Jean Pierre LOZA
Analyste Financier / *Equity Analyst*
jploza@genesta-finance.com
+ 33 1.45.63.68.87

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Noxxon Pharma

Une nouvelle collaboration dans le cancer du pancréas

Noxxon communique la signature et l'initiation d'un second accord de collaboration avec Merck pour l'utilisation du Keytruda en association avec le NOX-A12 dans le cancer du pancréas (phase II). Achat Fort avec un TP de 0,82 €.

A new collaboration in pancreatic cancer

Noxxon announces the signing and initiation of a second collaboration agreement with Merck for the use of Keytruda in combination with NOX-A12 in pancreatic cancer (phase II). Strong buy with a TP of € 0.82.

Recommendation	**1. Strong Buy**
Closing Price on 23 Jul. 2021	**0,35 €**
Target Price	**0,82 € (+135 %)**

Comme il fallait s'y attendre au regard des résultats obtenus par Noxxon avec sa molécule NOX-A12 dans ses différents essais cliniques, Merck a souhaité initier une nouvelle collaboration dans le cancer du pancréas cette fois.

La dynamique autour de Noxxon Pharma est particulièrement positive depuis quelques mois avec des résultats d'essais cliniques positifs, dans des cancers difficiles à soigner comme les cancers colorectaux, du pancréas ou du cerveau. Ces données, pour certaines préliminaires, montrent que le NOX-A12, qui en agissant sur le microenvironnement tumoral, peut renforcer l'immunothérapie anticancéreuse. Des éléments qui ont dû peser dans la décision de Merck de conclure un nouvel accord de collaboration avec Noxxon Pharma.

Nous maintenons ainsi notre opinion Achat Fort sur la valeur avec notre TP à 0,82 € par action.

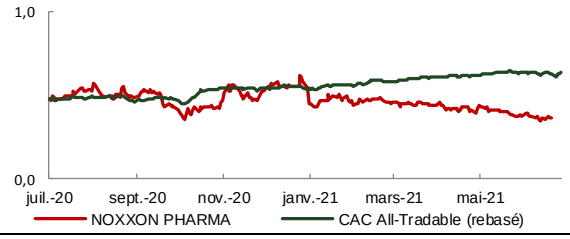
Not surprisingly, given the results obtained by Noxxon with its NOX-A12 molecule in its various clinical trials, Merck wanted to initiate a new collaboration in pancreatic cancer this time.

The momentum around Noxxon Pharma has been particularly positive in recent months with positive clinical trial results in difficult-to-treat cancers such as colorectal, pancreatic and brain cancer. These data, some of which are preliminary, show that NOX-A12, which acts on the tumor microenvironment, can reinforce anti-cancer immunotherapy. These elements must have weighed in Merck's decision to enter into a new collaboration agreement with Noxxon Pharma.

We maintain our Strong Buy opinion on the stock with our TP at € 0.82 per share.

Performances

Absolute perf.	1 month	6 months	12 months
	-5,4 %	-39,8 %	-26,9 %



Market data

Reuters / Bloomberg ticker	ALNOX.PA / ALNOX.FP
Market capitalisation (€m)	23,7 M€
Enterprise value (€m)	24,7 M€
Free Float	19,6 M€ (82,6 %)
Number of shares	67 871 047
Daily volume	1 062 291 €
Capital turnover rate (1 year)	115,2%
High (52 weeks)	0,61 €
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

Une étude clinique de phase II dans le cancer du pancréas

Noxxon Pharma envisage de réaliser un essai clinique de phase II évaluant l'effet de la combinaison NOX-A12 / pembrolizumab associé à deux régimes de chimiothérapie sur un certain nombre de paramètres comme la survie sans progression (SSP), par exemple à 6 mois, la meilleure réponse objective, la SSP globale ou encore la survie globale ou bien le temps jusqu'à l'échec thérapeutique. Dans le cadre de cet essai, Noxxon Pharma devrait recruter 70 patients présentant un cancer pancréatique métastatique (stade III ou IV) à microsatellites stables. L'étude, pour laquelle Merck fournira les lots cliniques de pembrolizumab, comprendra deux bras :

- Le bras 1 où les patients recevront le combo (NOX-A12 / pembrolizumab) ainsi que de la gemcitabine et du nab-paclitaxel ;
- Le bras 2 recevra le combo + le régime FOLFIRI (5-FU+leucovorine + irinotecan nano-liposomal).

De l'influence du microenvironnement

On sait depuis plusieurs années que les protocoles de chimiothérapie FOLFIRINOX ou FOLFIRI améliorent significativement la survie de patients ayant un cancer du pancréas métastatique, comparé au standard de traitement, la gemcitabine. Toutefois, les immunothérapies à base d'IPCI n'ont pas encore répondu aux espoirs. En effet, malgré une expression forte des marqueurs PD-1/PD-L1 (39 à 49%) au sein des tumeurs pancréatiques et une forte activité mutagène (tumeurs chaudes) de ces cancers, on assiste à une quasi résistance de ce cancer aux traitements à base d'IPCI. De nombreux cliniciens et scientifiques pensent que cette résistance serait liée au microenvironnement tumoral qui empêche physiquement la pénétration des lymphocytes T cytotoxiques à la proximité des cellules tumorales et favoriserait la présence de facteurs pro-tumoraux.

