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Noxxon Pharma

Réductions tumorales pour les 1ère et 2ème cohortes

Noxxon vient de communiquer des résultats positifs pour la 2ème cohorte NOX-A12+Radiothérapie dans le glioblastome. Le traitement aurait montré des signes d'efficacité chez près de 83% des patients. Achat Fort avec un TP de 0,83 €.

Tumoral reductions for the 1st and 2nd cohorts

Noxxon has reported positive results from the second NOX-A12 + Radiotherapy cohort in glioblastoma. The treatment reportedly showed signs of efficacy in nearly 83% of patients. Strong buy with a TP of 0.83 €.

Recommendation	**1. Strong Buy**
Closing Price on 1 Jun. 2021	**0,43 €**
Target Price	**0,83 € (+93 %)**

Comme convenu, les résultats de la 2ème cohorte de son essai (GLORIA) dans le glioblastome viennent de tomber et ils sont très positifs.

Ainsi, malgré la faible taille de l'échantillon, les premières données montrent que 5 patients sur 6 (83%) auraient vu leur tumeur se réduire durant ou à l'issue du traitement selon une échelle allant de 2% à 62%. Par ailleurs, 2 patients sur les 6 présenteraient des réponses objectives au traitement avec des réductions tumorales supérieures à 50%.

En termes d'efficacité clinique, 2 des 3 patients de la cohorte 1 (dose à 200 mg/semaine et sur laquelle le recul est le plus important) ont survécu au-delà la survie moyenne de 10 mois.

Nous maintenons ainsi notre opinion Achat Fort sur la valeur avec notre TP à 0,83 € par action.

As agreed, the results of the second cohort of its trial (GLORIA) in glioblastoma have just been released and they are very positive.

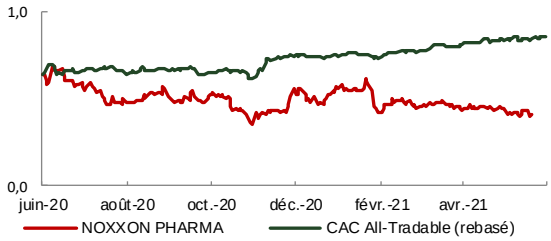
Despite the small sample size, initial data show that 5 out of 6 patients (83%) would have seen their tumor shrink during or after treatment on a scale ranging from 2% to 62%. In addition, 2 of the 6 patients showed objective responses to treatment with tumor reductions greater than 50%.

In terms of clinical efficacy, 2 of the 3 patients in cohort 1 (200 mg/week dose and the longest follow-up) survived beyond the mean survival of 10 months.

We maintain our Strong Buy opinion on the stock with our TP at € 0.83 per share.

Performances

Absolute perf.	1 month	6 months	12 months
	-2 %	-17,9 %	-32,5 %



Market data

Reuters / Bloomberg ticker	ALNOX.PA / ALNOX.FP
Market capitalisation (€m)	28,6 M€
Enterprise value (€m)	29,6 M€
Free Float	23,6 M€ (82,6 %)
Number of shares	66 462 447
Daily volume	1 518 025 €
Capital turnover rate (1 year)	96,0%
High (52 weeks)	0,69 €
Low (52 weeks)	0,35 €

Current shareholding structure

Free float : 87,5 % ; Kreos Capital: 7,4% ; Nyenburgh: 2,3% ;
NGN Biomed: 1,4% ; DEWB: 0,8%; ASO: 0,6%

Agenda

Q4 2021: 3rd (600mg) cohort top-line data GBM (GLORIA);
H2 2021: GLORIA Cohort expansion and Pancreas Cancer Trial

Key figures

	2019	2020	2021E	2022E	2023E
Revenues(M€)	0,3	0,1	6,6	13,4	62,2
Change (%)	-	-	-	-	-
EBITDA (M€)	-3,9	-5,8	-5,2	-5,2	15,2
EBIT (M€)	-4,0	-5,8	-5,3	-5,2	15,1
EBIT Margin (%)	*NS*	*NS*	*NS*	*NS*	*NS*
Net profit gp sh.	-0,9	-10,4	-8,3	-6,2	16,1
Net margin (%)	*NS*	*NS*	*NS*	*NS*	*NS*
EPS	-0,01	-0,45	-0,36	-0,27	0,70

