INVEST SECURITIES

ORYZON GENOMICS

BUY

TARGET PRICE : 8.8€ +113%

COMPANY UPDATE

VAFIDEMSTAT SHOWS PROMISE IN BPD AND ADHD

ORYZON GENOMICS presented clinical update from the Phase 2a REIMAGINE study of vafidemstat in neurodegenerative and psychiatric disorders. The results, presented at the European Congress of Psychiatry and the World Congress on ADHD, showed that in BPD and ADHD cohorts vafidemstat achieved significant improvements across several clinical measures. In our view, vafidemstat's results in BPD are especially encouraging as there is no approved pharmacotherapy for this hard-to-treat indication. We reiterate our BUY rating and TP of €8.8.

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REIMAGINE the treatment of aggression

In April 2019, the company presented clinical updates from its neuronal disorders franchise, the vafidemstat program, at the European Congress of Psychiatry and the World Congress on ADHD. Vafidemstat (ORY-2001), a dual LSD1/MAO-B inhibitor, is being evaluated in 3 Phase 2a studies: ETHERAL, SATEEN and REIMAGINE. The company presented an update from REIMAGINE study, which is assessing vafidemstat as a treatment for aggressive behavior across multiple psychiatric and neurodegenerative disorders, including Attention Deficit Hyperactivity Disorder (ADHD), Borderline Personality Disorder (BPD), Alzheimer's disease, Lewy Body Dementia and Autism Spectrum Disorder. The study's primary endpoints include the safety and tolerability of vafidemstat, while the secondary endpoints evaluate the efficacy of the drug based on relevant clinical scoring systems. The study was expected to recruit at least 6 patients in each disease arm and the presented results covered vafidemstat's activity in ADHD and BPD patients. Overall, Vafidemstat showed clean safety profile, with no hematologic impact, and encouraging clinical activity.

Vafidemstat shows promise in BPD

Vafidemstat showed statistically significant improvement across multiple clinical scales in patients with BPD (n=6). BPD is a complex psychiatric disease that is characterized by a persistent instability and disturbance of the self-image, interpersonal relationships, and impulsive control. Clinical hallmarks of this disease include emotional deregulation, impulsive aggression, repeated self-injury, and chronic suicidal tendencies. With the prevalence of 1.5% on the general population, there is still no curative treatment for BPD. While proper psychotherapy could improve the acute symptoms, such as self-harm, suicidal and impulsive behavior, the mood-disturbance, including intense anger, persist chronically.

We note that vafidemstat showed an improvement of aggression-related items in BPD patients as evaluated by 3 different scoring systems, borderline personality disorder checklist (BPDCL), neuropsychiatric inventory (NPI) and Clinical Global Impressions (CGI) (Exhibit 1). The BPD Checklist is a self-reported questionnaire that assesses the burden of BPD symptoms, including anger-control (on the scale from 4 to 20). NPI, on another hand, is a measure of disease performed by a doctor (although mostly used in dementing disorders, such as Alzheimer's disease), and it also showed the improvement of symptoms related to aggression-agitation (NPI-A/A).

in € / share	2018	2019e	2020e
Adjusted EPS	-0.03	-0.20	-0.30
chg.	*n.s.*	*n.s.*	*n.s.*
estimates chg.	*n.s.*	*n.s.*	*n.s.*

au 31/12	2018	2019e	2020e
PE	n.s.	n.s.	n.s.
EV/Sales	n.s.	516.9x	542.9x
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 (€)	4.1
Number of Shares (m)	39.1
Market cap. (€m)	162
Free float (€m)	111
ISIN	ES0167733015
Ticker	ORY-ES
DJ Sector	Health Technology

	1m	3m	Ytd
Absolute perf.	+16.2%	+29.1%	+90.8%
Relative perf.	+14.0%	+16.9%	+63.5%

