

31<sup>ST</sup> ECCMID

## COVID: PRELIMINARY RESULTS ARE ENCOURAGING!

ORYZON presented to the European Congress of Clinical Microbiology & Infectious Diseases (ECCMID) an update on its Phase II ESCAPE trial, which it launched in 2020 to explore the potential for using one of its leading drug candidates to manage patients with severe cases of Covid-19. Given the mechanism of action and anti-inflammatory activity of vafidemstat, the company quickly got this clinical trial up and running in April 2020, so that it could contribute to the collective effort to tackle the newly declared pandemic and help identify a potentially efficacious therapeutic solution. The preliminary results available to date are very encouraging, pointing to a reduction in the most severe symptoms that can lead to acute respiratory distress. We are standing behind our rating and target price.

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ESCAPE, a Phase II trial on 60 randomized patients with severe Covid progressing toward ARDS

On the first day of the 31st European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), taking place from July 9 to 12 2021, ORYZON presented preliminary data from its Phase II trial ESCAPE, evaluating the potential of its drug candidate vafidemstat (ORY-2001) to reduce inflammatory response in patients with severe forms of Covid-19.

ESCAPE is an open-label, randomized, double arm Phase II trial to evaluate the efficacy and tolerability of vafidemstat in combination with standard of care (SoC) treatment in the target indication, to prevent progression of severely ill Covid-19 patients with pneumonia to Acute Respiratory Distress Syndrome (ARDS), one of the leading causes of death in the disease, by reducing the patient's inflammatory response to the infection. Glucocorticoids were the most frequent SoC treatment (83% of patients, equally represented in both arms). The endpoints were assessed at days 5, 14 and 28.

EudraCT Number: 2020-001618-39		Sponsor Protocol Number: CL08-ORY-2001_COVID-19		Start Date*: 2020-04-24	
Sponsor Name: Oryzon Genomics S. A.					
Full Title: A Phase II, randomized, open-label study to evaluate the efficacy and tolerability of treatment with vafidemstat in combination with standard of care treatment to prevent Acute Respiratory Distress...					
Medical condition: Acute Respiratory Distress Syndrome (ARDS)					
Disease:	Version	SOC Term	Classification Code	Term	Level
	21.1	100000004855	10003083	ARDS	LLT
Population Age: Adults, Elderly			Gender: Male, Female		
Trial protocol: ES (Ongoing)					
Trial results: (No results available)					

Source: [clinicaltrialsregister.eu](https://clinicaltrialsregister.eu)

Invest Securities and the issuer have signed an analysis service agreement

in € / share	2021e	2022e	2023e
Adjusted EPS	-0,14	0,57	0,48
chg.	n.s.	n.s.	-15,6%
estimates chg.	n.s.	n.s.	n.s.
au 31/12	2021e	2022e	2023e
PE	n.s.	6,4x	7,6x
EV/Sales	n.s.	2,7x	4,6x
EV/EBITDA	n.s.	3,9x	5,5x
EV/EBITA	n.s.	3,9x	5,5x
FCF yield*	n.s.	12,2%	10,3%
Div. yield (%)	n.s.	n.s.	n.s.

\* After tax op. FCF before WCR

key points			
Share price (€)			3,7
Number of Shares (m)			53,1
Market cap. (€m)			194
Free float (€m)			157
ISIN			ESO167733015
Ticker			ORY-ES
DJ Sector			Health Technology
	1m	3m	Ytd
Absolute perf.	-6,5%	+5,6%	+4,7%
Relative perf.	-5,8%	+3,3%	-8,6%

Source: Factset, Invest Securities estimates

### Vafidemstat: Rationale for repurposing the drug to treat Covid

Vafidemstat (ORY-2001) is an oral small molecule that has been optimized for central nervous system (CNS) indications. It acts as a covalent inhibitor of the epigenetic enzyme Lysine Specific Demethylase-1, LSD1 (KDM1A), the most abundant Lysine Demethylase in the prefrontal cortex. LSD1 plays a fundamental role in the formation of the CNS, notably in neurogenesis, neuronal differentiation and axonal navigation.

Given the role this protein plays in the development of various disorders, both neurological and oncological, there is a strong rationale for modulating the enzyme, notably via inhibition, as a therapeutic strategy.

