ORYZON GENOMICS

BUY

TARGET PRICE : 6,6€ +140%

ASH-2021 CONGRESS

SOLID EFFICACY DATA FOR AML AT 36 MONTHS

During the 2021 international meeting of the American Society of Hematology (ASH), Oryzon presented new data for its Ph IIa Alice trial in acute myeloid leukemia (AML). The 36-month data presented showed that its drug candidate iadademstat, used in combination with chemotherapy drug azacitidine, significantly increases response rates: 78% responders with the combo vs. 28% with chemotherapy alone according to the literature, based on data obtained from elderly or unfit patients with AML. Moreover, in 77% of subjects with complete response, the duration of response was more than six months. Following these very encouraging results, patients will be monitored for an additional 12 months per the clinical protocol.

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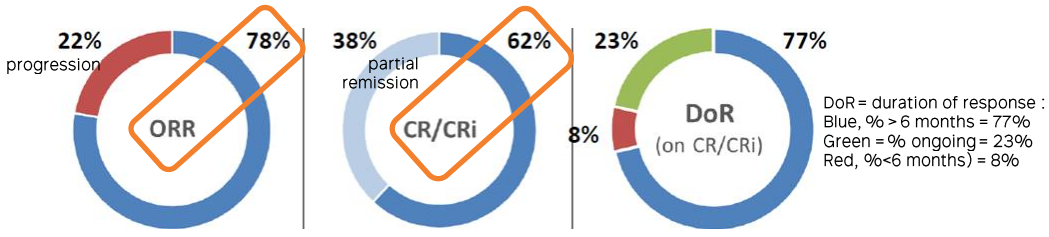
78% response rate at 36 months with the combo vs. 28% with azacitidine alone

The results showed an objective response rate (ORR) of 78% (i.e. 21 patients out of the 27 evaluable), of which 62% achieved complete remission (13 CR/CRi) and 38% partial remission (8 PR). In patients receiving iadademstat at 90 µg/m^2/d (dose selected for the next clinical steps), the ORR was 77%, with 80% achieving complete remission (13 CR/CRi). This data is all the more encouraging knowing that in the literature, the ORR with the standard chemotherapy (CT), azacitidine, is close to 28% in this target population (elderly or unfit patients with AML). Moreover, at this stage, the combination shows better efficacy than a recently approved treatment that combines venetoclax with azacitidine; the latter improved response rates in these patients with an ORR of 64% (vs. 78% with iadademstat based on the preliminary Ph IIa results) and median overall survival (mOS) of 14.7 months. However, while this new treatment does offer an alternative to chemotherapy alone, it should be noted that 25% of patients are refractory and 50% are subject to early relapse. There is thus an unmet medical need in this patient subpopulation, making the very good results obtained with the iadademstat/azacitidine combination extremely promising.

The median time to response is very short at two treatment cycles, or 55 days. The duration of response observed is also highly encouraging with 77% of CR/CRi having lasted more than six months, and the longest remission (ongoing) being more than 1,000 days (as of October 15, 2021 when data collection stopped for submission to the ASH).

Response rate in patients who received the Aza /iada combo at 90 µg/m^2/d



The responses shown are those reported preliminarily by investigators in the eCRF (electronic case report form).

Invest Securities and the issuer have signed an analyst coverage agreement.

in € / share	2021e	2022e	2023e
Adjusted EPS	-0,14	0,57	0,48
chg.	*n.s.*	*n.s.*	*-15,6%*
estimates chg.	*+98%*	*-594%*	*n.s.*

au 31/12	2021e	2022e	2023e
PE	n.s.	0,0x	0,0x
EV/Sales	n.s.	0,2x	-0,2x
EV/Adjusted EBITD	n.s.	0,2x	-0,2x
EV/Adjusted EBITA	n.s.	0,2x	-0,2x
FCF yield*	n.s.	198,8%	-292,2%
Div. yield (%)	n.s.	n.s.	n.s.