Merck et ses collaborations

Merck, avec son Keytruda,, a semble-t-il pris une avance considérable sur ses concurrents dans le monde des inhibiteurs de point contrôle immunitaire (IPCI), grâce notamment à ses différents enregistrements par la FDA. En effet, dès 2015, le pembrolizumab avait été reconnu comme efficace dans les cancers du poumon Non à petites cellules, avant d'être conforté par un enregistrement toujours à la FDA dans les cancers du poumon à petites cellules métastatiques en première. La FDA a reconnu la pertinence du pembrolizumab dans certaines autres tumeurs solides, qui présentent toutes la particularité d'être MSI-H (microsatellites hautement instables) ou à système de réparation de l'ADN déficient (dMMR), ce qui veut dire que ce sont à haut pouvoir de mutation et donc extrêmement immunogènes (donc de bonnes cibles pour une immunothérapie). Mais pour les cancers à microsatellites stables donc peu immunogènes qui constituent dans certains indications l'essentiel des cancers observés, les IPCI ne représentent pas une alternative thérapeutique satisfaisante, d'où l'intérêt pour la NOX-A12 et sa capacité à s'attaquer au microenvironnement ainsi qu'aux cellules MSS, qui rappelons-le représentent près de 90% des tumeurs pancréatiques et colorectales.

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 mis à jour des données de marché de 0,82 € / action.

Phase II clinical trial in pancreatic cancer

Noxxon Pharma plans to conduct a Phase II clinical trial evaluating the effect of NOX-A12 / pembrolizumab in combination with two chemotherapy regimens on a number of endpoints such as progression-free survival (PFS), e.g., at 6 months, best objective response, overall PFS, or time to treatment failure. In this trial, Noxxon Pharma is expected to enroll 70 patients with metastatic pancreatic cancer (stage III or IV) with stable microsatellites. The trial, for which Merck will provide the clinical batches of pembrolizumab, will have two arms:

- Arm 1 where patients will receive the combo (NOX-A12 / pembrolizumab) as well as gemcitabine and nab-paclitaxel;
- Arm 2 will receive the combo + FOLFIRI regimen (5-FU+leucovorin + irinotecan nano-liposomal).

The influence of the microenvironment

It has been known for several years that the chemotherapy protocols FOLFIRINOX or FOLFIRI significantly improve survival in patients with metastatic pancreatic cancer compared to the standard of care, gemcitabine. However, IPCI-based immunotherapies have not yet lived up to expectations. Indeed, despite a high expression of PD-1/PD-L1 markers (39-49%) in pancreatic tumors and a high mutagenic activity (hot tumors) of these cancers, there is a resistance of this cancer to IPCI-based treatments. Many clinicians and scientists believe that this resistance is related to the tumor microenvironment, which physically prevents the penetration of cytotoxic T lymphocytes in the vicinity of tumor cells and favors the presence of pro-tumor factors.

Merck and its collaborations

Merck, with its Keytruda, seems to have taken a considerable lead over its competitors in the world of immune checkpoint inhibitors (IPCI), thanks in particular to its various FDA registrations. Indeed, as early as 2015, pembrolizumab had been recognized as effective in Non-small cell lung cancer (NSCLC), before being backed up by a second approval at the FDA for metastatic small cell lung cancers (SCLC). The FDA has recognized the relevance of pembrolizumab in certain other solid tumors, all of which have the particularity of being MSI-H (highly unstable microsatellites) or DNA repair system deficient (dMMR), which means that they have high rates of mutation and are therefore extremely immunogenic (and thus good targets for immunotherapy). However, for cancers with stable microsatellites and therefore low immunogenicity, which in certain indications constitute the majority of observed cancers, IPCIs do not represent a satisfactory therapeutic alternative, hence the interest in NOX-A12 and its ability to attack the microenvironment as well as MSS cells, which represent nearly 90% of pancreatic and colorectal tumors.

These results, which support Noxxon's strategy, should generate a sustained newsflow and encourage us to maintain our Strong Buy opinion with an updated TP of market data of € 0.82 / 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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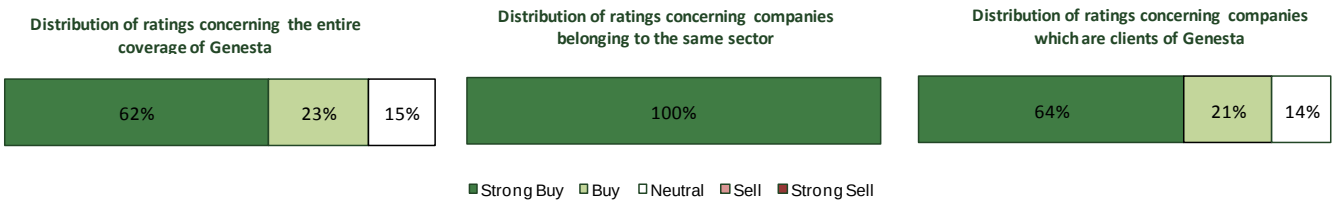
Rating and target price evolution throughout the last 12 months

Date of 1st publication	Rating	Target Price
27th July 2021	Equity Flash **Strong Buy**	**€ 0.82**
2nd 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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