The mechanism of action of vafidemstat, an LSD1 inhibitor, acts at two main levels:

- Reduction of cognitive impairment,
- Reduction of neuro-inflammation (effect reported by ORYZON scientists).

In animal models, vafidemstat was shown to restore memory and to significantly reduce the exacerbated aggressiveness observed in SAMP8 mice, a model for accelerated aging and Alzheimer's disease. It also reduced social avoidance and enhanced sociability. And vafidemstat has shown promising results for other severe indications with considerable unmet needs, such as multiple sclerosis (MS). Indeed, vafidemstat exhibited fast, strong and durable efficacy in several preclinical MS models, where it reduced neuro-inflammation (activity of most treatments currently available for MS), and in activities of great medical interest, including modulation of glial activity, neuroprotection and, importantly, the preservation of axonal integrity. Such effects are highly sought after by pharma companies exploring ways to treat neurodegenerative diseases.

The rationale for repositioning vafidemstat as a Covid-19 drug is based on its observed effects on inflammation. In preclinical models of acute inflammation, vafidemstat has been shown to produce a rapid and sharp decrease in IL-6, IL-1B, and other relevant immunomodulatory inflammatory cytokines such as TNF- $\alpha$  and IFN- $\gamma$ . In the recent ETHERAL clinical study in Alzheimer's disease, vafidemstat was shown to be very safe in long-term treatments and also demonstrated a significant decrease in a relevant marker of brain inflammation. This underpins the rationale for the drug's anti-inflammatory effects as well as its good safety profile.

### Strong efficacy signals relative to standard of care in Phase II trial

Between May 2020 and March 2021, 60 patients were randomized in the Phase II ESCAPE trial to determine the safety and efficacy of vafidemstat as an add-on to SoC treatment in Covid-19 severe patients. Follow-up data show that most of the patients in both arms (69% of the total cohort) were discharged before the first week of treatment, while four were admitted to ICU (two from each arm). Overall, vafidemstat appears to improve patients' general condition, since fewer interventions were required in the experimental arm vs. placebo: (i) mechanical ventilation required in 65.5% of the experimental arm (19 patients) vs. 77.4% in the control arm (24 patients), (ii) rescue medication (Tocilizumab = Actemra, ROCHE) required in 33% of the experimental arm (2 patients) vs. 67% in the control arm (4 patients), and (iii) one death due to Covid morbidities versus none in the vafidemstat arm.

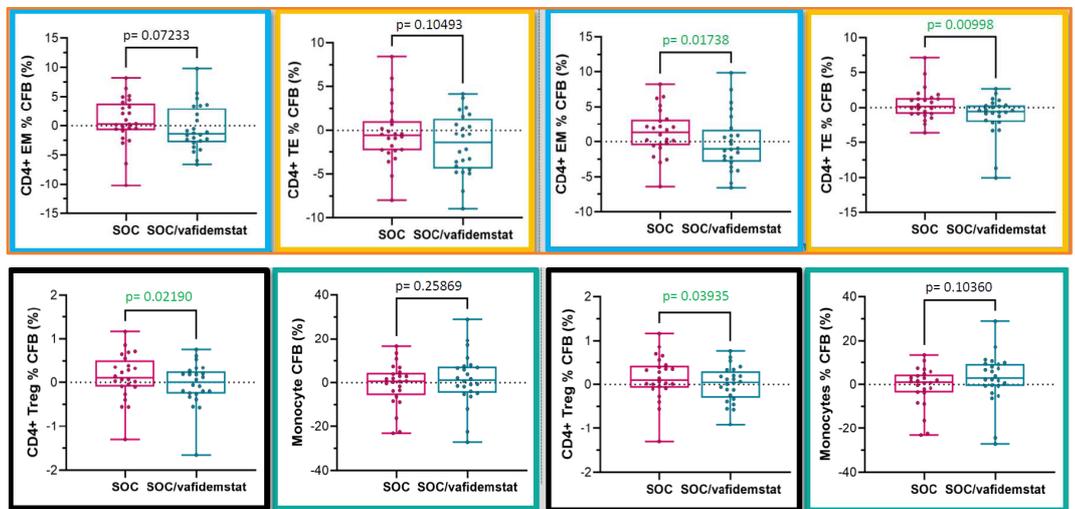
The primary endpoint of the study was to measure the difference in mortality between the vafidemstat + SoC arm vs. placebo + SoC. This endpoint now seems difficult to meet, given how the pandemic has trended and the sharp reduction in Covid-19-related mortality since the epidemic began. Indeed, hospital management of severely ill Covid-19 patients has improved considerably, and existing SoC treatments are proving efficacious in reducing mortality associated with SARS-CoV-2: Within the cohort of 60 patients with severe Covid-19, only one death was reported (in the placebo arm). This is why the primary endpoint set when the ESCAPE trial was being designed—measuring the difference in mortality between the two arms—is not relevant.