* After tax op. FCF before WCR

key points	
Closing share price 10/12/2021	2,7
Number of Shares (m)	53,1
Market cap. (€m)	146
Free float (€m)	118
ISIN	ES0167733015
Ticker	ORY-ES
DJ Sector	Health Technology

	1m	3m	Ytd
Absolute perf.	-11,5%	-20,2%	-21,6%
Relative perf.	-8,3%	-20,8%	-33,6%

Source : Factset, Invest Securities estimates

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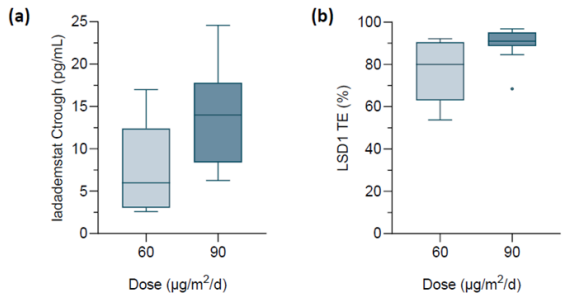
Next step: Clinical results of four-year follow-up

The ALICE trial is fully enrolled. It should be recalled that 36 patients were recruited for the study with a median age of 77 years, of which 27 were evaluable for measurements related to efficacy. Patients will now be monitored for 12 additional months to collect follow-up data at 48 months (four years). Based on initial efficacy data, and in a favorable scenario where clinical development is satisfactory and leads to approval, combination therapies with iadademstat could expand the range of therapeutic options for AML patients by adding a therapy not just for first-line treatment, but also for patients who are refractory or intolerant to BCL2 inhibitors.

Dose selected for the next phases of clinical development : 90 µg/m^2/d

The dose of iadademstat recommended for future clinical trials evaluating the Aza/iada combination is 90 µg/m^2/d since this is the dose that offered better exposure and higher LSD1 target engagement with no increase in the severity of adverse effects compared to the 60 µg/m^2/d dose.

Pharmacokinetics (a) and LSD1 target engagement (b) depending on dose



The levels presented were measured at day 5:

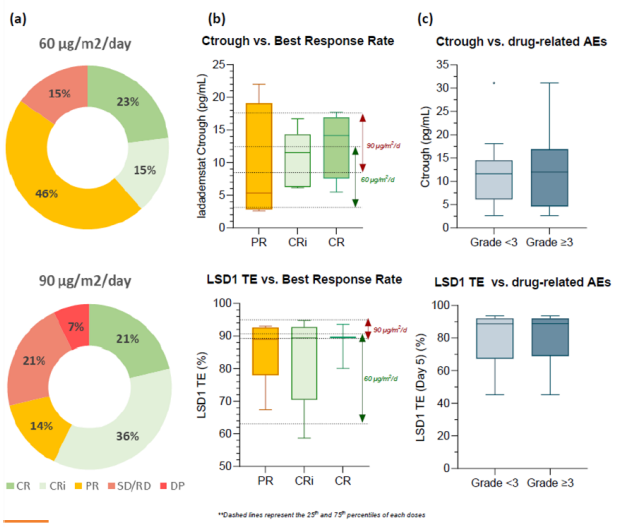
(a) Minimal plasma concentrations of iadademstat were determined by HPLC-MS/MS (LLOQ: 1 pg/mL),

(b) LSD1 target engagement was evaluated using an immno-enzymatic dose with a proprietary sandwich assay based on a chemoprobe.

→ better LSD1 engagement and better iada exposure at the 90 dose vs. 60 µg/m^2/d.

In addition to very promising signals of efficacy, and beyond what has been observed until now with no other treatment, the iadademstat-azacitidine combination continues to present a good safety profile: only two serious adverse events associated with the treatment were reported during this study. More generally, the most frequently reported adverse effect was a decrease in platelet count in 44% of patients, knowing that 61% of patients had thrombocytopenia (grade ≥3) at the time of recruitment. Beyond the hematological impact anticipated due to the type of cancer and mode of action of the therapy, no other significant non-hematological toxicity or other toxicity linked to the organs was observed.

Correlation between efficacy and iada exposure



(a) Responses per dose level: 60 vs. 90 µg/m^2/d,

(b) E-R (enzyme-receptor) relationship of iada exposure (Ctrough) and LSD1 target engagement (LSD1 TE) with efficacy response (best response rates),

(c) Safety profile (severity of adverse effects reported),

→ Preliminary data show a direct correlation between the quality of the clinical response and exposure to iada and LSD1 target engagement (TE). The 90 mg/m^2/d dose allowed the exposure and TE observed in patients who showed complete response to be achieved more systematically than the lower 60 µg dose, this without increasing the severity of adverse effects.

