ROTH Capital Partners

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COMPANY NOTE | EQUITY RESEARCH | April 09, 2019

Healthcare: Biotechnology

Oryzon Genomics SA | ORY.SM - €3.57 - MADRID | *Buy*

Company Update

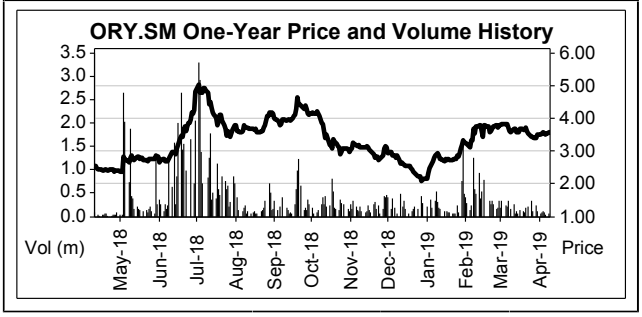
Stock Data	
52-Week Low - High	€2.06 - €5.18
Shares Out. (mil)	39.12
Mkt. Cap.(mil)	€139.67
3-Mo. Avg. Vol.	294,803
12-Mo.Price Target	€15.00
Cash (mil)	$39.3
Tot. Debt (mil)	$0.0

EPS $

Yr Dec	—2017—	—2018—	—2019E—
		Curr	Curr
1Q	-	(0.04)A	(0.05)E
2Q	-	0.06A	(0.05)E
3Q	-	(0.03)A	(0.05)E
4Q	-	(0.09)A	(0.05)E
YEAR	(0.20)A	(0.04)A	(0.20)E
P/E	NM	NM	NM

Revenue ($ millions)

Yr Dec	—2017—	—2018—	—2019E—
		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	0.0A	0.0E



ORY.SM: Dissecting the First Psych Data from Vafidemstat

Topline. In our view, the first clinical data from the Borderline cohort of Oryzon's ongoing basket psych study is suggestive of a clean drug with neuroactivity across a wide spectrum of symptoms.

Efficacy profile: Data is suggestive of activity across the neuro & psych spectrum. This cohort (n=6) with Borderline Personality Disorder (BPD) provides the first clinical data from the Phase 2 program of the LSD1/MAO-B inhibitor vafidemstat. While we certainly acknowledge why the data must be interpreted mindfully and conservatively (few patients, single center, open label), we are encouraged by the array of clinical scores all moving in the same positive direction. Of note, we like that while each overall score showed improvement (CGI, NPI, BPDCL), specific domains of the scores centered on agitation and aggression also showed improvement in and of themselves. In our view, this bodes well for the remaining cohorts, since the commonality targeted by vafidemstat in this basket trial is psychiatric aggression. Meanwhile, the parallel improvement in non-aggression domains suggests broader activity across psychiatric disease.

The results in context: What do we know about pharmacotherapy in BPD? Similarly to other personality disorders, BPD is primarily tackled with cognitive behavioral therapy (CBT) since pharmacotherapy has never demonstrated clear benefit. Our review of literature (see this meta-analysis, as example) reveals that certain neuroactive drugs do drive measurable benefit on relevant scales, however this is correlated to the type and nuance of the BPD itself (e.g. discouraged vs. impulsive disease) or the psych co-morbidities present (e.g. schizophrenia or major depression), once again reminding us of the wide spectrum of symptoms that need to be covered therapeutically in such disorders. For example, aripiprazole (second gen antipsychotic) is most active against psychotic and depressive symptoms in BPD (no surprise), while valproate (mood stabilizer) is most active in interpersonal problems and anger. We highlight the latter as a rather provocative historical precedent, because we all tend to forget that valproate is in fact an HDAC inhibitor and could be acting epigenetically (note that HDACs and vafidemstat's target LSD1 typically function in molecular complex). On the MAO-B front (vafidemstat's other target), we highlight that transdermal selegiline (MAO-B inhibitor typically used for major depression) can also be useful to treat anger and hostility in BPD, as per APA guidelines. Overall, consensus across literature is that different BPD patients likely experience different facets of the disorder, and so pharmacotherapeutic treatment should be targeted at defined symptoms. In our view, this bodes well for Oryzon's data (preliminary as it may be), especially the effect on aggression which could be leveraged into other psych disorders.

Continue below for thoughts on safety profile and upcoming catalysts.

