ORYZON GENOMICS

BUY

TARGET PRICE : 8.4€ +232%

COMPANY UPDATE

IADADEMSTAT SHOWS NOTABLE ACTIVITY IN SCLC

ORYZON GENOMICS presented a clinical update from its Phase 2a CLEPSIDRA study at ESMO 2019. CLEPSIDRA is evaluating iadademstat in combination with chemotherapy (carboplatin-etoposide) as a second-line treatment for patients with ED-SCLC, who are platinum-sensitive and positive for prespecified biomarkers. In 8 evaluable patients, the combination achieved 4 partial responses and 2 long-lasting stable diseases. Considering very poor prognosis for 2L ED-SCLC, we are encouraged by the observed clinical activity. We reiterate our BUY rating and TP of €8.4.

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Encouraging clinical activity in hard-to-treat population

The company presented a clinical update from its Phase 2a CLEPSIDRA study of iadademstat at the annual meeting of European Society for Medical Oncology (ESMO 2019). Recall, iadademstat (ORY-1001), a LSD1 selective inhibitor, is being evaluated in two Phase 2a studies, ALICE and CLEPSIDRA. CLEPSIDRA is assessing safety and efficacy of idademstat in combination with standard of care chemotherapy (carboplatin-etoposide) in patients with relapsed extensive-disease small cell lung cancer (ED-SCLC), who are positive for predictive biomarkers. According to CLEPSIDRA's trial design, the patients receive 4-6 cycles of the iadademstat plus carboplatin-etoposide therapy and thereafter treatment continues with iadademstat as monotherapy. The study includes 2 parts, and preliminary results from the Part 1 of CLEPSIDRA were presented at ESMO 2019.

The presented data showed that out of 8 evaluable patients, 4 achieved partial response (PR) and 2 long-lasting stable disease (SD) for more than 4 months (Exhibit 1). Notably, 1 patient with PR achieved substantial tumor reduction of 79% after 6 cycles of iadademstat plus chemotherapy. Moreover, tumor continued to shrink under monotherapy with iadademastat, reaching 86%, and the patient is still in remission after 6 cycles of iadademstat alone (currently at cycle 13 or nearly 10 months under treatment). The observed tumor response in this patient suggests that iadademstat could potentially achieve a long-lasting clinical effect. Another significant PR of 70% tumor reduction was achieved in patient, who died from unrelated medical cause. Among 2 other PRs: one developed into progressive disease (although patient did not receive the same amount of treatment due to hematoxicity) and another is currently ongoing (cycle 2 of therapy). Overall, considering that the backbone chemotherapy showed only 15-25% ORR in chemo-sensitive second-line SCLC patients, we believe that CLEPSIDRA's interim results suggest an encouraging clinical activity of iadademstat and supports further clinical development in this indication. CREPSIDRA is planning to recruit 36 patients, with expected topline results of the study in 2020.

ED-SCLC is a very aggressive type of cancer, with 2-year survival rate of ≤10%. Patients with SCLC have very poor prognosis and, while they respond well to initial chemotherapy, most of them develop recurrent disease. Moreover, while checkpoint inhibitors, such as anti-PD-1/L1 therapies, recently reshaped the landscape of treatment in non-small cell lung cancer (NSCLC), SCLC was shown to be less susceptible to these therapies.

in € / share	2019e	2020e	2021e
Adjusted EPS	-0.13	-0.29	-0.45
chg.	*n.s.*	*n.s.*	*n.s.*
estimates chg.	*n.s.*	*n.s.*	*n.s.*

au 31/12	2019e	2020e	2021e
PE	n.s.	n.s.	n.s.
EV/Sales	n.s.	n.s.	n.s.
EV/EBITDA	n.s.	n.s.	n.s.
EV/EBITA	n.s.	n.s.	n.s.
FCF yield*	n.s.	n.s.	n.s.
Div. yield (%)	n.s.	n.s.	n.s.

