	8,143	11,522	11,805	3,536	2,256	3,252	3,000	12,044	3,000	3,000	3,000	3,000	12,000	6,000
Net income (pretax)	**(5,186)**	**(3,339)**	**(4,301)**	**(5,269)**	**(2,044)**	**(1,872)**	**(1,800)**	**(2,461)**	**(8,177)**	**(2,691)**	**(2,932)**	**(3,184)**	**(3,449)**	**(12,255)**	**(25,532)**
Net financial & tax	1,047	(1,991)	(187)	(1,098)	89	(2,823)	36	50	(2,648)	50	50	50	50	200	220
Net income	**(6,233)**	**(1,348)**	**(4,114)**	**(4,171)**	**(2,133)**	**951**	**(1,836)**	**(2,511)**	**(5,529)**	**(2,741)**	**(2,982)**	**(3,234)**	**(3,499)**	**(12,455)**	**(25,752)**
EPS basic	**(0.20)**	**(0.04)**	**(0.10)**	**(0.08)**	**(0.04)**	**0.02**	**(0.03)**	**(0.05)**	**(0.10)**	**(0.05)**	**(0.05)**	**(0.05)**	**(0.06)**	**(0.21)**	**(0.41)**
EPS diluted	**(0.20)**	**(0.04)**	**(0.10)**	**(0.08)**	**(0.04)**	**0.02**	**(0.03)**	**(0.05)**	**(0.10)**	**(0.05)**	**(0.05)**	**(0.05)**	**(0.06)**	**(0.21)**	**(0.41)**
Basic shares outstanding	31,711	34,638	41,589	49,235	52,762	52,762	52,762	52,762	52,762	55,400	60,386	60,446	60,506	59,184	63,532
Diluted shares outstanding	31,711	34,638	41,565	49,235	52,762	52,762	52,762	52,762	52,762	55,400	60,386	60,446	60,506	59,184	63,532

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

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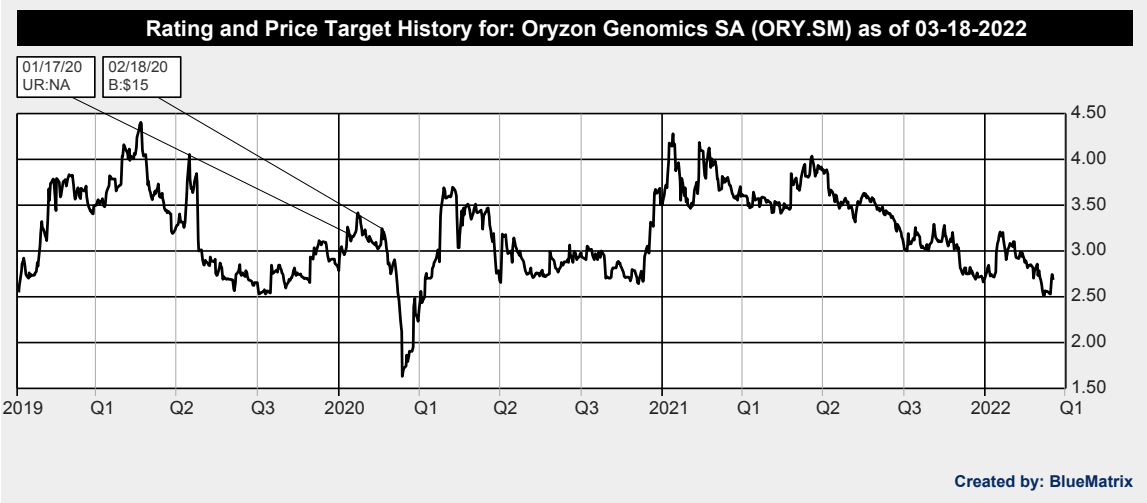
Disclosures:

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 03/21/22	
Rating	**Count**	**Percent**	**Count**	**Percent**
Buy [B]	**348**	**82.86**	**234**	**67.24**
Neutral [N]	**45**	**10.71**	**24**	**53.33**
Sell [S]	**0**	**0.00**	**0**	**0**
Under Review [UR]	**27**	**6.43**	**17**	**62.96**

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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