SUMMARY

Safety profile: Data looks fine to us, with no surprises. We are generally happy with the topline data around the safety & tolerability of the drug. First and foremost, there were no perturbations in blood counts, which in our view is very important for an epigenetic intervention in a chronic disease. This makes us comfortable writing off the infection-related AEs as unrelated to treatment (i.e. no immunosuppression; also of note, 4/6 infections took place in the same patient and appear related to influenza, which was on season during the study). Looking back to 2017, the hematologic impact only appeared around 2.5mg in Phase 1, far from the 1.2mg dosed in this study. We are also not concerned about the mild changes in creatine, LDH, and amylase all in the same subject, suggesting one underlying event likely unrelated to the study.

What to keep an eye on next? We will look for consistency in the drug's activity when we next see data from the ADHD cohort (25 April, ADHD Congress, Lisbon), and the ASD cohort (9 September, ECNP Congress, Copenhagen). In our view, clinical activity in similar or related scales will reinforce the thesis that vafidemstat is neuroactive and, importantly, may impact neuro/behavioral endpoints within a relatively short treatment term (i.e. weeks to months).

VALUATION

Our 12-month price target of €15/share (rounded: €4/share for ORY-1001 in AML + €10/share for ORY-2001 in AD + €1/share in cash) is based on a DCF-SoP analysis using a 12% discount rate and 1% growth rate. Factors which could impede the achievement of our target price include, but are not limited to: (1) failure and/or setbacks of the drugs in clinical studies; (2) failure of the drugs to gain regulatory approval; and (3) smaller than projected commercial opportunity due to changes in market size, competitive landscape, and drug pricing and reimbursement.

RISKS

Experimental therapeutic product risk. The company's risk profile is based primarily, in our belief, on the company's thesis being based on the clinical and commercial prospects of pipeline candidates. Current funding at the company is being directed toward these programs and should there be any missteps, negative trial data or delays, this could impact the stock negatively. Adding additional risk to both programs is their early stage nature. Drug development is fraught with failures and this risk is increased significantly during the earlier stages of development.

Development timeline risk. The company's shares could be subject to increased volatility, in our belief, based on the time frame required to get meaningful proof of concept data from the planned clinical program. Positive clinical data could yield a potential accelerated path toward approval, however we currently project that our modeled drug candidates ORY-1001 and ORY-2001 may only reach the market in 2023 and 2024, respectively. Investors may choose to delay investment in the company, despite potential excitement, until meaningful clinical data is generated.

Financing risk. As with a majority of development-stage biotechnology companies, the ability to maintain sufficient funding is critical to the progress of pipeline candidates. Should the company experience problems raising sufficient capital, its development programs' progress could be significantly impeded, leading to both delays in development timelines as well as potential negative effects on investor confidence. Each of these could have a negative impact on share price.

COMPANY DESCRIPTION

Oryzon Genomics S.A., headquartered in Barcelona, Spain, is a clinical stage biotechnology company focused on the discovery and development of epigenetic therapies in oncology and neurodegenerative diseases. Its first clinical asset, ORY-1001, an inhibitor of the histone demethylase LSD1, is currently advancing into a Phase 2 study in acute myelogenous leukemia (AML) and myelodysplastic syndrome (MDS), and a Phase 1 study in small cell lung cancer (SCLC). Its second clinical asset, ORY-2001, a dual inhibitor of LSD1 and MAO-B, is currently in proof-of-concept Phase 2 studies in Alzheimer's disease (AD) and multiple sclerosis (MS).

Oryzon Genomics, S.A.
Income Statement
(in $'1000s)

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	2015	2016	2017	Mar Q1:18	Jun Q2:18	Sep Q3:18	Dec Q4:18	2018	Mar Q1:19E	Jun Q2:19E	Sep Q3:19E	Dec Q4:19E	2019E
Collaborations	4,647	775	20	-	-	-	-	-	-	-	-	-	-
Total revenues	4,647	775	20	-	-	-	-	-	-	-	-	-	-
Research and development	4053	5,492	6,363	2,334	2,113	1,942	2,324	8,489	2,382	2,442	2,503	2,565	9,892
General and administrative	4624	5,011	4,502	887	838	816	539	2,993	857	900	945	992	3,693
Total operating expenses	8,677	10,503	10,865	3,221	2,951	2,758	2,863	11,482	3,239	3,341	3,447	3,557	13,585
Loss from operations	(4,030)	(9,728)	(10,845)	(3,221)	(2,951)	(2,758)	(2,863)	(11,482)	(3,239)	(3,341)	(3,447)	(3,557)	(13,585)
Other income	3774	4,903	5,659	2,458	1,960	1,776	2,177	8,143	957	967	977	987	3,888
Tax	-829	(918)	(1,047)	(499)	2,835	(153)	(178)	1,991	220	330	440	550	1,540
Net loss	(1,085)	(5,743)	(6,233)	(1,262)	1,844	(1,135)	(864)	(1,348)	(2,062)	(2,044)	(2,030)	(2,020)	(8,157)
Net loss per share	(0.04)	(0.21)	(0.20)	(0.04)	0.06	(0.03)	(0.09)	(0.04)	(0.05)	(0.05)	(0.05)	(0.05)	(0.20)
Weighted average shares	24,729	27,569	31,711	33,493	33,493	33,493	37,214	34,638	37,958	38,718	41,234	43,915	40,456

Source: www.oryzon.com and ROTH Capital Partners research.