That being said, the data collected show an undeniable clinical benefit, particularly with regard to the need for mechanical ventilation and the rescue medication Tocilizumab.

Clinical benefit confirmed at the cellular level...

The study showed that treatment with vafidemstat inhibited LSD1 at the cellular and molecular levels, producing significant effects on the immune response induced by Covid-19 infection. This immune response was observed at two levels: (i) circulating immune cell populations, and (ii) inflammatory mediators, including cytokines and chemokines.

Change in frequency of immune cell subpopulations



Source: ORYZON GENOMICS

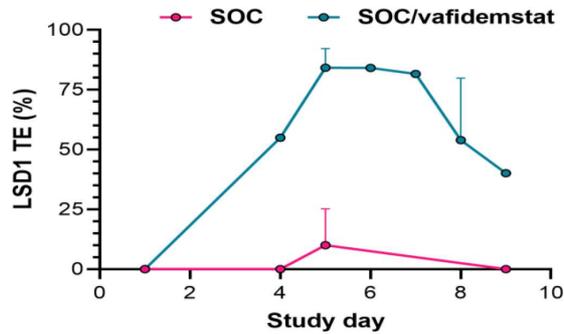
Furthermore, distinct changes in the frequency of several circulating immune cell populations were also observed, significantly affecting T CD4+ cell subsets, revealing that vafidemstat in combination with SoC treatment could help to control T-cell activation by significantly reducing the percentage of terminal effector, effector memory, and regulatory T cells. These specific immune cell subpopulations have been previously shown to be elevated in patients with Covid-19 pneumonia. Their presence may make patients more prone to developing a severe form of Covid-19 and a form associated with respiratory distress. Vafidemstat's effect on these cells in particular supports the case for its potential to prevent Covid-19 from evolving into very severe forms.

... and the molecular level: Action on cytokines and chemokines

Above and beyond clinical observations, and the drug's effects at the cellular level, treatment with 2.4mg/day of vafidemstat for five days resulted in an almost complete occupancy of the LSD1 target protein, which was sustained in most patients until they were discharged.

The graph below shows that LSD1 was still 70% occupied on average, even after treatment with vafidemstat ended. It also shows that in the absence of a treatment containing vafidemstat, the LSD1 rate remains low or even nonexistent throughout and after the entire treatment period.

