INVEST SECURITIES

BIOTECH

ORYZON GENOMICS

BUY

TARGET PRICE : 6,6€ +222%

RESULTS OF PHASE IIB IN BPD

SUCCESS OR FAILURE OF PORTICO? THE FDA TO DECIDE

After trading on Friday, the company unveiled the results of its Phase IIb trial PORTICO in borderline personality disorder (BPD). The results were mixed, with the trial's primary endpoints failing to reach statistical significance. However, two secondary endpoints were positive with a significant p-value, which should enable the company to obtain FDA approval for further development in a pivotal Phase III trial. Given the lack of approved treatments in this field and the medical need, we believe that the FDA could respond favourably to Oryzon's application. Pending initial feedback from the agency, we are making no change to our TP and reiterate our Buy rating.

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Document completed on 09/01/2024 7:37

Document published on 09/01/2024 7:37

Mixed results in a complex, multifactorial pathology

On Friday, the company published the topline results of its PORTICO Phase IIb trial in borderline personality disorder (BPD), which were negative in the two primary endpoints, despite showing a positive trend in favour of vafidemstat vs. placebo (statistically significant value not reached). However, out of the 11 criteria assessed, two were statistically significant in key areas: the severity of BPD symptoms and feelings of anger associated with aggression and agitation. In addition, an overall assessment of the trial's endpoints using GST (global statistical test p-value, useful for assessing the benefit of a potential treatment for a complex, multifactorial disease) confirmed a strong positive trend across all 11 trial endpoints in favour of vafidemstat treatment versus placebo.

BPD: a condition for which there is currently no approved treatment

Most clinical programmes in the area have failed to demonstrate efficacy. To date, there is no approved treatment for this complex condition. According to Oryzon Genomics, the PORTICO trial is the first study of this scale to have demonstrated efficacy in two criteria. As such, the company is confident in these results and believes it can obtain FDA approval for further development in a pivotal Phase III trial. We believe that in diseases where there is little clinical data and a relatively limited understanding of the mechanics underlying development of the disorder, regulatory agencies can indeed be flexible in their assessment of clinical results. Given the lack of effective treatments for BPD, the demonstration of a positive effect of vafidemstat on all the criteria assessed, including two that were significantly improved, is an opportunity for patients that regulatory agencies must consider, especially for a product with a generally satisfactory safety profile.

According to key opinion leaders (KOLs), a clinically effective product for BPD would be a drug candidate capable of achieving an improvement of at least 25% in the criteria assessed. In this respect, vafidemstat showed a mean improvement of 28.9% during weeks 8 to 12 of treatment for the BEST endpoint (measure of BPD symptom severity and adapted responses) with a p-value of 0.042, and a mean improvement of 46.7% for the STAXI-2 Trait Anger endpoint (anger and aggression/agitation) with a p-value of 0.026.

Invest Securities and the issuer have signed an analysis services agreement.

in € / share	2023e	2024e	2025e
Adjusted EPS	0,19	0,53	0,61
chg.	*n.s.*	*+174,4%*	*+15,2%*
estimates chg.	*-381%*	*-556%*	*n.s.*

au 31/12	2023e	2024e	2025e
PE	0,0x	0,0x	0,0x
EV/Sales	1,7x	0,6x	-0,2x
EV/Adjusted EBITD	2,5x	0,5x	-0,1x
EV/Adjusted EBITA	2,5x	0,5x	-0,1x
FCF yield*	n.s.	124,5%	-410,1%
Div. yield (%)	n.s.	n.s.	n.s.

