INVEST SECURITIES

BIOTECH

ORYZON GENOMICS

BUY

TARGET PRICE : 4,8€ +151%

CONGRESS EHA 2024

PH IB FRIDA WELL ORIENTED, GOOD SAFETY PROFILE

On the occasion of the EHA (European Hematology Association) congress being held from June 13 to 16, 2024, Oryzon presented interim results from its ongoing Phase Ib FRIDA trial in AML (acute myeloid leukemia) patients with FLT3-mutant (FLT3 mut+) who are resistant or relapsed. At this stage, the initial doses of iadademstat tested in combination with the targeted therapy gilteritinib (FLT3 inhibitor) have shown a good safety and tolerance profile, as well as promising early signals of efficacy. A third cohort aimed at evaluating a lower dose of treatment has started, with the trial planning to evaluate three doses under different conditions in nearly 45 patients in total (including expansion). Updated data is expected to be presented at ASH 2024 in early December. Our opinion BUY is maintained and our TP remains unchanged at €4.8.

Jamila El Bougrini, PhD, MBA
+33 1 44 88 88 09
jelbougrini@invest-securities.com

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

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Confirmed synergy between iadademstat and gilteritinib, noted clinical activity

On the occasion of the EHA, the company presented interim data from its Phase Ib FRIDA trial conducted in FLT3-mutant R/R (refractory/relapsed) AML patients on Friday. The results observed to date confirm a synergistic action for the iadademstat/gilteritinib combination biologically and clinically. Indeed, data related to complete LSD1 occupancy collected in the first two cohorts indicate that the dose needs to be reduced to optimize bone marrow recovery and achieve a higher number of complete responses. With the ability to quantify LSD1 occupancy levels, Oryzon should be able to follow the FDA's OPTIMUS guidelines to meet the targeted objectives. In terms of safety and tolerance, the primary criteria of this trial, no dose-limiting toxicity has been observed, and recruitment is continuing as planned.

In summary, the results obtained to date with the first two doses show:

- Good tolerance of the iadademstat/gilteritinib combination, which has proven to be safe, with no dose-limiting toxicity reported during the 28 days of treatment at iadademstat doses of 75µg and 100µg,
- No unexpected treatment-related adverse events (TEAE),
- Anti-leukemic activity observed in 9 of the 13 treated patients (response rate of 69%),
- Complete remission (CR) observed in 5 patients (38% of treated patients) with partial (CRh) or incomplete hematologic recovery (CRi),
- It is noteworthy that 11 of the 13 patients were refractory to previous standard treatments and 2 patients underwent hematopoietic stem cell transplantation.

Table 3. Preliminary responses

Best responses	Starting dose (n=6)	DL-1 (n=7)
CR	-	1 (1 HSCT)
CRh	-	1
CRi	2	1
MLFS	3 (1 HSCT)	1
NR	1	3
ORR	5 out of 6 83%	4 out of 7 57%
% CR/CRh/CRi	33%	43%

Source: Company – Poster EHA 2024

Invest Securities and the issuer have signed an analysis services agreement.

in € / share	2024e	2025e	2026e
Adjusted EPS	0,27	0,29	0,41
chg.	*+36,1%*	*+6,6%*	*+42,7%*
estimates chg.	*+36%*	*+6%*	*+15%*

au 31/12	2024e	2025e	2026e
PE	7,1x	6,7x	4,7x
EV/Sales	n.s.	n.s.	30,1x
EV/Adjusted EBITD	n.s.	61,4x	12,6x
EV/Adjusted EBITA	n.s.	61,4x	12,6x
FCF yield*	n.s.	n.s.	n.s.
Div. yield (%)	n.s.	n.s.	n.s.

* After tax op. FCF before WCR

key points	
Closing share price 14/06/2024	1,9
Number of Shares (m)	63,5
Market cap. (€m)	122
Free float (€m)	100
ISIN	ES0167733015
Ticker	ORY-ES
DJ Sector	Health Technology

	1m	3m	Ytd
Absolute perf.	-5,6%	+9,4%	+1,5%
Relative perf.	+4,9%	+13,7%	+3,2%

Source : Factset, Invest Securities estimates

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

The two doses tested so far have shown a high occupancy rate (nearly 90%) of LSD1 targets (enzyme inhibited by iadademstat) and, given the role of LSD1 in hematopoiesis, lower doses of iadademstat are being studied. The objective of this dose reduction is to maintain a high level of clinical efficacy while improving platelet recovery, in line with the FDA's OPTIMUS project, which requires identifying the minimal safe and biologically active dose (RP2D = recommended Phase II dose). Platelet count recovery has been slow in most patients, which at current doses has limited a rapid transition from morphologic leukemia-free state (MLFS) to complete remission (CR/CRh). Therefore, a third cohort (DL-2) is currently being recruited to test a dose of 75µg of iadademstat administered for 3 weeks per cycle. Additional cohorts are planned in the dose escalation protocol, including doses of 50µg of iadademstat administered for 3 or 4 weeks.

