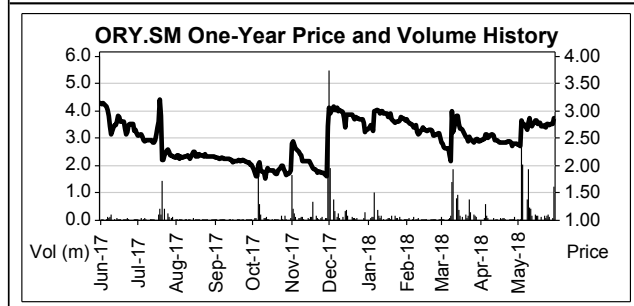


Healthcare: Biotechnology

Oryzon Genomics SA | ORY.SM - €2.87 - MADRID | Buy

Company Update

Stock Data			
52-Week Low - High	€1.75 - €3.40		
Shares Out. (mil)	34.16		
Mkt. Cap.(mil)	€98.0		
3-Mo. Avg. Vol.	315,826		
12-Mo.Price Target	€15.00		
Cash (mil)	€35.1		
Tot. Debt (mil)	€0.0		
EPS \$			
Yr Dec	—2017—	—2018E—	—2019E—
		Curr	Curr
1Q	-	(0.05)E	-
2Q	-	(0.05)E	-
3Q	-	(0.06)E	-
4Q	-	(0.06)E	-
YEAR	(0.20)A	(0.22)E	(0.26)E
P/E	NM	NM	NM
Revenue (\$ millions)			
Yr Dec	—2017—	—2018E—	—2019E—
		Curr	Curr
1Q	-	0.0E	-
2Q	-	0.0E	-
3Q	-	0.0E	-
4Q	-	0.0E	-
YEAR	0.0A	0.0E	0.0E



ORY.SM: Spotlight on Alzheimer's

We believe that Oryzon's epigenetic program in Alzheimer's (now clinical) is sufficiently differentiated from everything else in the field. Below we discuss why we believe that the ongoing Phase 2a study is likely to record positive signals in early 2019. Importantly, since in our view Oryzon still remains off-the-radar and the market is not expecting anything from this novel neuro program, a positive exploratory study will likely catapult Oryzon onto the map of Alzheimer's therapeutics, and upgrade its valuation appropriately.

What? As a reminder, Oryzon's lead neuro candidate, ORY-2001, is a selective dual inhibitor of LSD1 and MAO-B, which has shown preclinical effects in neuroinflammation and neuroprotection, as well as on behavioral phenomena such as aggression/agitation and social withdrawal. In our view, LSD1 (lysine specific demethylase 1) is a VIP epigenetic target, with good rationale and preclinical findings supporting its use in Alzheimer's disease (AD). Meanwhile, MAO-B (monoamine oxidase B) is a more classical neuro target (enzymatically degrades dopamine). We highlight that two MAO-B inhibitors (selegiline and rasagiline) are used today in Parkinson's.

When? Last year Oryzon cleared ORY-2001 through a 106-patient Phase 1 study, showing a clean safety profile, good brain penetrance, and continuous target coverage and engagement (half life 22 hrs; key for an epigenetic agent, in our view). Meanwhile, this May the ETHERAL Phase 2a study in AD started enrollment in Spain, and was approved to move forward in France and the UK. The 26-week study will enroll ~90 patients with mild/moderate AD, and report on a range of exploratory cognitive, functional, and biomarker endpoints. Oryzon expects a preliminary readout in early 2019.

How? If we take the LSD1 component out of the picture, as a thought experiment, we believe that the MAO-B component of ORY-2001 should be enough to show some clinical activity in the setting of this study. Our review of literature suggests that monotherapy in early disease is an ideal setting to flush out the activity of MAO-B inhibitors. Specifically, when looking at classical MAO-B inhibitors in different stages of AD from the past: (a) Lazabemide monotherapy in mild/moderate AD has shown cognitive and functional benefit (but was scratched due to tox); (b) Selegiline in moderate AD has shown no cognitive benefit, but some delay in functional deterioration; (c) Sembragiline combo with AChEI in moderate AD has shown no cognitive or functional benefit. In our view, these old studies together suggest that MAO-B targeting can be active in AD, but that activity emerges clinically only in earlier disease, before too much decline and before the start of conventional background therapy. Interestingly, this also happens to fit our own theory about the ideal application of an epigenetic therapy in AD, i.e., adding LSD1 targeting on top of MAO-B targeting. Overall, we believe that Oryzon's study design has maximized the chances of at least some clinical activity emerging, and that is before any epigenetic effects come into play. In our view, this an important consideration when thinking about a company whose pipeline and valuation still remain relatively undiscovered.

VALUATION

Our 12-month price target of €15/share (€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.

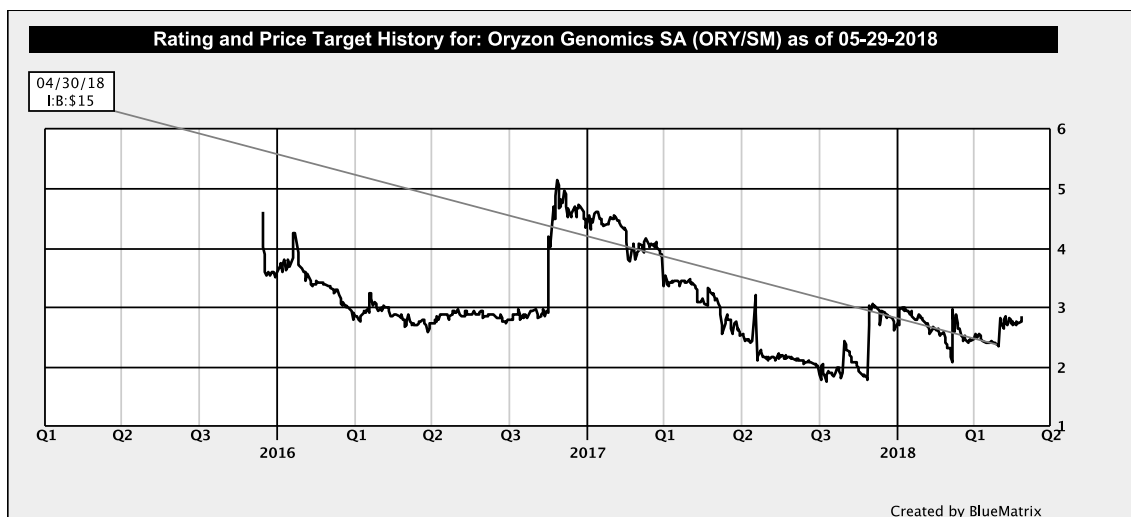
COMPANY DESCRIPTION

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).

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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

Rating	Count	Percent	IB Serv./Past 12 Mos. as of 05/30/18	
			Count	Percent
Buy [B]	250	70.82	135	54.00
Neutral [N]	51	14.45	22	43.14
Sell [S]	4	1.13	2	50.00
Under Review [UR]	47	13.31	25	53.19

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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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