* After tax op. FCF before WCR

key points	
Closing share price 08/01/2024	2,1
Number of Shares (m)	59,7
Market cap. (€m)	122
Free float (€m)	101
ISIN	ES0167733015
Ticker	ORY-ES
DJ Sector	Health Technology

	1m	3m	Ytd
Absolute perf.	-5,7%	+1,0%	+8,6%
Relative perf.	-8,6%	-4,2%	+9,5%

Source : Factset, Invest Securities estimates

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Next key stages: Q1 and Q2 2024

At this stage, Oryzon Genomics plans to prepare a complete file of data and analyses from its PORTICO trial by the end of Q1 2024, with a view to submitting an end-of-Phase II meeting application to the FDA at the beginning of Q2 2024. The aim is to discuss the results obtained with the agency in order to prepare the most appropriate pivotal Phase III trial, taking into account the observations and analyses from PORTICO. Based on statistical calculations of the design and results of the PORTICO trial, Oryzon estimates that a study involving between 300 and 500 patients would have achieved the statistical power necessary to obtain statistically significant results for the two primary endpoints. The plan is therefore to use the same calculation methodology to design a solid Phase III trial that will be submitted to the FDA for approval. The details of this trial will be refined and communicated at a later date following discussions with the FDA, the aim being to conduct a clinical trial on a larger number of patients (probably between 300 and 500) and over the same 12-week treatment period as PORTICO. The company does not plan to extend the treatment time because of the possible risk of patient disengagement and non-adherence, which could lead to bias in the study and prevent statistical significance from being achieved.

The full PORTICO data will probably be presented at a medical congress in mid-Q2 2024. The company is also awaiting further results from a biomarker analysis of PORTICO data. The aim is to identify patient profiles that are more likely to respond favourably to treatment with vafidemstat. If such a correlation is demonstrated, it will also be submitted to the FDA to enable patient segmentation and selection of the best responders with a view to recruitment for the Phase III trial the group would like to plan, the aim being to preserve the best possible chances of success for the trial. The results of the analysis of the biomarker data are expected at the end of Q1 2024 and will be included in the file being prepared for the FDA.

Buy rating maintained and TP unchanged at €6.6.for the moment

On the basis of the results obtained, it is difficult to consider the PORTICO trial as positive at this stage. However, it is also difficult for us to consider that the data collected and the results obtained at this stage are not a clinical success and cannot be considered promising for patients suffering from BPD. In our view, the trial's validity will depend on the FDA's assessment during the discussions scheduled in H1 2024. At this stage, we are making no change to our TP, pending the first feedback from the FDA and the agency's decision once it has reviewed the results and analyses submitted. With no effective treatment available in this field, we believe the results obtained to date remain promising and represent a real opportunity for BPD patients. However, the probability of concluding a licensing agreement based on these topline results now seems lower and will probably oblige Oryzon to use the €45m convertible bond financing line signed with Nice & Green at the end of 2023, with the associated risk of dilution and pressure on the share price. In our view, a potential partner would probably prefer to wait for feedback from the FDA before taking a position on vafidemstat, thereby making it less likely that a deal will be concluded in the short term. Pending feedback from the FDA, we are making no change to the probability of success of the PORTICO trial in our model, as the possibility of continuing the programme in Phase III remains subject to the FDA's decision. After the announcement of the results yesterday, the share opened trading up 8% and closed down 7.2%, reflecting the lukewarm reception to the results shared by the company during the webcast on Sunday evening. We are maintaining our Buy recommendation in view of still attractive upside and moderate risk in our view.

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FINANCIAL DATA

Share information	2018	2019	2020	2021	2022	2023e	2024e	2025e
Published EPS (€)	-0,03	-0,08	-0,08	0,07	-0,04	0,19	0,53	0,61
Adjusted EPS (€)	**-0,03**	**-0,08**	**-0,08**	**0,07**	**-0,04**	**0,19**	**0,53**	**0,61**
Diff. I.S. vs Consensus	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*
Dividend	0,00	0,00	0,00	0,00	0,00	0,00	0,00	1,00

Valuation ratios	2018	2019	2020	2021	2022	2023e	2024e	2025e
P/E	n.s.	n.s.	n.s.	0,0x	n.s.	0,0x	0,0x	0,0x
EV/Sales	n.s.	n.s.	n.s.	1,72x	1,73x	1,74x	0,65x	-0,21x
EV/Adjusted EBITDA	n.s.	n.s.	n.s.	6,1x	n.s.	2,5x	0,5x	-0,1x
EV/Adjusted EBITA	n.s.	n.s.	n.s.	6,1x	n.s.	2,5x	0,5x	-0,1x
Op. FCF bef. WCR yield	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	124,5%	-410,1%
Op. FCF yield	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	124,5%	-410,1%
Div. yield (%)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.