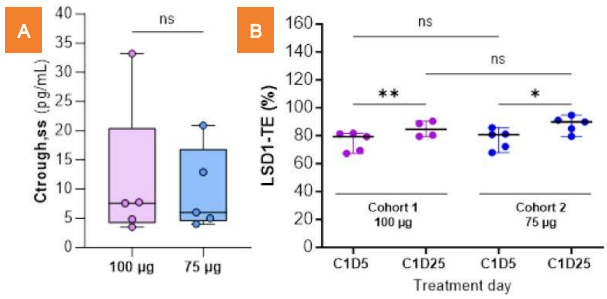


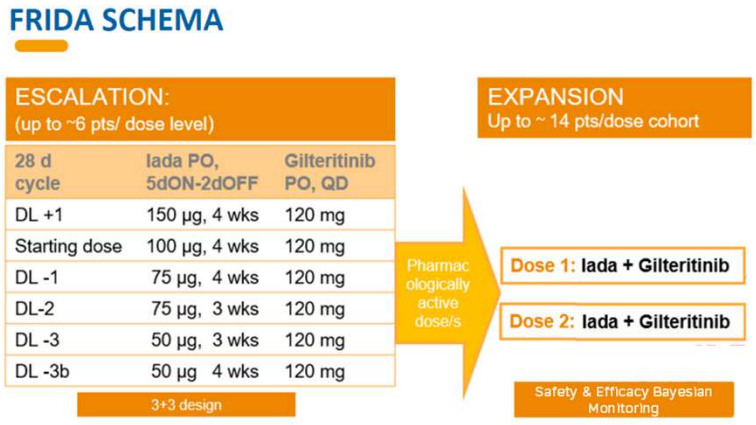
Figure 1: Iada exposure and LSD1 target engagement (TE)
A) Iada exposure (Ctrough) at C1D25 per assigned dose in available samples.
B) LSD1 TE achieved on C1D5 and C1D25. TE was measured as previously described6. Intra-cohort statistics (paired t-test); inter-cohort statistics (Mann-Whitney test).

Source: Company – Poster EHA 2024

The FRIDA study is being conducted in the US and was designed in accordance with the FDA's OPTIMUS project and includes two parts:

- Part 1, which will consist of evaluating the safety, tolerance, pharmacokinetics, pharmacodynamics, and emerging activity of the combination to identify the RP2D,
- Part 2, the expansion part at the RP2D dose identified during Part 1 of the trial to evaluate the activity of the iadademstat + gilteritinib combo in patients with FLT3-mut+ R/R AML.

In total, the trial plans to recruit approximately 45 patients: 6 per cohort tested in Part 1 of the trial. The expansion phase is expected to proceed with 2 cohorts of approximately 14 patients each. Updated results should be presented at ASH 2024.



Source: Company – Poster EHA 2024

To date, 50% of AML patients relapse after first-line treatment, and 30 to 40% of them have FLT3, which is correlated with an increased risk of relapse. Gilteritinib (FLT3 inhibitor) has demonstrated improved outcomes in FLT3-mut+ R/R AML patients, but the remission rate remains low and event-free survival is short.

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

FINANCIAL DATA

Share information	2019	2020	2021	2022	2023	2024e	2025e	2026e
Published EPS (€)	-0,08	0,14	0,13	0,22	0,20	0,27	0,29	0,41
Adjusted EPS (€)	**-0,08**	**0,14**	**0,13**	**0,22**	**0,20**	**0,27**	**0,29**	**0,41**
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	1,00	2,00

Valuation ratios	2019	2020	2021	2022	2023	2024e	2025e	2026e
P/E	n.s.	20,4x	27,1x	11,1x	11,1x	7,1x	6,7x	4,7x
EV/Sales	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	30,05x
EV/Adjusted EBITDA	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	61,4x	12,6x
EV/Adjusted EBITA	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	61,4x	12,6x
Op. FCF bef. WCR yield	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Op. FCF yield	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
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)	2019	2020	2021	2022	2023	2024e	2025e	2026e
Share price in €	*3,0*	*2,9*	*3,5*	*2,5*	*2,2*	*1,9*	*1,9*	*1,9*
Market cap.	141	139	159	124	114	122	104	104
Net Debt	-27	-29	-13	7	-1	-2	-2	8
Minorities	0	0	0	0	0	0	1	2
Provisions/ near-debt	0	0	0	0	0	0	0	0
+/- Adjustments	0	0	0	0	0	0	1	2
Entreprise Value (EV)	**114**	**110**	**146**	**131**	**113**	**120**	**105**	**117**

