

Jean Pierre LOZA
Analyste Financier / Equity Analyst
jean-pierre.loza@inextenso-finance.fr
+ 33 1.45.63.68.87

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TME Pharma

Survie globale supérieure à 17 mois + 50% de RC

Après plus de 17 mois de suivi, 4 patients sur 6 (67%) sont toujours en vie dans le bras d'expansion de GLORIA. Un résultat intermédiaire qui confirme l'effet de l'association RT+Bev+NOX-A12 sur le GBM. Opinion Achat fort avec un TP revu de 4,28€.

Overall Survival above 17 months + 50% CR

After more than 17 months of follow-up, 4 out of 6 patients (67%) in the GLORIA expansion arm are still alive. This interim result confirms the effect of the combination of RT+Bev+NOX-A12 on GBM. Strong Buy with a revised TP of €4.28.

Recommendation **1. Achat Fort**
Closing Price on 22 Sep. 2023 **1,25 €**
Target Price **4,28 € (+242,1 %)**

Mise à jour clinique : 4 patients en vie sur 6 dans le bras d'expansion GLORIA (RT+BEV+NOX-A12) avec un suivi médian supérieur à 17 mois et 50 % de réponse complète ou quasi-complète.

Avec ces données, la survie globale médiane devrait s'améliorer encore, puisque les 4 patients encore en vie reçoivent toujours le traitement ou des soins de suivi. TME Pharma, avec l'association RT+NOX-A12+BEV, obtient à 17 mois des taux de survie supérieurs à plusieurs études qui font référence dans le domaine. En outre, la médiane de survie globale devrait donc se situer autour des 18 à 19 mois ou même plus. Elles confortent par ailleurs, l'intérêt de l'association RT+NOX-A12+BEV dans le cancer du cerveau à promoteur MGMT non méthylé, qui est traditionnellement de mauvais pronostic.

Mais au regard de ces données, nous maintenons notre opinion Achat Fort sur la valeur avec notre TP revu à la hausse à 4,28 € par action.

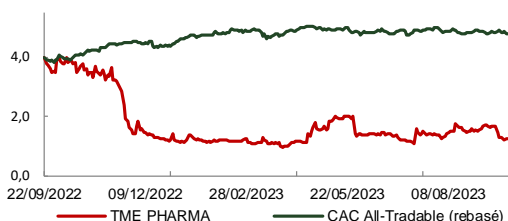
Clinical update: 4 out of 6 patients are alive on the GLORIA expansion arm (RT+BEV+NOX-A12) with a median follow-up of 17 months and 50 % complete or near-complete response.

With these data, median overall survival is expected to improve further, as the 4 patients still alive are still receiving treatment or follow-up care. TME Pharma, with its RT+NOX-A12+BEV combination, has achieved survival rates at 17 months that are higher than those achieved by several benchmark studies in the field. In addition, the median overall survival should be around 18 to 19 months or even more. They also confirm the value of the RT+NOX-A12+BEV combination in unmethylated MGMT-promoting brain cancer, which traditionally has a poor prognosis.

But in view of these data, we maintain our Strong Buy opinion on the stock with our TP revised upwards to €4.28 per share.

Performances

Absolute perf.	1 month	6 months	12 months
	-17%	-0.7%	-68.7%



Market data

Reuters / Bloomberg ticker	ALTME.PA / ALTME.FP
Market capitalisation (€m)	6.6
Enterprise value (€m)	8.6
Free Float (€m)	5.12 (77,2 %)
Number of shares	5,317,193
Daily volume (€)	156 462
Capital turnover rate (1 year)	NS
High (52 weeks)	€ 4.00
Low (52 weeks)	€ 0.32

Current shareholding structure

Not Specified

Agenda

Q4 2023: 2023 Half Year results ;
Q4 2023: 2023 SNO Annual Meeting, Vancouver (Nov., 16-19);
Q4 2023: GLORIA's Expansion Arm Follow on;

Key figures

	2021	2022	2023E	2024E	2025E
Revenues (€m)	0.12	0.03	0.04	5.04	15.04
Change (%)	ns	ns	ns	ns	ns
EBITDA (€m)	-13.28	-12.06	-14.34	-14.76	-13.04
EBIT (€m)	ns	ns	ns	ns	ns
EBIT Margin (%)	-13.28	-12.06	-14.34	-14.76	-13.04
Net profit gp sh. (€r)	-14.46	-15.16	-15.36	-14.78	-12.06
Net margin (%)	ns	ns	ns	ns	ns
EPS	-1.32	-1.38	-0.89	-0.53	0.2

Ratios

	2021	2022	2023E	2024E	2025E
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

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4 patients sur 6 sont en vie après 17 mois...