Source : Factset, Invest Securities estimates

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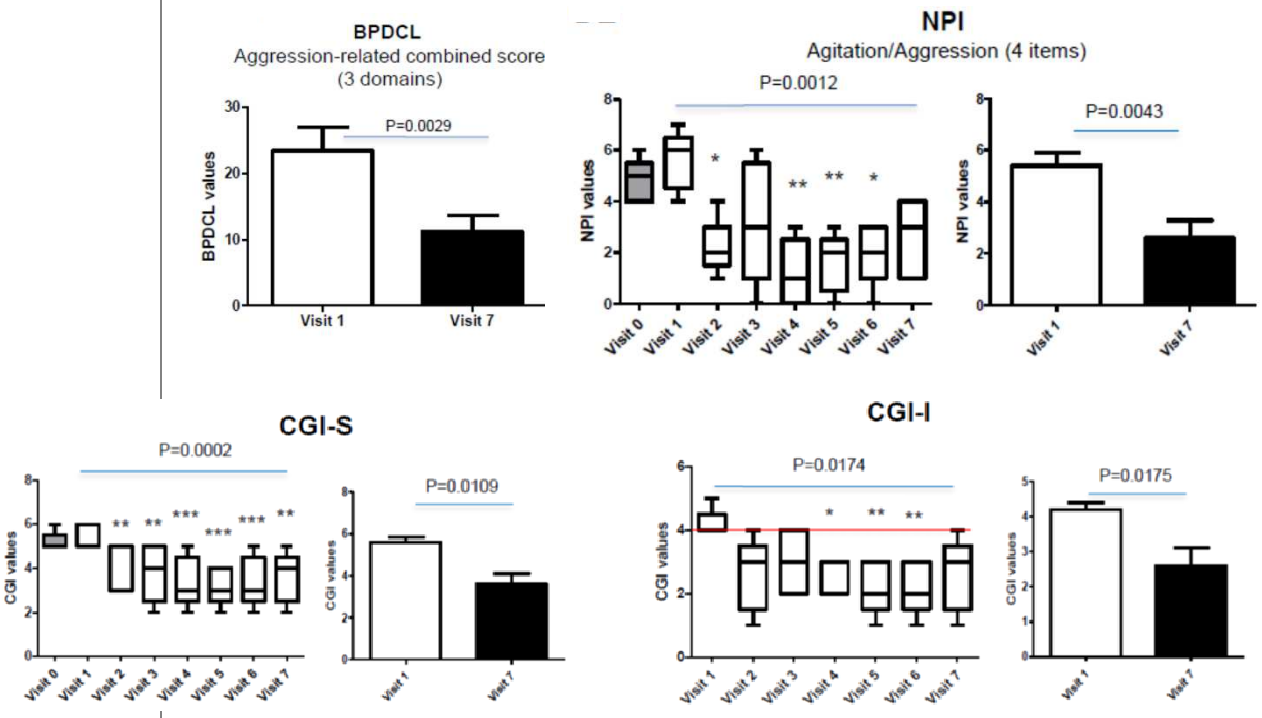
Exhibit 1: Vafidemstat improved Aggression-Agitation behavior in BPD

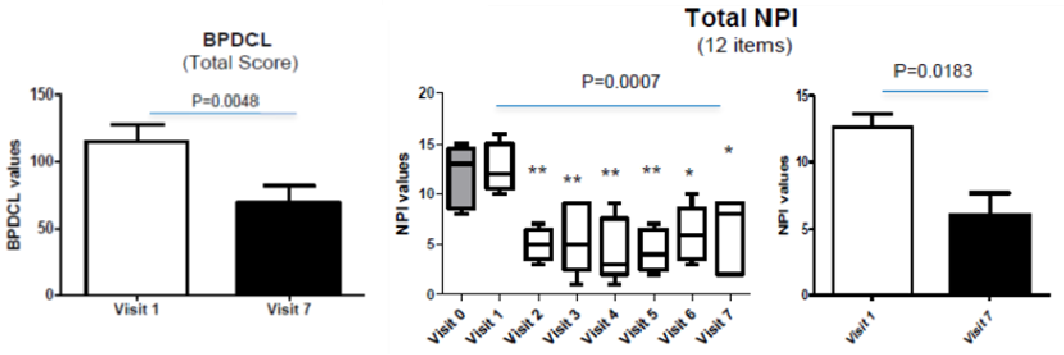


Source: Company's presentation at the European Congress of Psychiatry, 2019

Additionally, vafidemstat's effect on aggression was also assessed by less specialized methods, such as Clinical Global Impressions (CGI), which demonstrated similar positive results. CGI scoring was specifically developed for use in clinical trials to provide a brief assessment of the patient's functioning by the physician on the scale from 1 to 7, respectively corresponding to: i) "no" to "severe" sickness for CGI-S; and ii) "very much improved' to "very much worse" for CGI-I. We note that after 8 weeks of treatment with vafidemstat, CGI-S and CGI-I scores decreased at least by 1 point.