Income statement (€m)	2019	2020	2021	2022	2023	2024e	2025e	2026e
Sales	0,0	0,0	0,0	0,0	0,0	0,0	0,0	3,9
chg.	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*
Adjusted EBITDA	-4	-5	-8	-6	-5	-2	2	9
adjusted EBITA	**-4**	**-5**	**-8**	**-6**	**-5**	**-2**	**2**	**9**
chg.	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***+441,3%***
EBIT	-3,8	-5,3	-8,0	-5,9	-5,0	-2,0	1,7	9,2
Financial result	-1	13	15	18	17	19	20	22
Corp. tax	1	0	0	0	0	0	0	0
Minorities+affiliates	0	0	0	0	0	0	0	0
Net attributable profit	-3,7	7,6	6,9	12,5	12,1	16,7	22,1	31,6
Adjusted net att. profit	**-3,7**	**7,6**	**6,9**	**12,5**	**12,1**	**16,7**	**22,1**	**31,6**
chg.	***n.s.***	***n.s.***	***-10,0%***	***+81,6%***	***-3,0%***	***+38,2%***	***+32,4%***	***+42,7%***

Cash flow statement (€m)	2019	2020	2021	2022	2023	2024e	2025e	2026e
EBITDA	-3,7	-5,3	-8,0	-5,9	-5,0	-2,0	1,7	9,2
Theoretical Tax / EBITA	0,9	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Capex	-9,6	-9,1	-12,2	-17,0	-15,8	-17,4	-19,1	-21,0
Operating FCF bef. WCR	**-12,4**	**-14,4**	**-20,2**	**-22,9**	**-20,8**	**-19,3**	**-17,4**	**-11,8**
Change in WCR	0,3	-1,2	0,0	0,0	0,0	0,0	0,0	0,0
Operating FCF	**-12,1**	**-15,6**	**-20,2**	**-22,9**	**-20,8**	**-19,3**	**-17,4**	**-11,8**
Acquisitions/disposals	0,5	0,1	0,0	0,0	0,0	0,0	0,0	0,0
Capital increase/decrease	18,4	18,2	0,0	0,0	10,0	19,0	15,0	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	**6,7**	**2,7**	**-20,2**	**-22,9**	**-10,8**	**-0,3**	**-2,4**	**-11,8**

Balance Sheet (€m)	2019	2020	2021	2022	2023	2024e	2025e	2026e
Assets	42	52	64	81	97	114	133	154
Intangible assets/GW	40	49	61	78	94	112	131	152
WCR	-8	-5	-5	-5	-5	-5	-5	-5
Group equity capital	61	76	71	66	72	91	109	119
Minority shareholders	0	0	0	0	0	0	1	2
Provisions	0	0	0	0	0	0	0	0
Net financial debt	**-26,7**	**-29,1**	**-12,8**	**6,6**	**-0,6**	**-2,1**	**-1,6**	**8,3**

Financial ratios	2019	2020	2021	2022	2023	2024e	2025e	2026e
EBITDA margin	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	238,0%
EBITA margin	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	238,0%
Adjusted Net Profit/Sales	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	812,5%
ROCE	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	1,3%	6,2%
ROE adjusted	n.s.	10,0%	9,7%	18,9%	16,7%	18,4%	20,3%	26,5%
Gearing	n.s.	n.s.	n.s.	10,0%	n.s.	n.s.	n.s.	7,0%
ND/EBITDA (in x)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	-0,9x	0,9x