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FINANCIAL DATA

Share information	2017	2018	2019	2020	2021e	2022e	2023e	2024e
Published EPS (€)	-0,15	-0,03	-0,08	-0,08	-0,14	0,57	0,48	0,81
Adjusted EPS (€)	**-0,15**	**-0,03**	**-0,08**	**-0,08**	**-0,14**	**0,57**	**0,48**	**0,81**
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	0,00

Valuation ratios	2017	2018	2019	2020	2021e	2022e	2023e	2024e
P/E	n.s.	n.s.	n.s.	n.s.	n.s.	0,0x	0,0x	0,0x
EV/Sales	n.s.	n.s.	n.s.	n.s.	n.s.	0,16x	-0,16x	-0,32x
EV/Adjusted EBITDA	n.s.	n.s.	n.s.	n.s.	n.s.	0,2x	-0,2x	-0,7x
EV/Adjusted EBITA	n.s.	n.s.	n.s.	n.s.	n.s.	0,2x	-0,2x	-0,7x
Op. FCF bef. WCR yield	n.s.	n.s.	n.s.	n.s.	n.s.	198,8%	-292,2%	-86,2%
Op. FCF yield	n.s.	n.s.	n.s.	n.s.	n.s.	198,8%	-292,2%	-86,2%
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)	2017	2018	2019	2020	2021e	2022e	2023e	2024e
Share price in €	*4,6*	*0,0*	*3,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*
Market cap.	156	0	140	39	39	39	39	39
Net Debt	-17	-23	-27	-29	-15	-31	-43	-70
Minorities	0	0	0	0	0	0	0	0
Provisions/ near-debt	0	0	0	0	0	0	0	0
+/- Adjustments	0	0	0	0	0	0	0	0
Entreprise Value (EV)	**139**	**-22**	**113**	**10**	**24**	**8**	**-4**	**-31**

Income statement (€m)	2017	2018	2019	2020	2021e	2022e	2023e	2024e
Sales	0,0	0,0	0,0	0,0	0,0	50,0	26,5	96,3
chg.	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*
Adjusted EBITDA	-4	-3	-4	-4	-6	35	22	41
adjusted EBITA	**-4**	**-3**	**-4**	**-4**	**-6**	**35**	**22**	**41**
chg.	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***-36,3%***	***+87,6%***
EBIT	-4,7	-3,3	-3,8	-4,3	-6,8	34,1	21,5	40,7
Financial result	-1	-1	-1	0	0	0	0	0
Corp. tax	0	3	1	1	1	-9	0	-5
Minorities+affiliates	0	0	0	0	0	0	0	0
Net attributable profit	-5,2	-1,2	-3,7	-3,4	-5,9	25,0	21,1	35,2
Adjusted net att. profit	**-5,2**	**-1,2**	**-3,7**	**-3,4**	**-5,9**	**25,0**	**21,1**	**35,2**
chg.	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***-15,6%***	***+67,1%***

Cash flow statement (€m)	2017	2018	2019	2020	2021e	2022e	2023e	2024e
EBITDA	-3,9	-3,1	-3,7	-4,1	-6,5	34,5	22,0	41,2
Theoretical Tax / EBITA	0,1	2,5	0,9	1,4	1,4	-8,7	0,0	-5,1
Capex	0,6	-7,0	-9,6	-9,1	-9,5	-9,5	-9,5	-9,5
Operating FCF bef. WCR	**-3,2**	**-7,6**	**-12,4**	**-11,8**	**-14,6**	**16,3**	**12,5**	**26,7**
Change in WCR	-0,2	0,3	0,3	-1,2	0,0	0,0	0,0	0,0
Operating FCF	**-3,4**	**-7,3**	**-12,1**	**-13,1**	**-14,6**	**16,3**	**12,5**	**26,7**
Acquisitions/disposals	5,1	0,1	0,5	0,1	0,0	0,0	0,0	0,0
Capital increase/decrease	16,9	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	0,0
Other adjustments	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Published Cash-Flow	**18,5**	**4,7**	**6,7**	**5,3**	**-14,6**	**16,3**	**12,5**	**26,7**

