INVEST SECURITIES

BIOTECH

ORYZON GENOMICS

BUY

TARGET PRICE : 8,8€ (vs 9,3€) +207%

COMPANY UPDATE

RAISING EXPECTATIONS FOR 2019

Looking ahead of multiple clinical updates, we believe that Oryzon's lead programs could significantly advance in 2019. We expect the clinical updates from both neuronal and oncology franchises, as well as the first look into potential expansion indication, as the company launched REIMAGINE study. Following the 3Q18 results and recent capital raise, we have updated our financial model. As a result of these changes, we lower our TP to €8.8, down from €9.3. We reiterate our BUY recommendation ahead of the eventful year.

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Multiple catalysts to play out for Oryzon's neuronal franchise

In 2019, we expect several clinical updates from the company's neuronal disorders franchise, the vafidemstat program. Vafidemstat (ORY-2001), a dual LSD1/MAO-B inhibitor, is being evaluated in two Phase 2a studies: ETHERAL and SATEEN. Moreover, the company has recently initiated the third Phase 2a study of vafidemstat in the management of aggressive behavior.

■ Anticipating an interim look at ETHERAL and SATEEN data in 2H19

In our view, the results from the ETHERAL study is the most anticipated clinical milestone for the company. Recall, ETHERAL is evaluating vafidemstat in patients with mild to moderate Alzheimer's disease (AD). We remind that vafidemstat is designed to simultaneously target lysine specific demethylase 1 (LSD1) and monoamine oxidase B (MAO-B), enzymes that are involved in the epigenetic mechanisms of gene regulation. Epigenetics is one of the youngest fields in bioresearch and allows for the fine tuning of gene expression. In the preclinical studies, vafidemsat was able to restore the memory and to reduce the intensified aggression in a mouse model of AD.

ETHERAL, a 24-week double-blind randomized study, includes three arms: the two dosing regimens of vafidemstat and a placebo. The study is planned to enroll about 125 AD patients at the European clinical sites, and the interim look could be expected in 2H19. The primary endpoint of the study will assess the safety and the tolerability of vafidemstat, albeit, in our view, the most interesting would be a readout on the secondary exploratory endpoints, including cognitive and functional changes, as well as biomarker data. We note that the company is also planning to submit an IND with the FDA in December, 2018, and to launch a parallel twin study with 25 AD patients, with the potential interim look by the end of 2019. We currently project vafidemstat to enter the AD market in 2025 in the US and the EU, generating risk-adjusted revenues of €39M and growing to €495M by 2035.

A second Phase 2a study (SATEEN) is evaluating vafidemstat in patients with relapsing multiple sclerosis (rMS) and secondary progressive multiple sclerosis (SPMS). SATEEN is a 24-patient double-blind placebo-controlled trial that is assessing two different doses of vafidemstat against placebo.

in € / share	2018e	2019e	2020e
Adjusted EPS	-0,10	-0,34	-0,37
chg.	*n.s.*	*n.s.*	*n.s.*
estimates chg.	*n.s.*	*n.s.*	*n.s.*

au 31/12	2018e	2019e	2020e
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 (€)	2,9
Number of Shares (m)	39,1
Market cap. (€m)	112
Free float (€m)	77
ISIN	ES0167733015
Ticker	ORY-ES
DJ Sector	Health Technology

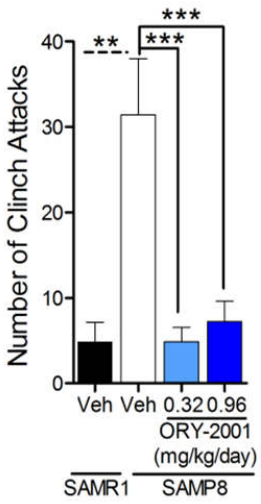
	1m	3m	Ytd
Absolute perf.	-7,3%	-24,6%	+9,6%
Relative perf.	-8,4%	-18,6%	+21,0%

Source : Factset, Invest Securities estimates

Similarly to ETHERAL, the study arms will be blinded, randomized and undergo the treatment for 36 weeks, followed by the unblinding and the open-label treatment. We believe that such trial design could potentially increase the number of treated patients with the appropriate dose of vafidemstat, should any of the doses show positive signs of clinical efficacy, once the study arms are unblinded. We expect the initial results from SATEEN in 2H19. We currently project vafidemstat to reach MS market in 2026 in the US and the EU, generating risk-adjusted revenues of €17M and growing to €167M by 2035.