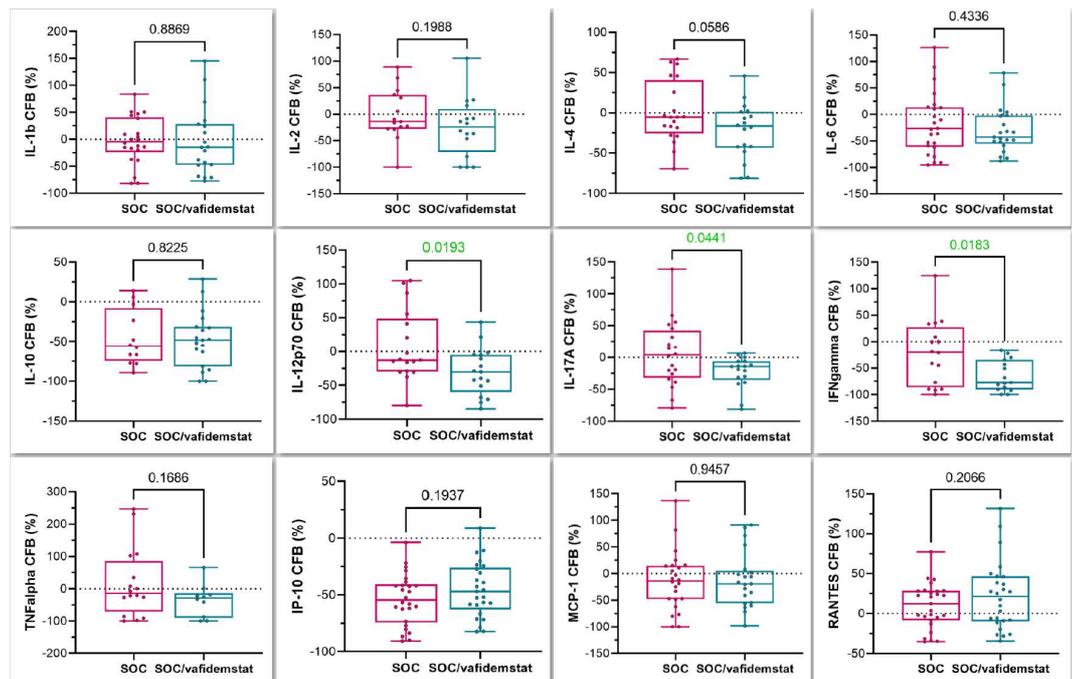
**Trend in LSD1 occupancy**



Source: ORYZON GENOMICS

LSD1 inhibition by vafidemstat resulted in significant effects on the immune response induced by Covid-19 infection both in terms of circulating immune cell populations and inflammatory mediators, including cytokines and chemokines. With regard to inflammatory mediators in particular, a clear tendency for decreased plasma levels of most of the cytokines evaluated was observed after five days of treatment with vafidemstat compared to the immunosuppressor effect already observed with the SoC alone, achieving statistical significance ( $p < 0.05$ ) for cytokines IL-12p70, IL -17A and IFN $\gamma$ . Regarding chemokines, vafidemstat treatment generated a trend towards elevation of RANTES (Regulated upon Activation, Normal T Cell Expressed and Presumably Secreted), known to play an important role in protecting Covid-19 patients from developing severe illness.

**Cytokines/chemokines in plasma in response to vafidemstat**



Source: ORYZON GENOMICS

In sum, data collected so far from the ESCAPE trial are fairly encouraging, since the vafidemstat arm has produced better anti-inflammatory indicators than the placebo arm. This is a clear example of the drug candidate's potential, especially when it comes to controlling the escalation of serious events that can potentially lead to severe or very severe illness in Covid-19 patients.

Vafidemstat modulates the immune response of Covid-19 patients at risk of rapidly becoming critical by controlling exacerbated CD4+ T cell activation and the subsequent release of inflammatory cytokines beyond the basal effect of the corticoids. Following the trial with Alzheimer's patients, the ESCAPE trial is the second clinical demonstration of the anti-inflammatory effects of vafidemstat for different indications.

### Satisfactory safety and tolerability profile

In terms of tolerability, the treatment was well tolerated on the whole with 13 adverse events (AEs) reported in 11 subjects during the study, none of them severe or serious. Nine of the AEs were in the vafidemstat + SoC arm, and all were mild and considered non-treatment related. This is an important outcome as it confirms that treatment with vafidemstat plus SoC, mainly corticoids, is safe and well tolerated.

Vafidemstat has to date been administered to more than 250 subjects through the multiple Phase I and II clinical trials completed or ongoing, and has been found to be safe and well tolerated.

### Final results of ESCAPE trial expected within the coming months

Heartened by these results, ORYZON will analyze different parameters to show vafidemstat's full potential for managing patients with Covid-19. Differences between the experimental arm (vafidemstat + SoC) and control arm (placebo + SoC) in terms of clinical response, including days of hospitalization or respiratory parameters, will be analyzed at a later date, once the database is hard-locked.

ORYZON has not yet provided a timeframe for the next steps. It will mainly be analyzing the data gathered under different parameters to measure the benefit of the treatment for patients even if the primary endpoint is not met for now. No additional information is available at this time, but we estimate that the full analysis will become available sometime around the middle of H2 2021.