Oryzon Genomics, S.A.
Valuation
(in €'MM, except per share values)

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ORY-1001 in AML	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
Total Revenue	0	0	0	0	0	50	156	221	256	290	297
Net Income	(3)	(4)	(4)	(9)	(14)	18	87	131	155	179	183
Periods	0.00	0.00	1.00	2.00	3.00	4.00	5.00	6.00	7.00	8.00	9.00
Discounted income	(3)	(4)	(4)	(9)	(14)	12	51	68	72	75	69

ORY-2001 in AD	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
Total Revenue	0	0	0	0	0	0	350	1,107	2,296	3,010	3,127
Net Income	(7)	(10)	(10)	(15)	(24)	(43)	190	682	1,468	1,962	2,063
Periods	0.00	0.00	1.00	2.00	3.00	4.00	5.00	6.00	7.00	8.00	9.00
Discounted income	(7)	(10)	(10)	(15)	(17)	(27)	106	337	646	767	718

ORY-1001, AML Valuation		
Discount Rate		12%
Growth Rate		1%
CPV		969.44
CPV/share	€	22.03
Adj CPV/share	€	4.41

ORY-2001, AD Valuation		
Discount Rate		12%
Growth Rate		1%
CPV		8,825.85
CPV/share	€	200.59
Adj CPV/share	€	10.03

Share Valuation					
	Probability		Adj Value		Full Value
ORY-1001, AML	20%	€	4	€	22
ORY-2001, AD	5%	€	10	€	201
Cash		€	1	€	1
Price Target		**€**	**15**	€	224

Source: ROTH Capital Partners research.

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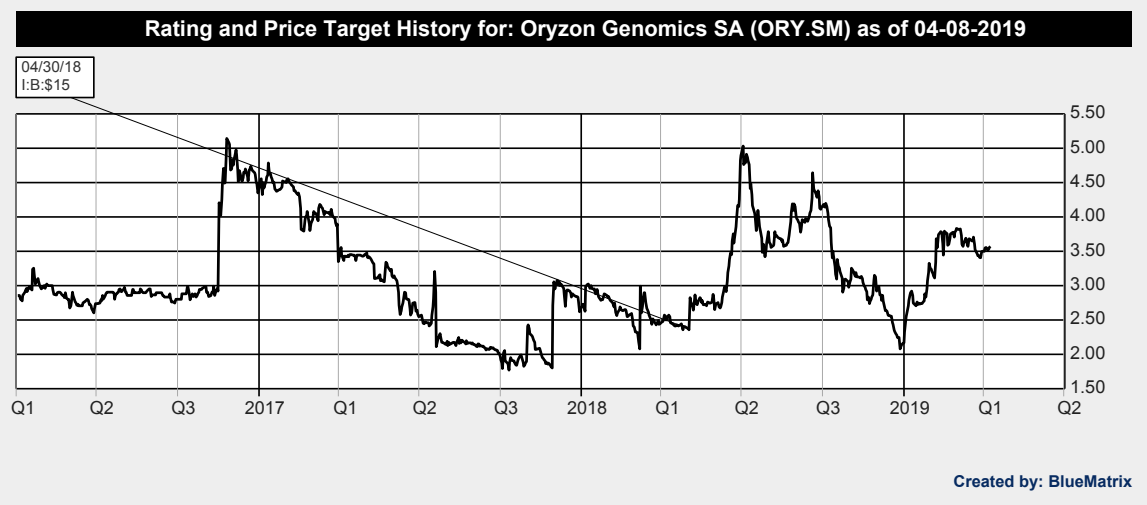
Disclosures:

Within the last twelve months, ROTH has received compensation for investment banking services from Oryzon Genomics SA.

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 04/09/19	
Rating	**Count**	**Percent**	**Count**	**Percent**
Buy [B]	**262**	**75.94**	**140**	**53.44**
Neutral [N]	**54**	**15.65**	**32**	**59.26**
Sell [S]	**3**	**0.87**	**1**	**33.33**
Under Review [UR]	**26**	**7.54**	**12**	**46.15**

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.