BIOTECH

ORYZON GENOMICS

BUY

TARGET PRICE : 8.4€ +180%

CLINICAL UPDATE

ENCOURAGING SIGNALS OF EFFICACY IN AML

On December 9, during the ASH annual conference in Orlando, ORYZON presented additional results of ALICE trial in AML. The abstract emphasized a ORR of 75% and a good safety profile despite one grade 5 AE that prompted the SMC to reduce iadademstat's dose to 60 µg/m²/d (vs 90). While it is difficult to draw any conclusions on such limited number of evaluable patients (n=8) and on such short follow-up (20 weeks), we are encouraged by the presented data. Awaiting for the full results of ALICE study, we reiterate our TP of €8,4/share and our BUY recommendation.

Thibaut Voglimacci - Stephanopoli
+33 1 44 88 77 95
tvoglimacci@invest-securities.com

Controlled safety profile despite a lower recommended dose

On December 9, during the ASH annual conference in Orlando, ORYZON presented additional results of ALICE trial. Recall, iadademstat (ORY-1001) is a selective inhibitor of lysine-specific demethylase 1 (LSD1), an enzyme that is involved in the epigenetic mechanisms of gene regulation. The open-label ALICE study is assessing the efficacy of the drug in combination with a chemotherapy agent azacitidine (Aza) as first-line therapy in older patients with acute myeloid leukemia (AML). AML is predominantly a disease of older patients with the median age at 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 (18 patients) and to show the clinical activity of the combination in Part 2, an expansion cohort of 18 patients. During EHA 2019 in June, the company presented the first clinical results of the combination trial on 6 patients. The clinical update presented yesterday was on 13 patients (8 evaluable for efficacy, 12 for toxicity).

As regards the safety profile, despite a good tolerance at the planned dose of iadademstat (90 µg/m²/d) for the first 6 patients (see flash of June 19), after the recruitment of additional patients, the Safety Monitoring Committee (SMC) decided to lower the dose to 60 µg/m²/d. This decision was made after the withdrawal of one patient that experienced severe fatigue and one death due to an intracranial hemorrhage. As reported in the "drug related side effects table" (exhibit 1), besides the intracranial hemorrhage for patient #11, the safety profile was comparable to the data presented in June with mostly neutropenia (4 patients) and thrombocytopenia (6 patients) as severe adverse events (Grade 4). Despite the reduction of the dose, as iadademstat is an epigenetic drug and AML itself is associated with myelosuppression, we believe that the reported toxicity of iadademstat is in agreement with its mechanism of action and bodes well for the future clinical development.

Encouraging signs of efficacy, further data needed

In terms of efficacy, the abstract presented data on 8 evaluable patients (vs 5 patients for the last clinical update). The ORR on 8 patients was 75% with 2 complete remissions (CR), 3 complete remissions with incomplete hematologic recovery (CRi) and 1 partial remission (PR). Looking at exhibit 2 and at the previous data, we are also encouraged by the fact that 1 PR patient (#5) achieved CRi and 1 CRi patient (#1) is now in CR.

1/6

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 (€)	3,0
Number of Shares (m)	45,8
Market cap. (€m)	137
Free float (€m)	101
ISIN	ES0167733015
Ticker	ORY-ES
DJ Sector	Health Technology

	1m	3m	Ytd
Absolute perf.	+12,1%	+9,5%	+38,6%
Relative perf.	+12,0%	+3,6%	+12,6%

Source : Factset, Invest Securities estimates

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Moreover, the mean Time to Response (TTR) was only 32 days which is shorter than the time to response achieved by Venclexta + Aza (36 days), the competing combination drug in first line treatment for elderly AML patients. Additionally, 2 of the 5 patients (40%) that have received more than 3 cycles of treatment have also become transfusion independent which is encouraging. Of note, In the previous studies in elderly patients with AML, Aza alone showed CR/CRi of only 27% (n=241) (vs 75% for iadademstat + Aza): complete remission (CR) of 20% (vs 25% for iadademstat + Aza) and CRi of 8% (vs 37,5% for iadademstat + Aza). In the same patient population, Venclexta in combination with aza achieved CR/CRi of 59% (n=22): CR of 27% and CRi of 32%. We note in the retrospective studies AML patients with CR had better relapse-free and overall survival rates than patients with CRi, patients with CRi still had significantly better outcomes than non-responders.

Overall, while it is difficult to draw any conclusions on such limited number of evaluable patients (n=8) and on such short follow-up (mean time of 20 weeks), we are encouraged by the presented iadademstat's data. We note that the preliminary clinical results were comparable to Venclexta, which set a relatively high bar for efficacy in AML. The next clinical updates will provide more mature data and an overview of the response rate at the 60 $\mu g/m^2/d$ dose. According to the SMC, this dosage is also able to saturate LSD1 target engagement with a clear biomarker effect.