REIMAGINE the treatment of aggression

On October 9th, the company has announced the initiation of the Phase 2a REIMAGINE study in the treatment of aggressive behavior across multiple neurodegenerative and psychiatric disorders. AD and dementia are often characterized by the aggressive behavior, resulting in the physical aggression in 11% - 46% of AD patients within the community and up to 42% of nursing home residents. Recall, vafidemstat, showed promising behavioral effects in the preclinical studies with SAMP8 mouse model. SAMP8 mice is a naturally occurring line with the accelerated aging phenotypes, including neurodegenerative condition (AD) and aggressive behavior. Vafidemstat (ORY-2001) reduced the exaggerated aggression of SAMP8 mice in the resident-intruder test. This test is based on the fact that an adult male mouse would attack unfamiliar males intruding its home cage.



Source: Company presentation, 2018

Interestingly, the REIMAGINE study will evaluate the clinical activity of vafidemstat across multiple indications, including AD, Lewy Body Dementia (LBD), Adult attention deficit hyperactivity disorder (ADHD), Borderline Personality Disorder (BPD) and Autism Spectrum Disorder (ASD). While the target diseases in the REIMAGINE study have different etiologies, we note that the aggression is a common behavioral symptom. Importantly, across the spectrum of REIMAGINE indications, aggression is one of the most distressing aspects for the family members and caregivers, often leading to the placement of these patients in the specialized centers or nursing homes. We also note that in AD, LBD, ADHD, BPD and ASD, the aggressive behavior is commonly treated with the antipsychotics, albeit without consistent efficiency.

According to the REIMAGINE trial design, presented at the Clinical trials for Alzheimer's Disease (CTAD) meeting in October 2018, at least 6 patients are expected be enrolled in each study arm, followed by 8-week treatment with vafidemstat. The study's primary endpoint will evaluate the safety of vafidemstat, while the secondary endpoint will assess the efficacy through the related clinical test for each disease. We expect the preliminary results from REIMAGINE to be released in 1Q19. Should vafidemstat show clinical activity in one of the basket trial's indications, we believe this could define the potential expansion indication and the developmental path forward for the drug.

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Expectations from the oncology franchise

In 1H19, we expect the preliminary results from the company's oncology franchise, the iadademstat program. Recall, iadademstat (ORY-1001), a LSD1 selective inhibitor, is being evaluated in two Phase 2a studies, ALICE and CLEPSIDRA. In-line with previous expectations, ALICE began the patient enrollment in 3Q18. Additionally, on October 17th, the company announced that CLEPSIDRA received a study approval from the Spanish Drug Agency and the patient enrollment to begin by the end of 2018.

▪ ALICE could strengthen iadademstat's position as an antileukemic therapy

The open-label ALICE study is assessing the efficacy of the drug in combination with a chemotherapeutic agent azacitidine as a first-line therapy in older patients with acute myeloid leukemia (AML). AML is predominantly a disease of older patients with the median age at a diagnosis of approximately 70 years. Older patients with AML have significant comorbidities, and only about 30% are eligible for conventional intensive chemotherapy. ALICE was designed as a two-part study to define the dosing of iadademstat in this patient population during Part 1 and to show clinical activity of the combination therapy in the Part 2. According to the company, the study would include 36 patients, and we believe that the preliminary data could be available in 1H19. We expect the upcoming clinical update to determine the appropriate dosing, to potentially show the signs of clinical activity and to pave the way for the Part 2. We currently project the topline results from ALICE to be available by the end of 2020. We also note that in the previous Phase 1/2a study iadedemstat showed encouraging clinical activity in hard-to-treat subtypes of AML, such as MLL and M6. Considering the recent approval of Venetoclax (Roche and Abbvie) in combination with azacitidine as a first-line therapy in elderly AML patients, we believe that the ALICE results could provide the supporting evidence to narrow down a more specific AML population (such as MLL) for the following pivotal study.

■ Anticipating more data to come from the SCLC front

Additionally, iadademstat is being evaluated in CLEPSIDRA trial in combination with platinum-etoposide chemotherapy in patients with relapsed, extensive-stage small cell lung cancer (SCLC), who are positive for predictive biomarkers. SCLC patients respond well to chemotherapy at first, but disease would eventually progress in the majority of patients (the relapsed SCLC population). Note that chemotherapy was shown to be effective in only about 10% of relapsed SCLC (rSCLC) patients with extensive disease, leaving room for the combination therapies to potentially improve this outcome. Similarly to ALICE, CLEPSIDRA was designed to include two parts: dose-defining (Part 1) and efficacy-evaluating (Part 2). We are expecting preliminary results from CLEPSIDRA to mostly cover the dose-finding part, potentially with the first interim look into the signs of activity and the biomarker-depended response. We currently expect topline results from CLEPSIDRA trial in 1Q21.