### Covid-19 treatments: Status of research and approvals

Whereas Covid-19 vaccine makers more or less kept their promise of delivering efficacious solutions in record time (the first vaccine using PFIZER/BIONTECH technology was approved in the UK in December 2020), the road has been bumpier for Covid-19 treatments. In the early days of the pandemic, most were betting on the treatment segment rather than vaccines, but the former is now regarded with great disappointment and skepticism. The fact is that colossal resources were quickly allocated to Covid-19 treatment and a large number of drugs and drug candidates were repurposed due to their known anti-inflammatory, antiviral and/or neuroprotective properties, but there is not much to show for these efforts today.

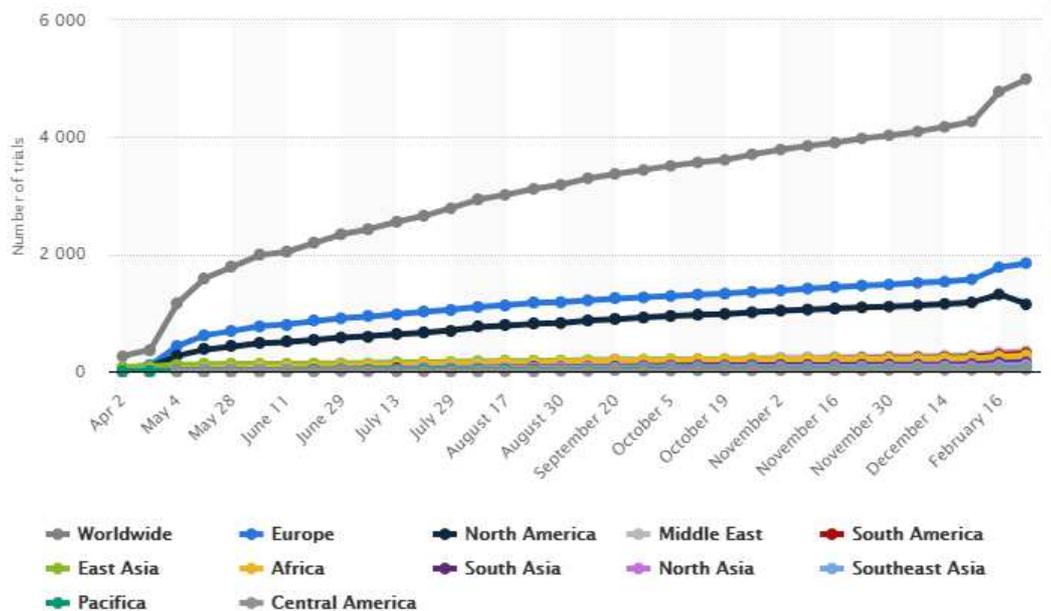
Yet the need for a treatment that works is undeniable, especially if the virus becomes endemic, as most in the health sector predict will happen. In line with statements from the CEOs of MODERNA and PFIZER, the WHO recently indicated that the most vulnerable will probably need to be vaccinated every year and the rest of the population every other year.

Moreover, while the vaccines, particularly those using mRNA technology, do appear to offer relatively good protection against Covid-19, a 100% vaccination rate will never be achieved. This means that the risk of severe Covid-19 patients needing hospitalization, respiratory assistance and acute care will remain. It is therefore indispensable to identify treatments that can prevent the disease from progressing to such severe stages, with three primary goals:

- Reduce mortality associated with Covid-19
- Reduce hospitalizations and the risk of hospitals filling up due to a new wave of infections
- Keep contamination in check to limit the risk of spread.

According to Statista, some 5,000 Covid-19 clinical programs were listed as active across the world on the ClinicalTrials.gov website in March 2021, a very large majority of them in the field of therapeutics. It is imperative that all SARS-Cov-2 solutions and strategies be considered as part of a whole. Until such time as a prophylactic approach proves effective in protecting the entire population, despite the potential roadblocks known today (delays in vaccinating low-income areas, emergence of more or less resistant variants, vaccine defiance in certain parts of the population, vaccines offering less than 100% protection, moderate durability of protection, etc.), the therapeutic arsenal must be as broad and complementary as possible. Indeed, even if countries are less focused on the therapeutic segment for now, it remains a priority for public health and within the scientific/medical community that is continuing the R&D work to deliver differentiating solutions. This is especially important if we consider that most experts believe the pandemic could quickly evolve into an endemic, meaning the virus may not be fully eradicated and that we may have to live with different variants during different seasons, similar to the flu.