Source : company, Invest Securities Estimates

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

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

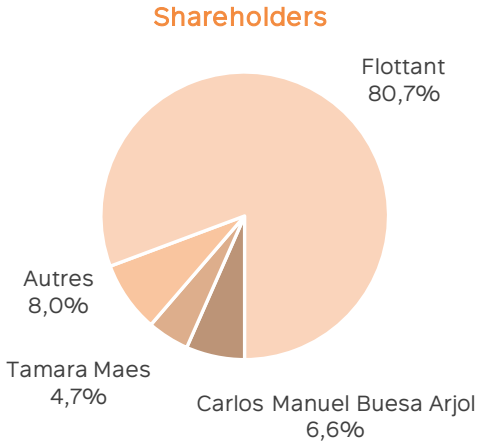
OPPORTUNITIES

- Potential partnership
- Extension of indications

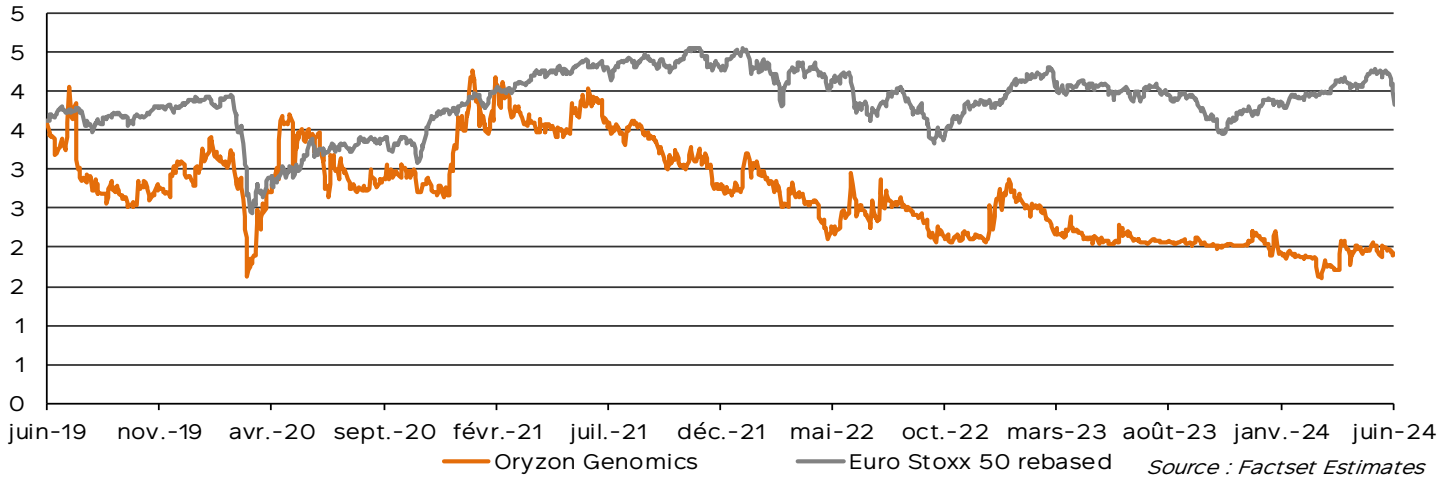
THREATS

- Clinical and regulatory risk
- Commercial risks
- Legal risks

ADDITIONAL INFOMATION



SHARE PRICE CHANGE FOR 5 YEARS



Source : Factset Estimates

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

Ratings assigned by the Invest Securities analysis office are defined as follows:

- 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

73, bd Haussmann - 75008 Paris
T : +33 (0)1 80 97 22 01
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12-MONTHS HISTORY OF OPINION

The table below reflects the history of recommendation and price target changes made by Invest Securities' research department over the last 12 months.

Company Name	Main Author	Release Date	Rating	Target Price	Potential
Oryzon Genomics	Jamila El Bougrini	27-févr.-24	ACHAT	4,8	+156%

DETECTION OF CONFLICTS OF INTEREST

	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

Invest Securities's conflict of interest management policy is available on the Invest Securities website in the Complicance section. A list of all recommendations released over 12 months as well as the quarterly publication of "BUY, SELL, NEUTRAL, OTHERS" over 12 months, are available on the Invest Securities research platform.

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

Pascal Hadjedj
Deputy Managing Director and Head of Primary Market Sales
+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

Stéphane Afonso
Financial analyst, Real Estate
+33 1 73 73 90 25
safonso@invest-securities.com

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

Jamila El Bougrini
Financial analyst, Biotech/Healthtech
+33 1 44 88 88 09
jelbougrini@invest-securities.com

Benoît Faure-Jarrosson
Senior Advisor, Real Estate
+33 1 73 73 90 25
bfaure-jarrosson@invest-securities.com

Claire Meilland
Financial analyst, CleanTech
+33 1 73 73 90 34
cmeilland@invest-securities.com

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

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

TRADING FLOOR

Raphael Jeannet
Institutional Sales
+33 1 55 35 55 62
rjeannet@invest-securities.com

Edouard Lucas
Institutional Sales
+33 1 55 35 55 74
elucas@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

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

CORPORATE BROKING & ISSUER MARKETING

Thierry Roussilhe
Head of CB & Issuer Marketing
+33 1 55 35 55 66
troussilhe@invest-securities.com

Fabien Huet
Liquidity
+33 1 55 35 55 60
fhuet@invest-securities.com

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