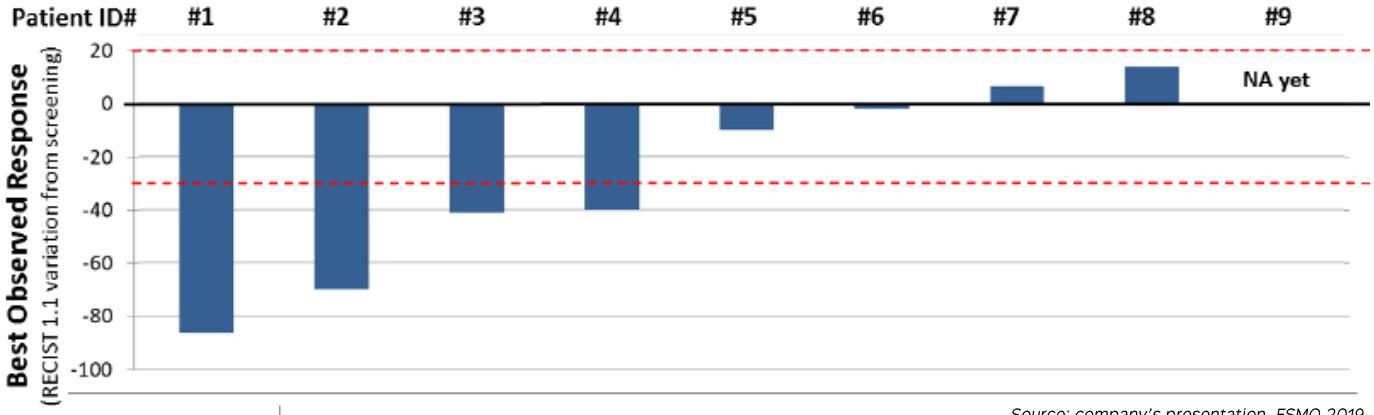
* After tax op. FCF before WCR

key points	
Share price (€)	2.5
Number of Shares (m)	45.8
Market cap. (€m)	116
Free float (€m)	85
ISIN	ES0167733015
Ticker	ORY-ES
DJ Sector	Health Technology

	1m	3m	Ytd
Absolute perf.	-1.9%	-23.4%	+16.9%
Relative perf.	-1.8%	-20.7%	+2.6%

Source : Factset, Invest Securities estimates

Exhibit 1: Efficacy of iadademstat plus chemo in second-line ED-SCLC



Source: company's presentation, ESMO 2019

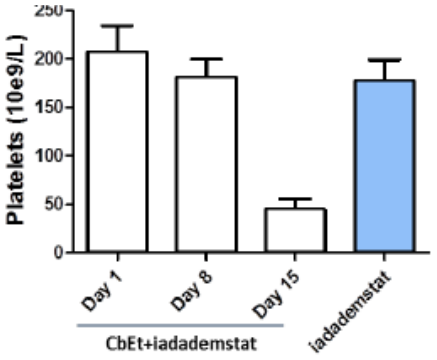
For instance, ROCHE's anti-PD-L1 therapy, Tecentriq, was recently approved as a first-line treatment in combination with chemotherapy for ED-SCLC, albeit improving an overall survival (OS) to only 12.3 months (vs 10.3 months for placebo). In the second-line setting, checkpoint inhibitors as monotherapy have shown 10-30% ORR and OS of up to 10 months.

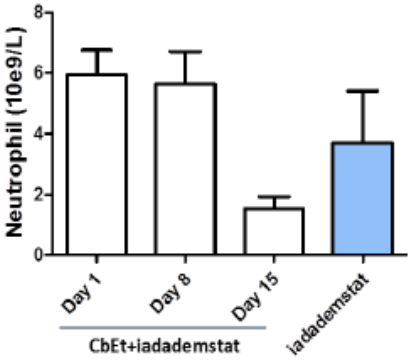
Hematologic toxicities are attributed to chemotherapy

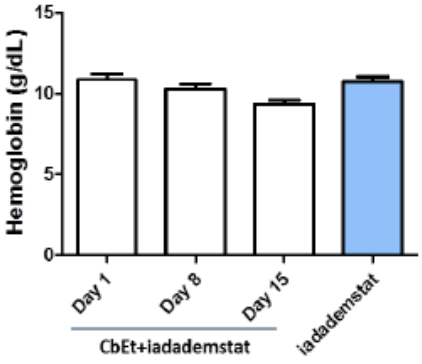
CLEPSIDRA's results also showed that while iadademstat plus chemotherapy treatment resulted in substantial hematologic toxicity (Grade 3 neutropenia 65%), it was mostly due to chemotherapy agents (Exhibit 2). We note that in previous studies, carboplatin plus etoposide also showed Grade 3-4 hematologic adverse events (neutropenia 16%, anemia 11%, thrombocytopenia 3%) as well as Grade 3-4 fatigue (20%) and Grade 3-4 anorexia (19%).