Importantly, vafidemstat aided the overall BPD condition as measured by BPDCL (Exhibit 2). According to BPDCL scoring system, BPD manifestation is indicated by the value higher than 100 points, whereas 67 could serve as a clinical cutoff for recovery. Thus, we believe that achieved improvement in BPDCL score underlines vafidemstat's potential as a pharmacological treatment for this hard-to-treat indication.

Exhibit 2: Vafidemstat improved overall BPD progression



Source: Company's presentation at the European Congress of Psychiatry, 2019

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Additionally, as a part of safety profile, treatment with vafidemstat was evaluated based on Columbia-Suicide Severity Rating Scale (C-SSRS), which showed that the drug also improved suicidal symptoms. Suicide-related behavior has a profound impact on BPD patients and their caregivers and is reported in up to 84% of cases. Therefore, in our view, the reduction in C-SSRS bodes well with the clinical activity of vafidemstat in BPD.

Overall, while the BPD cohort in REIMAGINE study included only 6 patients and was not controlled for background psychotherapy, we note that vafidemstat showed statistically significant clinical activity across multiple psychiatric scales. We also note that currently there is no approved pharmacological therapy for BPD. Common treatment guidelines consider psychotherapy as a treatment of choice for BPD and assign only an adjunctive role to the pharmacological intervention. At the same time, while any drug prescription in BPD is off-label, up to 82% of BPD patients still receive pharmacotherapy to directly target BPD symptoms. Antidepressants are most commonly used, but there is no standard of treatment. Currently, the there is a broad consensus among psychiatrists that no single drug is able to treat BPD itself and, if successful, vafidemstat could change this treatment paradigm.

Since it is difficult to estimate the market potential for BPD, in our view, bipolar disorder could serve as a proxy for the sales estimates. Bipolar disorder is a mental illness that causes dramatic shifts in a person's mood and BPD sometimes is misdiagnosed as bipolar disorder. While the suicide rate in bipolar disorder is higher, both diseases have similar prevalence and both are treated with antidepressants (albeit in case of BPD, off-label). According to *Evaluate Pharma,* the market projections for bipolar disorder, including such drugs as Lumateperone from INTRA-CELLULAR THERAPIES and Vraylar from ALLERGAN, are expected to reach $800M by 2024. Thus, with the absence of an approved therapy, we believe that the potential market for BPD could be worth more than $800M by 2024.

ADHD provides another PoC for Vafidemstat

The clinical update from another REIMAGINE's cohort, with ADHD, was also presented recently, at World Congress on ADHD. The presented results showed that vafidemstat improved aggression-agitation associated behavior in adults with ADHD as well (Exhibit 3). Adult ADHD is a psychiatric disorder with prevalence of nearly 5% in general population. The symptoms include a combination of persistent problems, such as difficulty paying attention, hyperactivity and impulsive behavior. ADHD patients often display clinically significant aggression, with impulsive aggression being the predominant subtype. Although impulsive aggression is more common in children and preadolescents, it could represents a clinical and public health problem in adults as well. Additionally, in preadolescents, impulsive aggression is predictive of an unfavorable developmental trajectory for the disease. Although adjunctive aggression-targeted therapy is widely recommended when aggressive behavior is not contained with primary ADHD therapy (such as psychostimulants), there is no standard of treatment or aggression-specific approved therapy.