Ratios

	2019	2020	2021E	2022E	2023E
VE / CA	NS	NS	NS	NS	NS
VE / EBIT	NS	NS	NS	NS	NS
VE / REX	NS	NS	NS	NS	NS
P / E	NS	NS	NS	NS	NS
Gearing (%)	NS	NS	NS	NS	NS
Net debt/ EBITDA	NS	NS	NS	NS	NS
RCE (%)	NS	NS	NS	NS	NS

Résultats de la 2ème cohorte (dose : 400 mg)

Noxxon communique les premiers résultats sur la dose 400 mg/semaine en association avec la radiothérapie (RT) pour le traitement des glioblastomes nouvellement diagnostiqués. Ceux-ci montent que le traitement est bien toléré et sûr en termes d'utilisation. Chez 5 patients / 6 premiers (soit 83%) ayant reçu soit 200 mg/semaine, soit 400 mg/semaine, on note une réduction de la taille de la tumeur cérébrale mesurée par IRM. Ces réductions, qui surviennent durant ou après le traitement, s'échelonnent entre 2 et 62% par rapport au niveau initial.

Biologie : réponses objectives (33%) et réductions tumorales

Deux réponses objectives (2/6, soit 33%) ont été observées (une dans chaque cohorte). Elles ont été déterminées par la mesure en IRM de la tumeur, qui dans ces deux cas s'est réduite de plus de 50%. De plus, chez 3 patients / 6, des lésions satellites présentes à l'initiation du traitement avaient disparu à l'issue de celui-ci. En outre, au niveau physiologique, les méthodes IRM utilisées ont montré une réduction du flux sanguin en proximité des tumeurs, laissant envisager une action anti-angiogénique (blocage de la repousse des vaisseaux sanguins) de NOX-A12 associé à la RT. Cette action de NOX-A12 est aussi confortée pharmacologiquement par une quasi-disparition des molécules de CXCL12 dont on sait aujourd'hui qu'elles participent aux phénomènes de résistance médicamenteuse observés avec la RT (mobilisation des cellules souches cancéreuses) ou encore le temolozomide (notamment en favorisant la migration et l'invasivité des cellules de glioblastome en régulant à la hausse le gène FOXM1).

Résultats cliniques : cohorte 1

Ces résultats, qui peuvent se comparer favorablement à des données parues dans la littérature (toutes choses étant égales par ailleurs), démontrent leur pertinence. Ainsi, les premières données des essais de phase I/II de l'Enzastaurin® d'Eli Lilly/Denovo Pharmaceuticals s'inscrivent elles dans la même logique. Néanmoins, Noxxon Pharma devra compléter ses premiers résultats sur la biologie de la tumeur (réduction, etc.) par des données cliniques sur notamment la survie des patients (survie globale, survie sans progression, etc.). En effet, les premières données cliniques montrent que 2 des 3 patients de la cohorte 1 (dosage : 200 mg/semaine) présentaient une survie supérieure à la survie moyenne prévue de 10 mois. Ainsi, l'association NOX-A12 + RT semble avoir un effet sur la survie globale des patients. Toutefois, afin de confirmer ces premières données, Noxxon devra réaliser des analyses statistiques plus approfondies sur les deux dernières cohortes.

Avancées cliniques : Lots cliniques et financement

Comme nous l'évoquons plus haut, le mécanisme d'action de l'association NOX-A12 / Radiothérapie, en réduisant les résistances (chimiothérapiques et radiothérapiques) induites par la voie métabolique CXCL12 / CXCR4, devrait permettre à Noxxon de lancer dès 2022 une étude pivot (NOX-A12 + radiothérapie) en première ligne chez des patients atteints d'un GBM MGMT non-méthylé, donc non sensible au temolozomide (traitement de référence). Pour cela, Noxxon a non seulement initié la production de lots cliniques de NOX-A12, mais aussi de NOX-E36 afin de réaliser ses futures études. Cela a eu pour effet de déclencher l'émission de 2 368 obligations convertibles, d'un montant unitaire de 1 000 €, soit 2,3 M€, selon l'accord de financement précédemment signé avec Atlas Special Opportunities en décembre 2020.

Ces résultats, qui confortent la stratégie de Noxxon, devraient générer un newsflow soutenu et nous incitent à maintenir notre opinion Achat Fort avec un TP rehaussé de 0,83 € / action.