**Number of coronavirus trials conducted between April 2020 and March 2021**



Source: Statista (ClinicalTrials.gov)

Various therapeutic solutions have already been approved in different parts of the world. In the US, the FDA has issued several emergency use authorizations (EUAs) since April 30, 2020 for different drugs and medical devices. Some of these EUAs have since been amended due to a failure to demonstrate efficacy per the initial use protocol (convalescent plasma and the combination of bamlanivimab/etesevimab antibodies). To date, the FDA has issued 11 EUAs:

- Treatments: Remdesivir, Covid-19 convalescent plasma, Baricitinib, REGEN-COV, bamlanivimab/etesevimab, Sotrovimab, and Actemra.
- Medical devices: MultiFiltrate PRO System by Fresenius, Fresenius Kabi Propoven 2%, REGIOCIT, Propofol-Lipuro 1%.

Europe's EMA has been more conservative, approving only one Covid-19 treatment to date: Veklury (remdesivir). A marketing authorization application is being reviewed for Olumiant (baricitinib), and four other products are under rolling review: the bamlanivimab/etesevimab combo, Regdanvimab, REGN-COV2 and Sotromvimab.

**Covid-19 treatments approved or under review in Europe and the US**

	Product	Manufacturer	Comments	EUA first delivery
 Authorization granted Marketing authorisation application submitted	Veklury (remdesivir)	Gilead Sciences		03/07/2020
	Olumiant (baricitinib)	Eli Lilly		
 Currently under rolling review	- Bamlanivimab and etesevimab	Eli Lilly		
	- Regdanvimab	Celltrion		
 Treatments        Medical devices	- REGN-COV2 (casirivimab / imdevimab)	Regeneron (Roche)		
	- Sotrovimab	GSK and Vir Biotechnology		
	- Actemra (Tocilizumab)	Roche		06/24/2021
	- Sotrovimab	GSK and Vir Biotechnology	* Pause in distribution of bamlanivimab/etesevimab	05/26/2021
	- Bamlanivimab and Etesevimab*	Eli Lilly		02/09/2021
	- REGEN-COV (Casirivimab and Imdevimab)	Regeneron (Roche)	nationwide (from ASPR and FDA, June 25, 2021)	11/21/2020
	- Baricitinib (Olumiant) in Combination with remdesivir (Veklury)	Eli Lilly		11/19/2020
	- COVID-19 convalescent plasma**	N/A	** Letter Granting EUA	08/23/2020
	- Remdesivir for Certain Hospitalized COVID-19 Patients	Gilead	Amendment (June 2, 2021)	05/01/2020
	- Propofol-Lipuro 1%	B. Braun		03/12/2021
	- REGIOCIT	Baxter		08/13/2020
- Fresenius Kabi Propoven 2%	Fresenius		05/08/2020	
- Fresenius Medical, multiFiltrate PRO System and multiBic/multiPlus Solutions	Fresenius		04/30/2020	

Source: EMA and FDA

## DONNÉES FINANCIÈRES

Share information	2018	2019	2020	2021e	2022e	2023e	2024e
Published EPS (€)	-0,03	-0,08	-0,08	-0,14	0,57	0,48	0,81
<b>Adjusted EPS (€)</b>	<b>-0,03</b>	<b>-0,08</b>	<b>-0,08</b>	<b>-0,14</b>	<b>0,57</b>	<b>0,48</b>	<b>0,81</b>
<i>Diff. I.S. vs Consensus</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>
Dividend	0,00	0,00	0,00	0,00	0,00	0,00	0,00