Valuation unchanged, BUY reiterated

With historical response rates of 27% in first line treatment of elderly patients with Aza alone and a manageable safety profile, the current results are supportive for a significant synergistic effect from iadademstat. Awaiting for the full results of ALICE study (part 1 and part 2) to reinforce this hypothesis, we don't change our rNPV. We currently project iadademstat to reach the market for the treatment in first line elderly AML patients in 2025 in the US and the EU, generating peak sales revenues of €142M by 2031. We reiterate our BUY rating with a TP of €8,4/share.

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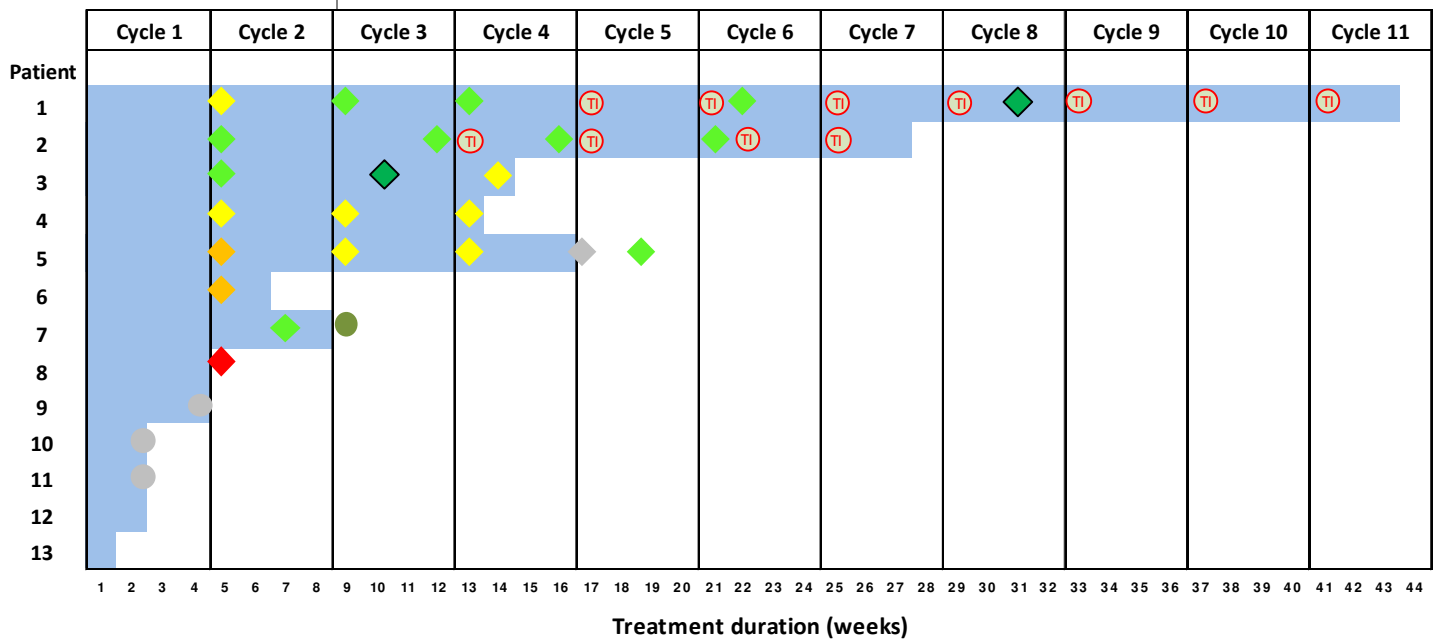
invest-securities.com