Exhibit 2: Safety profile of iadademstat on combination with chemo

	CbEt+iada	iadademstat Monotherapy
Completed cycles	29	9
Hematological toxicity*	40	0
Thrombocytopenia (≥ Grade III)	19 (65.5%)	0
Neutropenia (≥ Grade III)	11 (37.9%)	0
Anemia (≥ Grade III)	10 (34.5%)	0







Source: company's presentation, ESMO 2019

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Considering that chemotherapy is widely used in the clinic, we believe that clinicians are accustomed to managing hematologic adverse events associated with chemotherapeutic agents. Additionally, in our view, the treatment regimen could be modified further to improve the safety profile of iadademstat plus carboplatin-etoposide combination.

Reinforced sentiment for accelerated approval in SCLC

With high unmet medical need and recent failures of Rova-T from ABBVIE and Opdivo from BRISTOL-MAYERS SQUIBB in second-line SCLC, the FDA seems to be willing to ease the regulatory hurdles for novel therapies in this indication. As an example, the agency recently signaled a green light to PHARMAMAR to submit its chemotherapy, lurbinectedin, for accelerated approval in second-line SCLC. The Phase 2 basket study of lurbinectedin (Zepsyre) included 60 patients with second-line chemo-sensitive ED-SCLC. In this cohort, the drug achieved an overall response rate (ORR) of 45% and median duration of response of 6.2 months. In overall second-line SCLC population (n=105), lurbinectedin showed ORR of 35% and SD of 33%, with medium overall survival of 9.3 months. PHARMAMAR has also initiated the registration Phase 3 Atlantis study of lurbinectedin plus chemotherapeutic agent, doxorubicin, in comparison to other chemotherapy regimens (including topotecan and CAV) to move the drug through the regulatory approval. The readout of Atlantis study was expected in 2020, albeit in August 2019, the company announced that the FDA has accepted the accelerated approval filling based on the Phase 2 data. According to company, the results from Atlantis study would still be incorporated into the final lurbinectedin's regulatory filling, although there is no pressure to generate the outstanding data.

Thus, we believe that iadademstat could also aim for shortened clinical path and potentially accelerated approval in the future. We are currently expecting the full results of CLEPSIDRA study to reinforce this hypothesis. We currently project iadademstat to reach the market for second-line ED-SCLC in 2024 in the US and the EU, generating sales revenues of €81M and growing to €574M by 2031.

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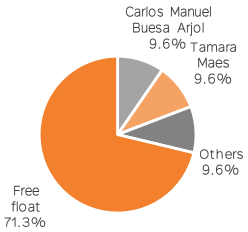
ORYZON GENOMICS

INVESTMENT CASE

ORYZON is a Spanish biotech specializing in the treatment of neurodegenerative diseases and cancer. In all its development programs, the company identifies biomarkers through its genetic and proteomic platforms in order to develop small molecule drugs. Looking ahead of multiple clinical updates, we believe that Oryzon's lead programs could significantly advance in 2019.