Valuation ratios	2018	2019	2020	2021e	2022e	2023e	2024e
P/E	n.s.	n.s.	n.s.	n.s.	6,4x	7,6x	4,5x
EV/Sales	n.s.	n.s.	n.s.	n.s.	2,67x	4,57x	0,98x
VE/EBITDA	n.s.	n.s.	n.s.	n.s.	3,9x	5,5x	2,3x
VE/EBITA	n.s.	n.s.	n.s.	n.s.	3,9x	5,5x	2,3x
Op. FCF bef. WCR yield	n.s.	n.s.	n.s.	n.s.	12,2%	10,3%	28,3%
Op. FCF yield	n.s.	n.s.	n.s.	n.s.	12,2%	10,3%	28,3%
Div. yield (%)	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	2021e	2022e	2023e	2024e
<i>Share price in €</i>	<i>3,7</i>	<i>2,9</i>	<i>3,7</i>	<i>3,7</i>	<i>3,7</i>	<i>3,7</i>	<i>3,7</i>
Market cap.	125	138	164	164	164	164	164
Net Debt	-23	-27	-29	-15	-31	-43	-70
Minorities	0	0	0	0	0	0	0
Provisions/ near-debt	0	0	0	0	0	0	0
+/- Adjustments	0	0	0	0	0	0	0
<b>Entreprise Value (EV)</b>	<b>103</b>	<b>112</b>	<b>135</b>	<b>150</b>	<b>133</b>	<b>121</b>	<b>94</b>

Income statement (€m)	2018	2019	2020	2021e	2022e	2023e	2024e
Sales	0,0	0,0	0,0	0,0	50,0	26,5	96,3
<i>chg.</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>
EBITDA	-3	-4	-4	-6	35	22	41
<b>EBITA</b>	<b>-3</b>	<b>-4</b>	<b>-4</b>	<b>-6</b>	<b>35</b>	<b>22</b>	<b>41</b>
<i>chg.</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	<b>-36,3%</b>	<b>+87,6%</b>
EBIT	-3,3	-3,8	-4,3	-6,8	34,1	21,5	40,7
Financial result	-1	-1	0	0	0	0	0
Corp. tax	3	1	1	1	-9	0	-5
Minorities+affiliates	0	0	0	0	0	0	0
Net attributable profit	-1,2	-3,7	-3,4	-5,9	25,0	21,1	35,2
<b>Adjusted net att. profit</b>	<b>-1,2</b>	<b>-3,7</b>	<b>-3,4</b>	<b>-5,9</b>	<b>25,0</b>	<b>21,1</b>	<b>35,2</b>
<i>chg.</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>	<b>-15,6%</b>	<b>+67,1%</b>

Cash flow statement (€m)	2018	2019	2020	2021e	2022e	2023e	2024e
EBITDA	-3,1	-3,7	-4,1	-6,5	34,5	22,0	41,2
Theoretical Tax / EBITDA	2,5	0,9	1,4	1,4	-8,7	0,0	-5,1
Capex	-7,0	-9,6	-9,1	-9,5	-9,5	-9,5	-9,5
<b>Operating FCF bef. WCR</b>	<b>-7,6</b>	<b>-12,4</b>	<b>-11,8</b>	<b>-14,6</b>	<b>16,3</b>	<b>12,5</b>	<b>26,7</b>
Change in WCR	0,3	0,3	-1,2	0,0	0,0	0,0	0,0
<b>Operating FCF</b>	<b>-7,3</b>	<b>-12,1</b>	<b>-13,1</b>	<b>-14,6</b>	<b>16,3</b>	<b>12,5</b>	<b>26,7</b>
Acquisitions/disposals	0,1	0,5	0,1	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
Dividends paid	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
<b>Published FreeCash Flow</b>	<b>4,7</b>	<b>6,7</b>	<b>5,3</b>	<b>-14,6</b>	<b>16,3</b>	<b>12,5</b>	<b>26,7</b>

Balance Sheet (€m)	2018	2019	2020	2021e	2022e	2023e	2024e
Assets	32	42	52	61	70	79	88
Intangible assets/GW	29	40	49	58	68	77	86
WCR	-9	-8	-5	-5	-5	-5	-5
Group equity capital	45	61	76	70	95	116	151
Minority shareholders	0	0	0	0	0	0	0
Provisions	0	0	0	0	0	0	0
<b>Net financial debt</b>	<b>-22,6</b>	<b>-26,7</b>	<b>-29,1</b>	<b>-14,5</b>	<b>-30,8</b>	<b>-43,3</b>	<b>-69,9</b>