Exhibit 1 : Preliminary Safety and Tolerability

Study-drug related TEAEs (ADRs) by SOC and PT (n= 12)					
Number of Patients (%) Event Count					
System Organ Class Preferred Term (SOC) Preferred Term(PT)	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
Blood and lymphatic system disorders					
Anaemia	3(25.0)12	3(25)11	4(33.3)10	0(0.0)0	0(0.0)0
Leukocytosis	1(8.33)1	0(0.0)0	0(0.0)0	0(0.0)0	0(0.0)0
Neutropenia	4(33.3)6	4(33.3)7	5(41.6)13	4(33.3)10	0(0.0)0
Thrombocytopenia	3(25.0)6	3(25)10	4(33.3)10	6(50.0)14	0(0.0)0
Ear and labyrinth disorders					
Hypoacusis	1(8.33)1	0(0.0)0	0(0.0)0	0(0.0)0	0(0.0)0
Gastrointestinal disorders					
Nauseas	1(8.33)1	2(16.66)2	0(0.0)0	0(0.0)0	0(0.0)0
Constipation	1(8.33)1	1(8.33)1	0(0.0)0	0(0.0)0	0(0.0)0
Vomiting	1(8.33)1	0(0.0)0	0(0.0)0	0(0.0)0	0(0.0)0
Gingival bleeding	1(8.33)1	1(8.33)1	0(0.0)0	0(0.0)0	0(0.0)0
General disorders and administration site conditions					
Asthenia	4(33.3)6	1(8.33)2	1(8.33)1	0(0.0)0	0(0.0)0
Pyrexia	1(8.33)1	0(0.0)0	0(0.0)0	0(0.0)0	0(0.0)0
Hepatobiliary disorders					
Hyperbilirubinaemia	1(8.33)1	1(8.33)1	0(0.0)0	0(0.0)0	0(0.0)0
Investigations					
Blood bilirubin increased	0(0.0)0	1(8.33)1	0(0.0)0	0(0.0)0	0(0.0)0
Platelet count decreased	0(0.0)0	0(0.0)0	0(0.0)0	1(8.33)1	0(0.0)0
Metabolism and nutrition disorders					
Decreased appetite	2(16.66)3	0(0.0)0	0(0.0)0	0(0.0)0	0(0.0)0
Hypomagnesaemia	1(8.33)1	0(0.0)0	0(0.0)0	0(0.0)0	0(0.0)0
Hyponatraemia	2(16.66)2	0(0.0)0	0(0.0)0	0(0.0)0	0(0.0)0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
Differentiation syndrome	0(0.0)0	0(0.0)0	1(8.33)1	0(0.0)0	0(0.0)0
Nervous system disorders					
Dysgeusia	3(25.0)6	0(0.0)0	1(8.33)1	0(0.0)0	0(0.0)0
Haemorrhage intracranial	0(0.0)0	0(0.0)0	0(0.0)0	0(0.0)0	1(8.33)1
Respiratory, thoracic and mediastinal disorders					
Dyspnoea	0(0.0)0	1(8.33)1	0(0.0)0	0(0.0)0	0(0.0)0
Skin and subcutaneous tissue disorders					
Rash	3(25.0)3	0(0.0)0	0(0.0)0	0(0.0)0	0(0.0)0

Source: company's presentation, ASH 2019

Exhibit 2 : Iadademstat plus aza shows efficacy in elderly AML patients



Source: company's presentation, ASH 2019

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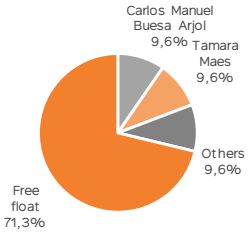
73, bd Haussmann - 75008 Paris
T : +33 (0)1 80 97 22 01
invest-securities.com

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 2020.

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%*	*+8,0%*					
Dividend								

Valuation ratios	2017	2018	2019e	2020e	2021e	2022e	2023e	2024e
P/E	n.s.	n.s.	n.s.	n.s.	n.s.	5,8x	7,0x	4,0x
EV/Sales	8265,92x	n.s.	n.s.	n.s.	n.s.	2,74x	4,73x	1,03x
VE/EBITDA	n.s.	n.s.	n.s.	n.s.	n.s.	4,3x	6,4x	2,6x
VE/EBITA	n.s.	n.s.	n.s.	n.s.	n.s.	4,3x	6,4x	2,6x
Op. FCF bef. WCR yield	n.s.	n.s.	n.s.	n.s.	n.s.	11,9%	9,9%	26,8%
Op. FCF yield	n.s.	n.s.	n.s.	n.s.	n.s.	11,9%	9,9%	26,8%
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*	*3,0*	*3,0*	*3,0*	*3,0*	*3,0*	*3,0*	*3,0*
Market cap.	156	102	141	141	141	141	141	141
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**	**80**	**112**	**132**	**152**	**137**	**125**	**99**