We also note that checkpoint inhibitors did not show overwhelming results in both AML and SCLC. In view of the recently published scientific findings that LSD1 inhibition overcomes resistance to anti-PD-1 therapy in a mouse melanoma model, we believe there is a scientific rationale for the combination approach with iadademstat and checkpoint inhibitors. In our view, the expansion into immuno-oncology could be a potential future turn for the Oryzon's oncology franchise. We currently project iadademstat to reach the market for AML (MLL subtype) and rSCLC in 2024 in the US and the EU, generating risk-adjusted revenues of €24M and growing to €176M by 2031.

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Updates to our valuation model

On November 2nd, Oryzon Genomics reported 3Q18 financial results. The company reported no revenues and the operating expenses of €2.8M, in-line with our estimates. At the end of 3Q18 the company held €26.2M in cash, cash equivalents and marketable securities. After the reporting of 3Q18 financial results, Oryzon raised additional €13M through the private placement transaction, closed on October, 31st. As a result of this transaction, the company's *pro forma* cash and cash equivalents totaled €39.2M, which we believe is sufficient to maintain operations into 2H20.

We have updated our financial model to reflect the 3Q18 results and recent equity capital raise. As the equity capital raise (at €2.62 per share) was more dilutive compared to our previous estimates, we lower our TP to €8.8, down from €9.3.

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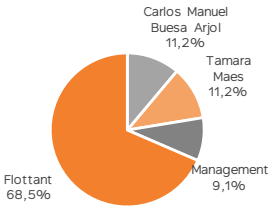
ORYZON GENOMICS

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. We expect the clinical updates from both neuronal and oncology franchises, as well as the first look into potential expansion indication, as the company launched REIMAGINE study.

FINANCIAL DATA

Shareholders



Share information	2016	2017	2018e	2019e	2020e	2021e	2022e	2023e
Published EPS (€)	-0,19	-0,15	-0,10	-0,34	-0,37	-0,49	0,46	0,38
Adjusted EPS (€)	**-0,19**	**-0,15**	**-0,10**	**-0,34**	**-0,37**	**-0,49**	**0,46**	**0,38**
Diff. I.S. vs Consensus	*+12,5%*	*-0,3%*	*+56,0%*	*+89,1%*	*#DIV/0!*	*#DIV/0!*	*#DIV/0!*	*#DIV/0!*
Dividend								

Valuation ratios	2016	2017	2018e	2019e	2020e	2021e	2022e	2023e
P/E	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	6,2x	7,6x
EV/Sales	111,47x	8265,92x	n.s.	n.s.	n.s.	n.s.	2,75x	4,73x
VE/EBITDA	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	4,4x	6,8x
VE/EBITA	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	4,4x	6,8x
Op. FCF bef. WCR yield	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	11,4%	9,7%
Op. FCF yield	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	11,4%	9,7%
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)	2016	2017	2018e	2019e	2020e	2021e	2022e	2023e
Share price in €	*3,0*	*4,6*	*2,9*	*2,9*	*2,9*	*2,9*	*2,9*	*2,9*
Market cap.	85	156	98	137	137	137	137	137
Net Debt	-3	-17	-21	-1	5	16	0	-12
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)	**82**	**139**	**77**	**136**	**142**	**153**	**137**	**125**

Income statement (€m)	2016	2017	2018e	2019e	2020e	2021e	2022e	2023e
Sales	0,7	0,0	0,0	0,0	0,0	0,0	50,0	26,5
chg.	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*
EBITDA	-4	-4	-5	-14	-15	-20	31	18
EBITA	**-4**	**-4**	**-5**	**-14**	**-15**	**-20**	**31**	**18**
chg.	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***-40,4%***
EBIT	-4,9	-4,7	-6,4	-15,2	-16,5	-21,7	29,1	16,4
Financial result	-1	-1	2	0	0	0	0	0
Corp. tax	0	0	0	0	0	0	-9	0
Minorities+affiliates	0	0	0	0	0	0	0	0
Net attributable profit	-5,4	-5,2	-3,6	-14,8	-16,0	-21,3	20,2	16,5
Adjusted net att. profit	**-5,4**	**-5,2**	**-3,6**	**-14,8**	**-16,0**	**-21,3**	**20,2**	**16,5**
chg.		***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***-18,5%***

Cash flow statement (€m	2016	2017	2018e	2019e	2020e	2021e	2022e	2023e
EBITDA	-4,1	-3,9	-5,4	-14,0	-15,0	-20,0	31,0	18,5
Theoretical Tax / EBITA	0,0	0,1	0,0	0,0	0,0	0,0	-9,3	-0,3
Capex	-7,1	0,6	-6,0	-6,0	-6,0	-6,0	-6,0	-6,0
Operating FCF bef. WCR	**-11,2**	**-3,2**	**-11,4**	**-20,0**	**-21,0**	**-26,0**	**15,7**	**12,2**
Change in WCR	-0,1	-0,2	0,0	0,0	0,0	0,0	0,0	0,0
Operating FCF	**-11,3**	**-3,4**	**-11,4**	**-20,0**	**-21,0**	**-26,0**	**15,7**	**12,2**
Acquisitions/disposals	0,7	5,1	0,0	0,0	0,0	0,0	0,0	0,0
Capital increase/decrease	0,3	16,9	12,9	0,0	15,0	15,0	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	**-10,2**	**18,5**	**1,5**	**-20,0**	**-6,0**	**-11,0**	**15,7**	**12,2**