NB : valuation based on annual average price for past exercise

Entreprise Value (€m)	2018	2019	2020	2021	2022	2023e	2024e	2025e
Share price in €	*0,0*	*2,5*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*
Market cap.	0	123	39	39	39	39	39	39
Net Debt	-23	-27	-29	-24	-13	-13	-27	-45
Minorities	0	0	0	0	0	0	0	1
Provisions/ near-debt	0	0	0	0	0	0	0	0
+/- Adjustments	0	0	0	0	0	0	0	1
Entreprise Value (EV)	**-22**	**97**	**10**	**15**	**26**	**26**	**12**	**-4**

Income statement (€m)	2018	2019	2020	2021	2022	2023e	2024e	2025e
Sales	0,0	0,0	0,0	9,0	15,0	15,0	18,0	21,0
chg.	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*
Adjusted EBITDA	-3	-4	-4	3	0	11	26	30
adjusted EBITA	**-3**	**-4**	**-4**	**3**	**0**	**11**	**26**	**30**
chg.	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***+142,6%***	***+15,7%***
EBIT	-3,3	-3,8	-4,3	2,2	-0,9	10,1	25,0	29,0
Financial result	-1	-1	0	0	0	0	0	0
Corp. tax	3	1	1	1	0	-1	-2	-2
Minorities+affiliates	0	0	0	0	0	0	0	0
Net attributable profit	-1,2	-3,7	-3,4	3,1	-1,8	8,4	23,0	26,5
Adjusted net att. profit	**-1,2**	**-3,7**	**-3,4**	**3,1**	**-1,8**	**8,4**	**23,0**	**26,5**
chg.	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***+174,4%***	***+15,2%***

Cash flow statement (€m)	2018	2019	2020	2021	2022	2023e	2024e	2025e
EBITDA	-3,1	-3,7	-4,1	2,5	-0,5	10,5	25,5	29,5
Theoretical Tax / EBITA	2,5	0,9	1,4	1,4	-0,5	-1,2	-1,5	-2,0
Capex	-7,0	-9,6	-9,1	-9,5	-9,5	-9,5	-9,5	-9,5
Operating FCF bef. WCR	**-7,6**	**-12,4**	**-11,8**	**-5,6**	**-10,5**	**-0,2**	**14,5**	**18,1**
Change in WCR	0,3	0,3	-1,2	0,0	0,0	0,0	0,0	0,0
Operating FCF	**-7,3**	**-12,1**	**-13,1**	**-5,6**	**-10,5**	**-0,2**	**14,5**	**18,1**
Acquisitions/disposals	0,1	0,5	0,1	0,0	0,0	0,0	0,0	0,0
Capital increase/decrease	11,9	18,4	18,2	0,0	0,0	0,0	0,0	0,0
Dividends paid	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Other adjustments	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Published Cash-Flow	**4,7**	**6,7**	**5,3**	**-5,6**	**-10,5**	**-0,2**	**14,5**	**18,1**

Balance Sheet (€m)	2018	2019	2020	2021	2022	2023e	2024e	2025e
Assets	32	42	52	61	70	79	88	97
Intangible assets/GW	29	40	49	58	68	77	86	95
WCR	-9	-8	-5	-5	-5	-5	-5	-5
Group equity capital	45	61	76	79	77	86	109	135
Minority shareholders	0	0	0	0	0	0	0	1
Provisions	0	0	0	0	0	0	0	0
Net financial debt	**-22,6**	**-26,7**	**-29,1**	**-23,5**	**-13,1**	**-12,9**	**-27,4**	**-45,4**