Financial ratios	2018	2019	2020	2021e	2022e	2023e	2024e
EBITDA margin	n.s.	n.s.	n.s.	n.s.	69,0%	83,1%	42,8%
EBITA margin	n.s.	n.s.	n.s.	n.s.	69,0%	83,1%	42,8%
Adjusted Net Profit/Sales	n.s.	n.s.	n.s.	n.s.	49,9%	79,6%	36,5%
ROCE	n.s.	n.s.	n.s.	n.s.	53,0%	29,6%	49,5%
ROE adjusted	n.s.	n.s.	n.s.	n.s.	26,3%	18,1%	23,3%
Gearing	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
ND/EBITDA (in x)	n.s.	n.s.	n.s.	n.s.	-0,9x	-2,0x	-1,7x

Source : company, Invest Securities Estimates

## 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

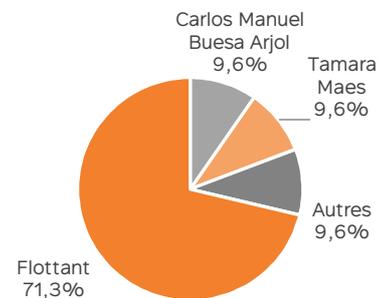
- Potential partnership
- Extension of indications

### THREATS

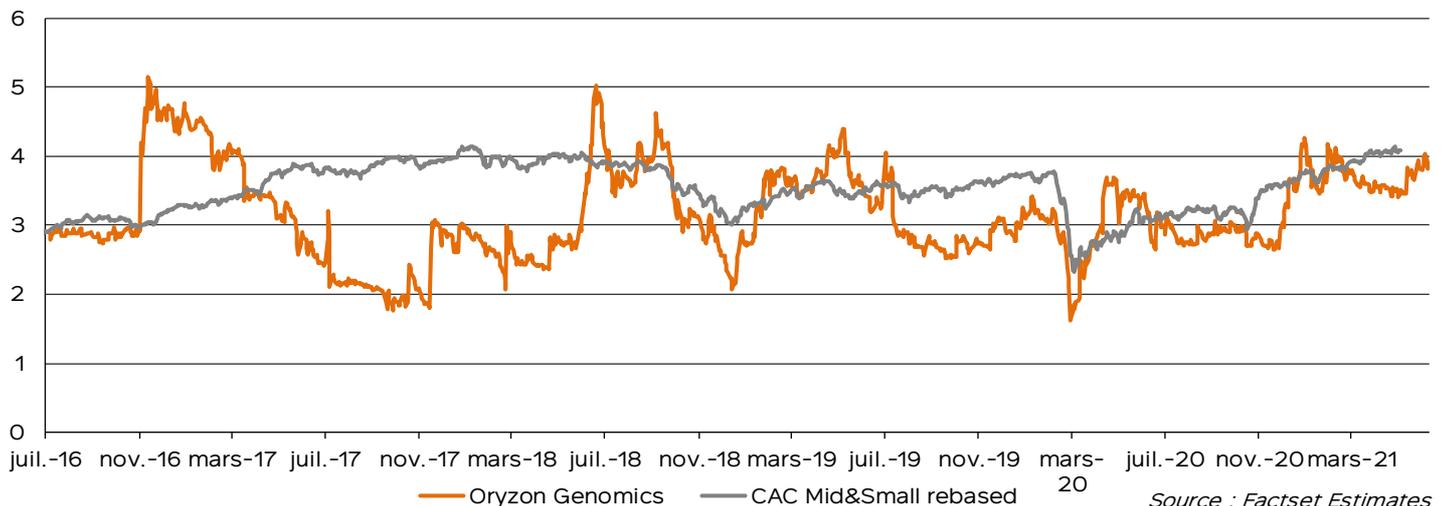
- Clinical and regulatory risk
- Commercial risks
- Legal risks

## ADDITIONAL INFORMATION

### Shareholders



## SHARE PRICE CHANGE FOR 5 YEARS



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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

## 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 covered	Principal Analyst	Date of publication	Opinion	Target price	Potential vs TP
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## DETECTION OF CONFLICTS OF INTEREST

	ORYZON
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
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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' conflict of interest policy is available on the Invest Securities website in the Regulation section. A list of all recommendations issued over 12 months as well as the quarterly publication of the share of "BUY, SELL, NEUTRAL, OTHER" over 12 months is available on the Invest Securities research website.

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