Balance Sheet (€m)	2016	2017	2018e	2019e	2020e	2021e	2022e	2023e
Assets	21	25	30	36	40	45	50	54
Intangible assets/GW	19	22	28	33	38	43	47	52
WCR	-1	-8	-8	-8	-8	-8	-8	-8
Group equity capital	23	34	44	29	28	22	42	58
Minority shareholders	0	0	0	0	0	0	0	0
Provisions	0	0	0	0	0	0	0	0
Net financial debt	**-2,6**	**-17,2**	**-21,0**	**-1,0**	**5,0**	**16,0**	**0,3**	**-11,9**

Financial ratios	2016	2017	2018e	2019e	2020e	2021e	2022e	2023e
EBITDA margin	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	62,0%	69,8%
EBITA margin	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	62,0%	69,8%
Adjusted Net Profit/Sales	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	40,5%	62,3%
ROCE	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	73,5%	39,7%
ROE adjusted	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	48,4%	28,3%
Gearing	n.s.	n.s.	n.s.	n.s.	17,8%	73,9%	0,6%	n.s.
ND/EBITDA (in x)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	0,0x	-0,6x

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

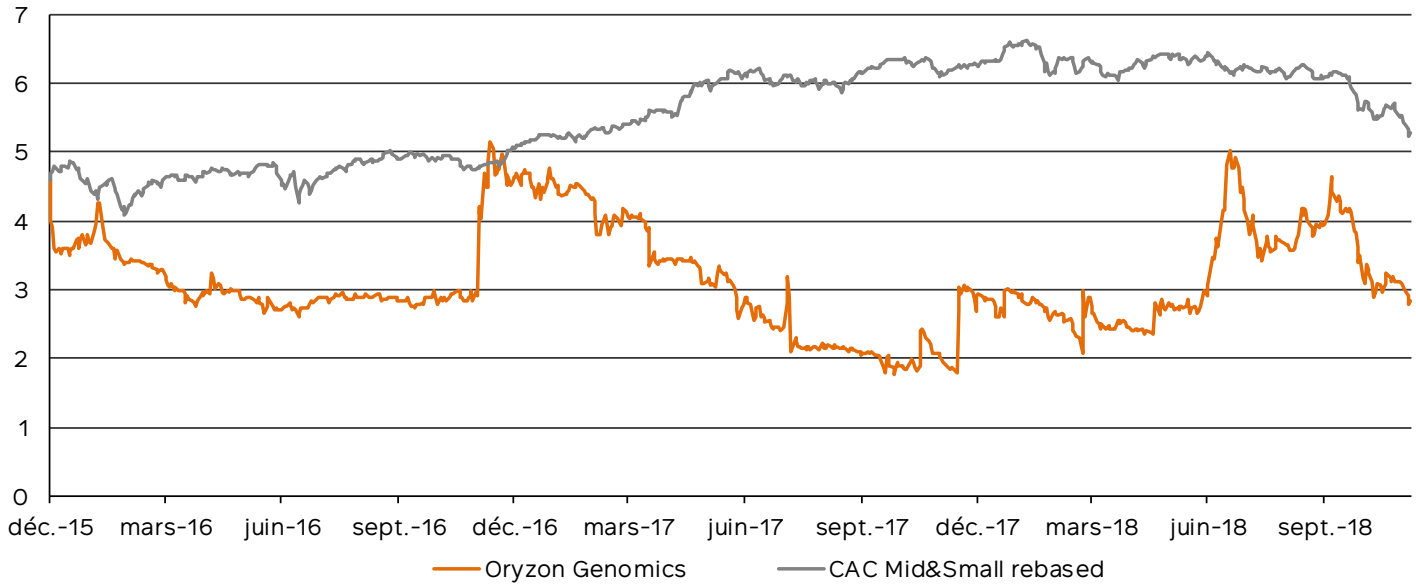
OPPORTUNITIES

- 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	Détention capitalistique de l'émetteur	Communication préalable à l'émetteur	Intérêt personnel de l'analyste	Contrat de liquidité	Listing Sponsor	Contrat d'analyse
Oryzon Genomi	Non	Non	Oui	Non	Non	Non	Oui

DISCLAIMER

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