Financial ratios	2018	2019	2020	2021	2022	2023e	2024e	2025e
EBITDA margin	n.s.	n.s.	n.s.	28,0%	n.s.	70,1%	141,8%	140,6%
EBITA margin	n.s.	n.s.	n.s.	28,0%	n.s.	70,1%	141,8%	140,6%
Adjusted Net Profit/Sales	n.s.	n.s.	n.s.	34,3%	n.s.	56,0%	128,0%	126,3%
ROCE	n.s.	n.s.	n.s.	4,5%	n.s.	14,2%	30,7%	32,0%
ROE adjusted	n.s.	n.s.	n.s.	3,9%	n.s.	9,8%	21,2%	19,6%
Gearing	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
ND/EBITDA (in x)	n.s.	n.s.	n.s.	-9,3x	n.s.	-1,2x	-1,1x	-1,5x

Source : company, Invest Securities Estimates

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INVESTMENT CASE

ORYZON GENOMICS is a Spanish biotechnology company specializing in the treatment of neurodegenerative diseases and cancer. Specializing in the field of epigenetics, the company aims, in all of its development programs, to identify biomarkers through its genetic and proteomic platforms in order to develop small molecule drugs. The company has delivered interesting results with its most advanced programs in areas more or less invested in terms of overall R&D efforts, cancer but also Covid-19 and cognitive disorders associated with neurodegenerative diseases or disorders of the personality.

SWOT ANALYSIS

STRENGTHS

- Epigenetic platform
- Extensive development pipeline
- Differentiating positioning