FINANCIAL DATA

Shareholders



Share information	2017	2018	2019e	2020e	2021e	2022e	2023e	2024e
Published EPS (€)	-0.15	-0.03	-0.13	-0.29	-0.45	0.52	0.43	0.75
Adjusted EPS (€)	**-0.15**	**-0.03**	**-0.13**	**-0.29**	**-0.45**	**0.52**	**0.43**	**0.75**
Diff. I.S. vs Consensus	*-0.3%*	*-14.1%*	*-20.2%*					
Dividend								

Valuation ratios	2017	2018	2019e	2020e	2021e	2022e	2023e	2024e
P/E	n.s.	n.s.	n.s.	n.s.	n.s.	4.9x	5.9x	3.4x
EV/Sales	8265.92x	n.s.	n.s.	n.s.	n.s.	2.42x	4.13x	0.87x
VE/EBITDA	n.s.	n.s.	n.s.	n.s.	n.s.	3.8x	5.6x	2.2x
VE/EBITA	n.s.	n.s.	n.s.	n.s.	n.s.	3.8x	5.6x	2.2x
Op. FCF bef. WCR yield	n.s.	n.s.	n.s.	n.s.	n.s.	13.5%	11.4%	32.0%
Op. FCF yield	n.s.	n.s.	n.s.	n.s.	n.s.	13.5%	11.4%	32.0%
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	2019e	2020e	2021e	2022e	2023e	2024e
Share price in €	*4.6*	*2.5*	*2.5*	*2.5*	*2.5*	*2.5*	*2.5*	*2.5*
Market cap.	156	86	125	125	125	125	125	125
Net Debt	-17	-23	-30	-10	11	-5	-16	-42
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**	**64**	**96**	**116**	**136**	**121**	**109**	**83**

Income statement (€m)	2017	2018	2019e	2020e	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.*
EBITDA	-4	-3	-6	-12	-19	32	19	39
EBITA	**-4**	**-3**	**-6**	**-12**	**-19**	**32**	**19**	**39**
chg.	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***-39.2%***	***+98.9%***
EBIT	-4.7	-3.3	-6.2	-12.2	-19.3	31.7	19.1	38.3
Financial result	-1	-1	-1	-1	-1	-1	-1	-1
Corp. tax	0	3	1	0	0	-9	0	-5
Minorities+affiliates	0	0	0	0	0	0	0	0
Net attributable profit	-5.2	-1.2	-5.7	-12.7	-19.8	22.5	18.6	32.8
Adjusted net att. profit	**-5.2**	**-1.2**	**-5.7**	**-12.7**	**-19.8**	**22.5**	**18.6**	**32.8**
chg.	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***-17.3%***	***+76.0%***

Cash flow statement (€m)	2017	2018	2019e	2020e	2021e	2022e	2023e	2024e
EBITDA	-3.9	-3.1	-6.0	-12.0	-19.0	32.0	19.5	38.7
Theoretical Tax / EBITA	0.1	2.5	1.0	0.0	0.0	-8.7	0.0	-5.1
Capex	0.6	-7.0	-7.0	-7.0	-7.0	-7.0	-7.0	-7.0
Operating FCF bef. WCR	**-3.2**	**-7.6**	**-12.0**	**-19.0**	**-26.0**	**16.3**	**12.5**	**26.7**
Change in WCR	-0.2	0.3	0.0	0.0	0.0	0.0	0.0	0.0
Operating FCF	**-3.4**	**-7.3**	**-12.0**	**-19.0**	**-26.0**	**16.3**	**12.5**	**26.7**
Acquisitions/disposals	5.1	0.1	0.0	0.0	0.0	0.0	0.0	0.0
Capital increase/decrease	16.9	11.9	20.0	0.0	6.0	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 FreeCash Flow	**18.5**	**4.7**	**8.0**	**-19.0**	**-20.0**	**16.3**	**12.5**	**26.7**

Balance Sheet (€m)	2017	2018	2019e	2020e	2021e	2022e	2023e	2024e
Assets	25	32	39	46	53	60	67	74
Intangible assets/GW	22	29	36	44	51	58	65	71
WCR	-8	-9	-9	-9	-9	-9	-9	-9
Group equity capital	34	45	59	47	33	55	74	107
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**	**-29.8**	**-10.0**	**10.8**	**-4.7**	**-16.4**	**-42.3**