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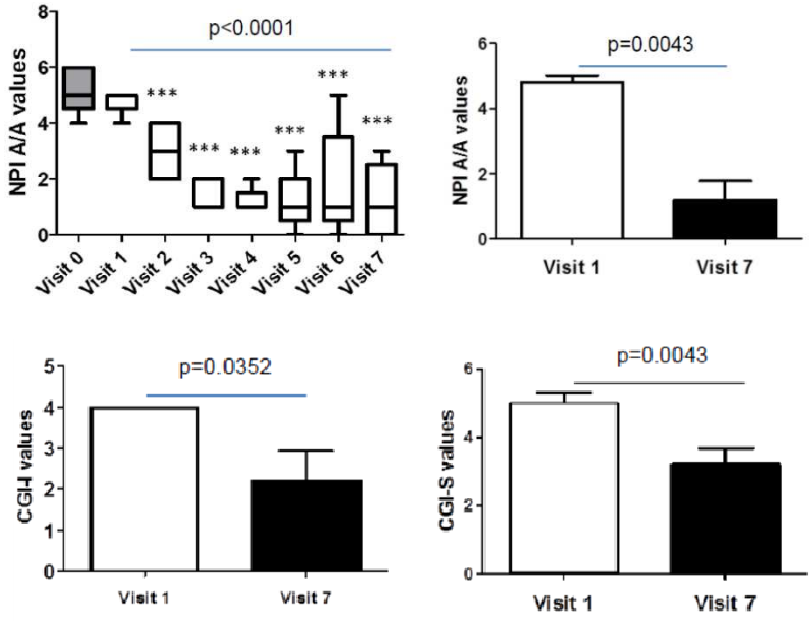
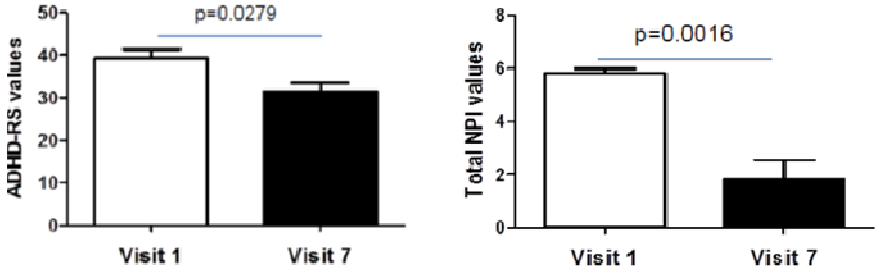
Exhibit 3: Vafidemstat improves Aggression-Agitation in adults with ADHD



Source: Company's presentation at the World Congress on ADHD, 2019

Similarly to BPD cohort, vafidemstat also improved the overall condition of ADHD patients, as evaluated by NPI and ADHD-RS (Exhibit 4). The ADHD Rating Scale (ADHD-RS), performed by a caregiver and scored by a doctor, reflects the frequency of each ADHD symptom. Importantly, the ADHD-specific scoring system, ADHD-RS, showed statistically significant decrease in the frequency of ADHD symptoms.

Exhibit 4: Vafidemstat improved overall ADHD progression



Source: Company's presentation at the World Congress on ADHD, 2019

We note that ADHD market grew to up to $5.5B in 2017 (according to *Evaluate Pharma*), albeit it is overcrowded with psychostimulants, such as Adderall, Ritalin, Concerta and Vyvanse. Though there are concerns regarding the abuse of this class of drugs, as well as pricing pressure from generics. In the non-stimulants class, such as norepinephrine reuptake inhibitor, beyond marketed generics there are few drug candidates in the late-stage clinical trials, which showed a statistically significant decrease in ADHD-RS-5 of at least 10 points. We also highlight SUPERNUS' asset, SPN-810, as it is being developed specifically for impulse aggression in ADHD with Phase 3 readout expected in 2H19, albeit the drug is targeting pediatric and adolescent populations.

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Overall, considering the competitive pressure, we see ADHD as a riskier option for an expansion indication for vafidemstat. Albeit we also note that the drug candidates, currently in development for ADHD, are mostly based on the repurposing or augmenting medications that are already in use. With about 40% of caregivers unsatisfied with currently available ADHD treatment, we believe that there is a room for a novel therapeutic class.

Looking ahead of the readouts from ASD and AD cohorts

We currently expect the company to present the readouts from other REIMAGINE's cohorts in 2H19. Specifically, the results on the vafidemstat's safety and efficacy in the patients with Autism Spectrum Disorder (ASD) at the ECNP Congress, in September 2019, and in patients with Alzheimer's disease (effect on aggression) by the end of 2019. Considering the consistent data from BPD and ADHD populations, in our view, should the results from ASD and AD cohorts show similar efficacy trend, it could significantly increase the confidence in vafidemstat as a neuroactive therapy. We remind that the other Phase 2a studies of vafidemstat (ETHERAL in AD and SATEEN in multiple sclerosis) could provide an interim look in 2H19 as well.

According to management, the company is currently in the dialogue with KOLs to finalize the future clinical development path for vafidemstat in psychiatric indications. While we are encouraged by the positive results from the BPD and ADHD cohorts, we currently do not include this indications in our financial valuation awaiting for the defined development strategy.