WEAKNESSES

- No partnership
- Risky indications (CNS)
- Intense competition in oncology

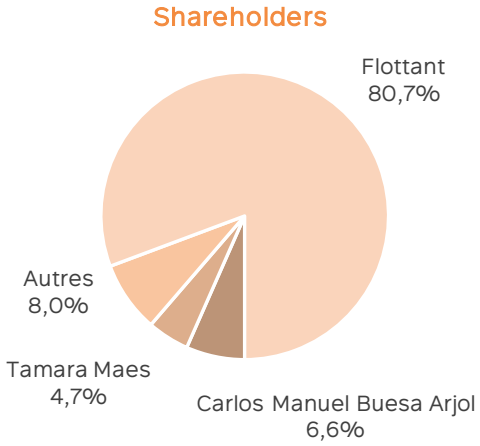
OPPORTUNITIES

- Potential partnership
- Extension of indications

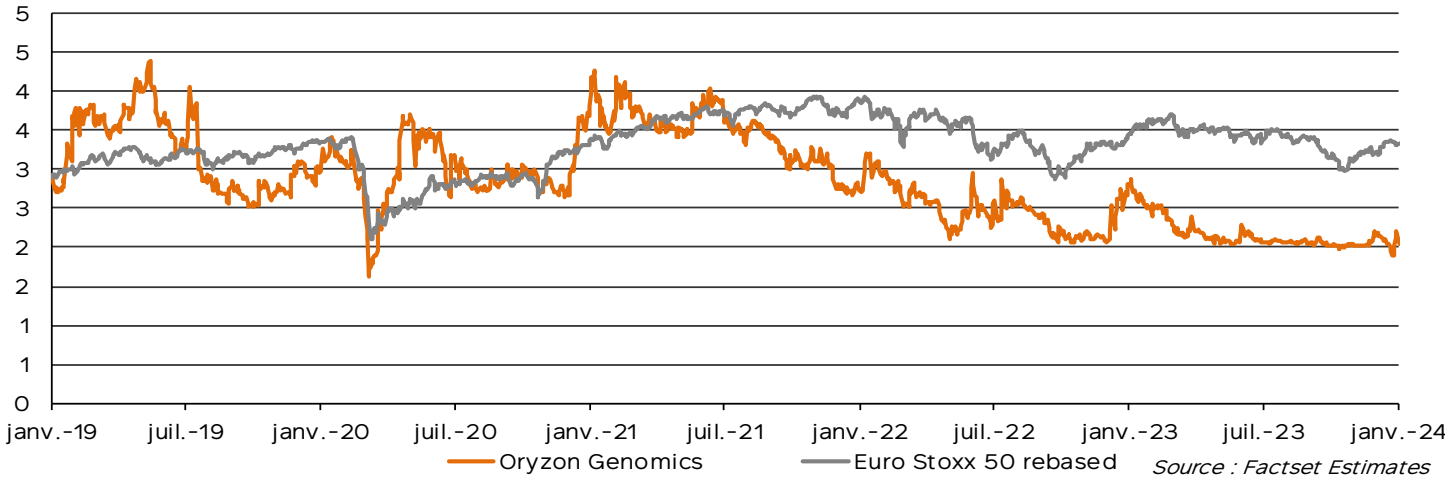
THREATS

- Clinical and regulatory risk
- Commercial risks
- Legal risks

ADDITIONAL INFOMATION



SHARE PRICE CHANGE FOR 5 YEARS



Source : Factset Estimates

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TARGET PRICE AND RECOMMENDATION

Our analyst ratings are dependent on the expected absolute performance of the stock on a 6- to 12-month horizon. They are based on the company’s risk profile and the target price set by the analyst, which takes into account exogenous factors related to the market environment that may vary considerably. The Invest Securities analysis office sets target prices based on a multi-criteria fundamental analysis, including, but not limited to, discounted cash flows, comparisons based on peer companies or transaction multiples, sum-of-the-parts value, restated net asset value, discounted dividends.

Ratings assigned by the Invest Securities analysis office are defined as follows:

- BUY: Upside potential of more than 10% (the minimum upside required may be revised upward depending on the company’s risk profile)
- NEUTRAL: Between -10% downside and +10% upside potential (the maximum required may be revised upward depending on the company’s risk profile)
- SELL: Downside potential of more than 10%
- TENDER or DO NOT TENDER: Recommendations used when a public offer has been made for the issuer (takeover bid, public exchange offer, squeeze-out, etc.)
- SUBSCRIBE or DO NOT SUBSCRIBE: Recommendations used when a company is raising capital
- UNDER REVIEW: Temporary recommendation used when an exceptional event that has a substantial impact on the company’s results or our target price makes it impossible to assign a BUY, NEUTRAL or SELL rating to a stock

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12-MONTHS HISTORY OF OPINION

The table below reflects the history of recommendation and price target changes made by Invest Securities' research department over the last 12 months.

Company Name	Main Author	Release Date	Rating	Target Price	Potential

DETECTION OF CONFLICTS OF INTEREST

	Oryzon Genomics
Invest Securities was lead manager or co-lead manager in a public offer concerning the financial instruments of this issuer during the last twelve months.	No
Invest Securities has signed a liquidity contract with the issuer.	No
Invest Securities and the issuer have signed a research service agreement.	Yes
Invest Securities and the issuer have signed a Listing Sponsor agreement.	No
Invest Securities has been remunerated by this issuer in exchange for the provision of other investment services during the last twelve months (RTO, Execution on behalf of third parties, advice, placement, underwriting).	No
This document was sent to the issuer prior to its publication. This rereading did not lead the analyst to modify the valuation.	No
This document was sent to the issuer for review prior to its publication. This rereading led the analyst to modify the valuation.	No
The financial analyst has an interest in the capital of the issuer.	No
The financial analyst acquired equity securities of the issuer prior to the public offering transaction.	No
The financial analyst receives remuneration directly linked to the transaction or to an investment service provided by Invest Securities.	No
An executive officer of Invest Securities is in a conflict of interest with the issuer and was given access to this document prior to its completion.	No
Invest Securities or the All Invest group owns or controls 5% or more of the share capital issued by the issuer.	No
Invest Securities or the All Invest group holds, on a temporary basis, a net long position of more than 0.5% of the issuer's capital.	No
Invest Securities or the All Invest group holds, on a temporary basis, a net short position of more than 0.5% of the issuer's capital.	No
The issuer owns or controls 5% or more of the capital of Invest Securities or the All Invest group.	No

Invest Securities's conflict of interest management policy is available on the Invest Securities website in the Complicance section. A list of all recommendations released over 12 months as well as the quarterly publication of "BUY, SELL, NEUTRAL, OTHERS" over 12 months, are available on the Invest Securities research platform.

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