Results of the 2nd cohort (dose: 400 mg)

Noxxon reports initial results for the 400 mg/week dose in combination with radiation therapy (RT) for the treatment of newly diagnosed glioblastoma. These show that the treatment is well tolerated as well as safe to use. In 5 over 6 patients (ie 83%) who received either 200 mg/week or 400 mg/week, there was a reduction in brain tumor size as measured by MRI. These reductions, which occurred during or after treatment, ranged from 2 to 62% from baseline.

Biology: Objective responses (33%) and tumor reductions

Two objective responses (2/6, or 33%) were observed (one in each cohort). They were determined by MRI measurement of the tumor, which in these two cases was reduced by more than 50%. In addition, in 3/6 patients, satellite lesions present at the initiation of treatment had disappeared at the end of the treatment. In addition, at the physiological level, the MRI methods used showed a reduction in blood flow in the vicinity of the tumors, suggesting an anti-angiogenic action (blockage of blood vessel regrowth) of NOX-A12 associated with RT. This action of NOX-A12 is also supported pharmacologically by a virtual disappearance of CXCL12 molecules, which are now known to be involved in the drug resistance phenomena observed with RT (mobilization of cancer stem cells) or temolozomide (in particular by promoting the migration and invasiveness of glioblastoma cells by upregulating the FOXM1 gene).

Clinical results: cohort 1

These results, which compare favorably with data published in the literature (all other things being equal), demonstrate their relevance. The initial data from the Eli Lilly/Denovo Pharmaceuticals Phase I/II trials of Enzastaurin® are consistent with this. Nevertheless, Noxxon Pharma will need to complement its initial results on tumor biology (reduction, etc.) with clinical data on patient survival (overall survival, progression-free survival, etc.). Indeed, the first clinical data show that 2 of the 3 patients in cohort 1 (dosage: 200 mg/week) had a survival greater than the expected average survival of 10 months. Thus, the combination of NOX-A12 + RT seems to have an effect on the overall survival of patients. However, in order to confirm these initial data, Noxxon will need to perform further statistical analyses on the last two cohorts.

Clinical Advances: Clinical Batches and Funding

As discussed above, the mechanism of action of NOX-A12/RT, which reduces resistance (chemotherapy and radiation) induced by the CXCL12/CXCR4 metabolic pathway, should enable Noxxon to launch as early as 2022 a pivotal study (NOX-A12 + RT) in (1L) first-line patients with non-methylated MGMT GBM, which is not responsive to temolozomide (Gold Standard therapy). To this end, Noxxon not only initiated clinical batch production of NOX-A12, but also of NOX-E36 for future studies. This has triggered the issuance of 2,368 convertible bonds of €1,000 each or €2.3 million, as per the financing agreement previously signed with Atlas Special Opportunities in December 2020.

These results, which support Noxxon's strategy, should generate a sustained newsflow and encourage us to maintain our Strong Buy opinion with an increased TP of € 0.83 / share.

Important Disclosure

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1. Strong buy	The absolute share price performance is expected to be at least +25 %
2. Buy	The absolute share price performance is expected to be comprised between +10 % and +25 %
3. Neutral	The absolute share price performance is expected to be comprised between +10 % et -10 %
4. Sell	The absolute share price underperformance is expected to be comprised between -10 % et -25 %
5. Strong Sell	The absolute share price underperformance is expected to be at least -25 %

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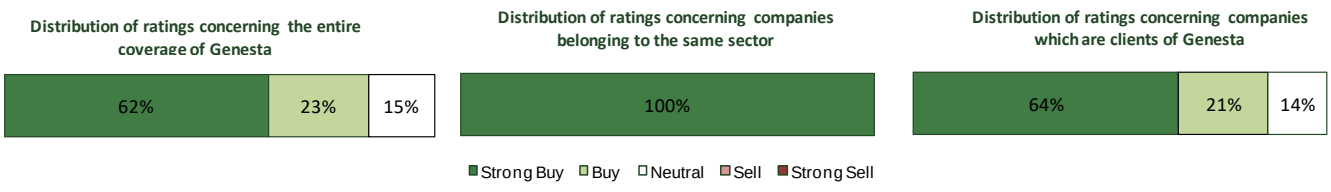
Rating and target price evolution throughout the last 12 months

Date of 1st publication	Rating	Target Price
3rd June 2021	Equity Flash **Strong Buy**	**€ 0.83**
12th May 2021	Equity Flash **Strong Buy**	**€ 0.80**
2nd February 2021	Equity Flash **Strong Buy**	**€ 0.80**
24th November 2020	Equity Flash **Strong Buy**	**€ 1.05**

Ratings distribution



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