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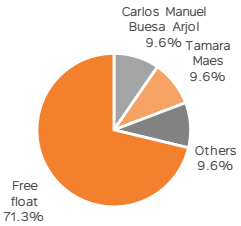
INVESTMENT CASE

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	2016	2017	2018	2019e	2020e	2021e	2022e	2023e	2024e
Published EPS (€)	-0.19	-0.15	-0.03	-0.20	-0.30	-0.47	0.49	0.40	0.71
Adjusted EPS (€)	**-0.19**	**-0.15**	**-0.03**	**-0.20**	**-0.30**	**-0.47**	**0.49**	**0.40**	**0.71**
Diff. I.S. vs Consensus	*+12.5%*	*-0.3%*	*-11.2%*	*+11.0%*					
Dividend									

Valuation ratios	2016	2017	2018	2019e	2020e	2021e	2022e	2023e	2024e
P/E	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	8.4x	10.4x	5.9x
EV/Sales	111.47x	8265.92x	n.s.	516.95x	542.95x	n.s.	3.45x	6.05x	1.42x
VE/EBITDA	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	5.4x	8.3x	3.5x
VE/EBITA	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	5.4x	8.3x	3.5x
Op. FCF bef. WCR yield	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	9.4%	7.8%	19.5%
Op. FCF yield	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	9.4%	7.8%	19.5%
Div. yield (%)	n.s.	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	2018	2019e	2020e	2021e	2022e	2023e	2024e
Share price in €	*3.0*	*4.6*	*4.1*	*4.1*	*4.1*	*4.1*	*4.1*	*4.1*	*4.1*
Market cap.	85	156	141	180	180	180	180	180	180
Net Debt	-3	-17	-23	-8	1	9	-8	-20	-46
Minorities	0	0	0	0	0	0	0	0	0
Provisions/ near-debt	0	0	0	0	0	0	0	0	0
+/- Adjustments	0	0	0	0	0	0	0	0	0
Entreprise Value (EV)	**82**	**139**	**119**	**172**	**181**	**189**	**173**	**160**	**134**

Income statement (€m)	2016	2017	2018	2019e	2020e	2021e	2022e	2023e	2024e
Sales	0.7	0.0	0.0	0.3	0.3	0.0	50.0	26.5	94.6
chg.	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*
EBITDA	-4	-4	-3	-8	-12	-19	32	19	38
EBITA	**-4**	**-4**	**-3**	**-8**	**-12**	**-19**	**32**	**19**	**38**
chg.	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***-39.4%***	***+97.0%***
EBIT	-4.9	-4.7	-3.3	-9.2	-13.4	-21.0	29.8	17.0	35.4
Financial result	-1	-1	-1	0	0	0	0	0	0
Corp. tax	0	0	3	0	0	0	-9	0	-5
Minorities+affiliates	0	0	0	0	0	0	0	0	0
Net attributable profit	-5.4	-5.2	-1.2	-8.9	-13.1	-20.7	21.4	17.3	30.8
Adjusted net att. profit	**-5.4**	**-5.2**	**-1.2**	**-8.9**	**-13.1**	**-20.7**	**21.4**	**17.3**	**30.8**
chg.		***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***-19.0%***	***+77.8%***

Cash flow statement (€m)	2016	2017	2018	2019e	2020e	2021e	2022e	2023e	2024e
EBITDA	-4.1	-3.9	-3.1	-7.9	-11.9	-19.2	31.8	19.2	37.9
Theoretical Tax / EBITA	0.0	0.1	2.5	0.0	0.0	0.0	-8.7	0.0	-5.0
Capex	-7.1	0.6	-7.0	-6.8	-6.8	-6.8	-6.8	-6.8	-6.8
Operating FCF bef. WCR	**-11.2**	**-3.2**	**-7.6**	**-14.7**	**-18.7**	**-26.0**	**16.3**	**12.5**	**26.2**
Change in WCR	-0.1	-0.2	0.3	0.0	0.0	0.0	0.0	0.0	0.0
Operating FCF	**-11.3**	**-3.4**	**-7.3**	**-14.7**	**-18.7**	**-26.0**	**16.3**	**12.5**	**26.2**
Acquisitions/disposals	0.7	5.1	0.1	0.0	0.0	0.0	0.0	0.0	0.0
Capital increase/decrease	0.3	16.9	11.9	0.0	10.0	18.0	0.0	0.0	0.0
Dividends paid	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Other adjustments	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Published FreeCash Flow	**-10.2**	**18.5**	**4.7**	**-14.7**	**-8.7**	**-8.0**	**16.3**	**12.5**	**26.2**