Balance Sheet (€m)	2017	2018	2019	2020	2021e	2022e	2023e	2024e
Assets	25	32	42	52	61	70	79	88
Intangible assets/GW	22	29	40	49	58	68	77	86
WCR	-8	-9	-8	-5	-5	-5	-5	-5
Group equity capital	34	45	61	76	70	95	116	151
Minority shareholders	0	0	0	0	0	0	0	0
Provisions	0	0	0	0	0	0	0	0
Net financial debt	**-17,2**	**-22,6**	**-26,7**	**-29,1**	**-14,5**	**-30,8**	**-43,3**	**-69,9**

Financial ratios	2017	2018	2019	2020	2021e	2022e	2023e	2024e
EBITDA margin	n.s.	n.s.	n.s.	n.s.	n.s.	69,0%	83,1%	42,8%
EBITA margin	n.s.	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.	n.s.	49,9%	79,6%	36,5%
ROCE	n.s.	n.s.	n.s.	n.s.	n.s.	53,0%	29,6%	49,5%
ROE adjusted	n.s.	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.	n.s.
ND/EBITDA (in x)	n.s.	n.s.	n.s.	n.s.	n.s.	-0,9x	-2,0x	-1,7x

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

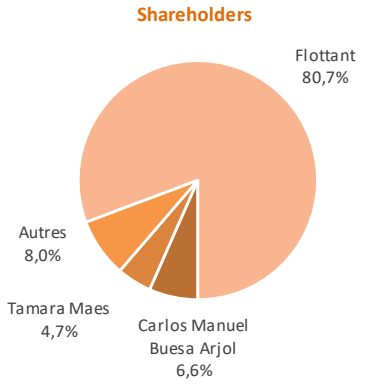
OPPORTUNITIES

- Potential partnership
- Extension of indications

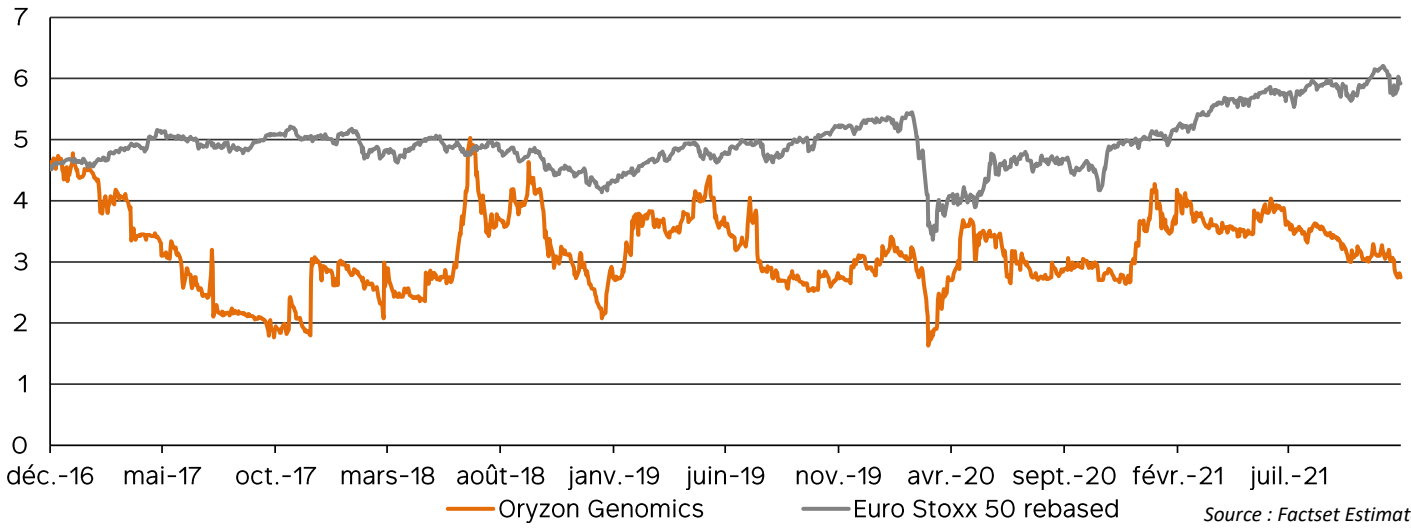
THREATS

- 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.

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- 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

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Company Name	Main Author	Release Date	Rating	Target Price	Potential

	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.	No
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

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