Financial ratios	2017	2018	2019e	2020e	2021e	2022e	2023e	2024e
EBITDA margin	n.s.	n.s.	n.s.	n.s.	n.s.	64.0%	73.5%	40.2%
EBITA margin	n.s.	n.s.	n.s.	n.s.	n.s.	64.0%	73.5%	40.2%
Adjusted Net Profit/Sales	n.s.	n.s.	n.s.	n.s.	n.s.	45.0%	70.4%	34.0%
ROCE	n.s.	n.s.	n.s.	n.s.	n.s.	62.8%	33.6%	59.8%
ROE adjusted	n.s.	n.s.	n.s.	n.s.	n.s.	40.5%	25.1%	30.7%
Gearing	n.s.	n.s.	n.s.	n.s.	32.6%	n.s.	n.s.	n.s.
ND/EBITDA (in x)	n.s.	n.s.	n.s.	n.s.	n.s.	-0.1x	-0.8x	-1.1x

Source : company, Invest Securities Estimates

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ORYZON GENOMICS

SWOT ANALYSIS

STRENGTHS

- Epigenetic platform
- Numerous clinical development programs
- Solid cash position

WEAKNESS

- No partnership
- Numerous failures in lead indication (AD)
- Tight competition in oncology indications

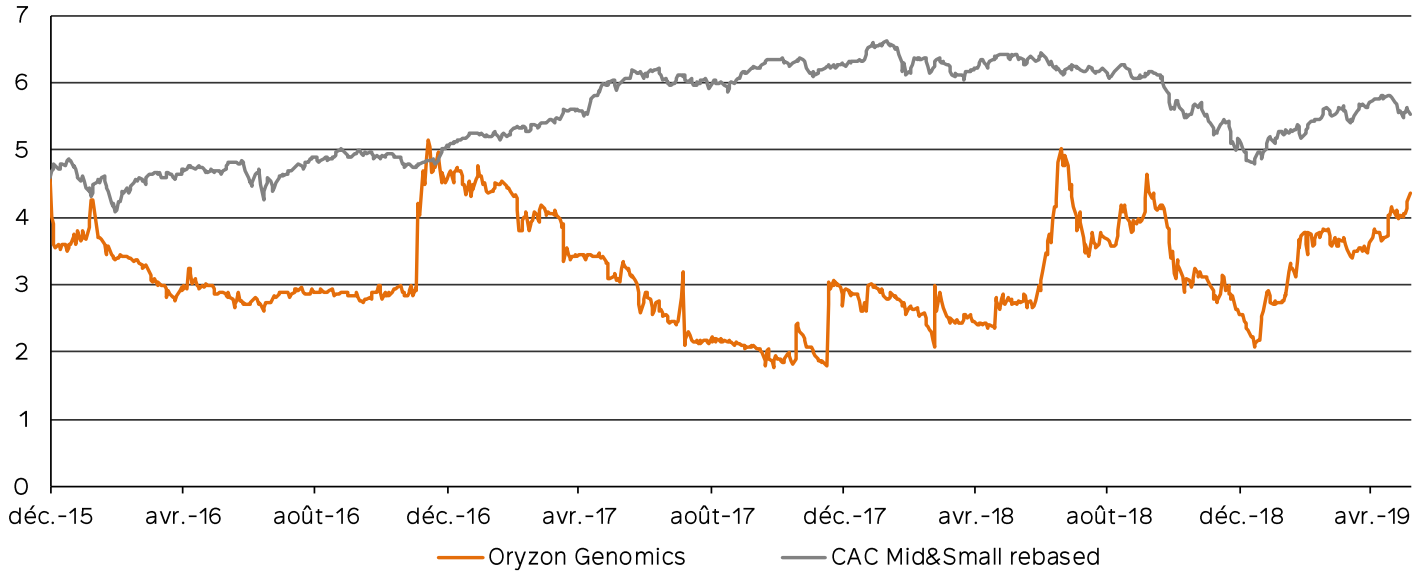
OPPORTUNITIES

- Potential partnership agreement
- Expansion indications for clinical programs
- Preclinical programs to move into clinic

THREATS

- Clinical and regulatory risks
- Commercial risks
- Legal risks

SHARE PRICE CHANGE FOR 5 YEARS



DETECTION OF CONFLICTS OF INTEREST

	Corporate Finance	Treasury stocks holding	Prior communication to company	Analyst's personal interest	Liquidity contract	Listing Sponsor	Research Contract
Oryzon Genomics	No	No	Yes	No	No	No	Yes

DISCLAIMER

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