Balance Sheet (€m)	2016	2017	2018	2019e	2020e	2021e	2022e	2023e	2024e
Assets	21	25	32	38	43	48	54	58	63
Intangible assets/GW	19	22	29	35	41	46	51	56	61
WCR	-1	-8	-9	-9	-9	-9	-9	-9	-9
Group equity capital	23	34	45	36	33	30	52	69	100
Minority shareholders	0	0	0	0	0	0	0	0	0
Provisions	0	0	0	0	0	0	0	0	0
Net financial debt	**-2.6**	**-17.2**	**-22.6**	**-8.0**	**0.7**	**8.7**	**-7.6**	**-20.0**	**-46.2**

Financial ratios	2016	2017	2018	2019e	2020e	2021e	2022e	2023e	2024e
EBITDA margin	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	63.6%	72.7%	40.1%
EBITA margin	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	63.6%	72.7%	40.1%
Adjusted Net Profit/Sales	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	42.8%	65.5%	32.5%
ROCE	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	71.5%	39.0%	70.2%
ROE adjusted	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	41.2%	25.0%	30.8%
Gearing	n.s.	n.s.	n.s.	n.s.	2.2%	28.6%	n.s.	n.s.	n.s.
ND/EBITDA (in x)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	-0.2x	-1.0x	-1.2x

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

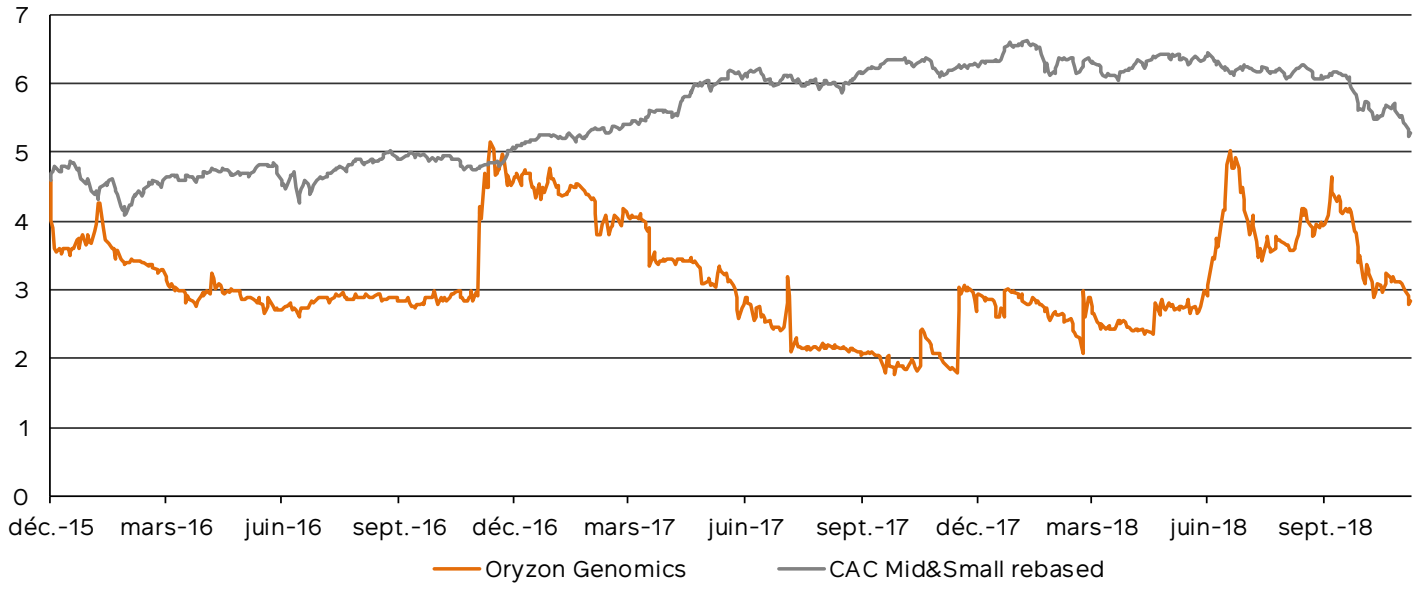
OPPORTUNITIES

- 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

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