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

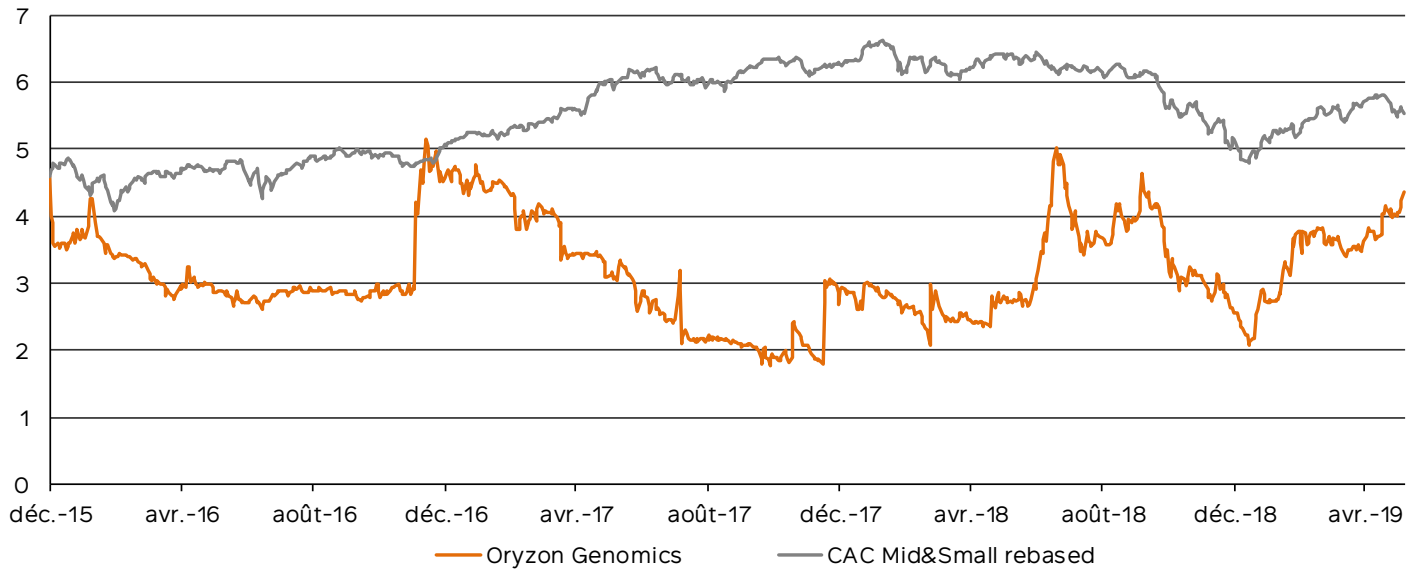
OPPORTUNITIES

- 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

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73, bd Haussmann - 75008 Paris
T : +33 (0)1 80 97 22 01
invest-securities.com

MANAGEMENT

Marc-Antoine Guillen
CEO
+33 1 44 88 77 80
maguillen@invest-securities.com

Jean-Emmanuel Vernay
Managing Director
+33 1 44 88 77 82
jevernay@invest-securities.com

Anne Bellavoine
Managing Director
+33 1 55 35 55 75
abellavoine@invest-securities.com

Pascal Hadjedj
Deputy Managing Director
+33 1 55 35 55 61
phadjedj@invest-securities.com

EQUITY RESEARCH

Maxime Dubreil
Head of Equity Research
+33 1 44 88 77 98
mdubreil@invest-securities.com

Johann Carrier
Stock-Picking
+33 1 44 88 77 88
jcarrier@invest-securities.com

Bruno Duclos
Real Estate
+33 1 73 73 90 25
bduclos@invest-securities.com

Benoit Faure-Jarrosson
Real Estate
+33 1 44 88 77 88
bfaure-jarrosson@invest-securities.com

Christian Guyot
Consumer Goods
+33 1 80 97 22 01
cguyot@invest-securities.com

Matthieu Lavillunière, CFA
Technology
+33 1 73 73 90 34
mlavilluniere@invest-securities.com

Ludovic Martin, CFA
Consumer Goods
+33 1 73 73 90 36
lmartin@invest-securities.com

Vladimir Minot
Real Estate
+33 1 73 73 90 25
vminot@invest-securities.com

Thibault Morel
Technology
+33 1 44 88 77 97
tmorel@invest-securities.com

Jean-Louis Sempé
Automotive
+33 1 73 73 90 35
jlsempe@invest-securities.com

Olga Smolentseva
Biotechs
+33 1 44 88 88 09
osmolentseva@invest-securities.com

Thibaut Voglimacci
Medtechs / Biotechs
+33 1 44 88 77 95
tvoglimacci@invest-securities.com

TRADING FLOOR

François Habrias
Institutional Sales
+33 1 55 35 55 70
fhabrias@invest-securities.com

Dominique Humbert
Sales trading
+33 1 55 35 55 64
dhumbert@invest-securities.com

Bertrand Le Mollé-Montanguon
Institutional Sales
+33 1 55 35 55 74
blmm@invest-securities.com

Ralph Olmos
Institutional Sales
+33 1 55 35 55 72
rolmos@invest-securities.com

Kaspar Stuart
Institutional Sales
+33 1 55 35 55 65
kstuart@invest-securities.com

Renaud Vallette Viallard
Institutional Sales
+33 1 72 38 26 32
rvv@invest-securities.com

Frédéric Vals
Institutional Sales
+33 1 55 35 55 71
fvals@invest-securities.com

CORPORATE BROKING & ISSUER MARKETING

Thierry Roussilhe
Head
+33 1 55 35 55 66
troussilhe@invest-securities.com

Claude Bouyer
Senior Advisor
+33 1 44 88 88 02
cbouyer@invest-securities.com

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