...de traitement avec l'association RT+NOX-A12+BEV. La **survie médiane globale (mSG)** de cette cohorte se situe donc à date à **67% (à 17 mois)**. Autrement dit, **67% des patients sont encore en vie à l'issue des 17 mois de suivi**. Des données qui se comparent **très favorablement** aux résultats de plusieurs études de références dans le domaine pour les populations résistantes à la chimiothérapie avec des thérapies en développement ou approuvées. L'intervalle se situe entre **13,4 et 16,5 mois** de mSG, tandis que pour le dispositif médical TTF (Tumor Treating Fields) approuvé par la FDA en 2015, la survie médiane était à **16,9 mois**.

Par ailleurs, **le taux de réponse globale** (ORR, Objective Response Rate) pour RT+NOX-A12+BEV se situant à **83%** (qui aurait été de **100%**, si l'un des patients traités et répondant au traitement n'était mort d'une propagation antérieure du cancer au liquide céphalo-rachidien) est bien au-delà des données de la littérature (intervalle **3 – 7,8%**). Ainsi donc, si la dynamique actuelle de l'essai d'expansion se poursuit, nous pourrions voir la survie globale médiane atteindre des valeurs bien au-delà des 18 ou 19 mois.

...et 50 % des patients ont une réponse complète...

...ainsi un patient dont la meilleure réponse antérieure était de 89,9% a continué à évoluer pour présenter **une réduction quasi-complète de la taille de la tumeur**, qui n'était **plus détectable par IRM**. En fait, le lecteur central d'IRM indépendant de l'étude GLORIA et de son bras d'expansion a considéré que ce patient présente **une réponse complète (RC)** à l'association RT+NOX-A12. C'est donc **un troisième patient sur six** qui présente une réponse complète (RC) ou quasi-complète au traitement portant donc le pourcentage à 50%. Selon l'Inca (Institut National du Cancer) « *Le terme de réponse complète s'applique quand tous les signes de la maladie ont disparu après le traitement. On parle aussi de rémission complète. Une rémission peut être complète même s'il existe une masse résiduelle mais non évolutive...* ».

Les données actuelles sont impressionnantes. En effet, si 100% des patients ont montré une **réponse radiographique partielle** (réduction de la tumeur > 50%) au traitement, le niveau de réponse complète serait de l'ordre de 50%. La signification de ces données qui restent à confirmer dans un échantillon plus important de patients est que l'association RT+NOX-A12+BEV est efficace à 100% pour agir sur des tumeurs de glioblastomes imparfaitement ou non réséqués. En outre, chez trois (3) patients sur 6, soit 50% des patients du bras d'expansion, les données d'imagerie montrent que leur tumeur est à des niveaux non mesurables permettant de les classer dans les patients en réponse complète. Cette réduction complète de leur tumeur en imagerie est donc une confirmation de l'efficacité du traitement pour des patients avec un glioblastome nouvellement diagnostiqué et à **promoteur MGMT non méthylé (donc résistant aux chimiothérapies standards : temozolomide)**.

...et conforte notre vision positive du titre.

Ces nouvelles données de TME Pharma sont particulièrement enthousiasmantes car elles indiquent deux choses. Tout d'abord que l'association RT+NOX-A12+BEV agit sur les tumeurs de ces patients leur apportant un bénéfice thérapeutique avéré :

- Réduction des tumeurs objectivée par l'imagerie dans 100% des cas : **cela fonctionne**.
- Réduction presque totale des tumeurs chez trois (3) patients/6, soit **50% de réponses complètes**.
- Amélioration de la **médiane de survie (> 17 mois)** de ces patients pour la plupart en impasse thérapeutique dont le pronostic n'était que de **9 mois avec le standard de soins** actuel. (survie X2).

A notre sens, la qualité de ces résultats de survie dans l'extension de GLORIA, place cette association RT+NOX-A12+BEV à **l'avant-garde** des molécules en développement dans cette indication de glioblastome nouvellement diagnostiqué et à promoteur MGMT non méthylé. Devant **la portée de ces dernières données**, il nous semble évident que rapidement, à l'issue de la réunion annuelle de la SNO (où des données plus pourraient être communiqués) et peut-être même avant plusieurs acteurs du GBM devraient se rapprocher de TME Pharma. C'est pourquoi **nous maintenons notre opinion Achat Fort avec un OC mis à jour de 4,28 € / action**.

4 out of 6 patients alive after 17 months...

...treatment with RT+NOX-A12+BEV. The **median overall survival** of this cohort is now 67% (at 17 months). In other words, **67% of patients are still alive at the end of 17 months' follow-up**. These data compare **very favorably** with the results of several benchmark studies in the field for the chemotherapy-resistant population, using therapies in development or approved. The range is between **13.4 and 16.9 months** of mOS, while for the TTF (Tumor Treating Fields) medical device approved by the FDA in 2015, median survival was **16.9 months**.

Furthermore, the **overall response rate** (ORR, Objective Response Rate) for RT+NOX-A12+BEV of **83%** (which would have been **100%**, had one of the patients treated and responding to the treatment not died of a previous spread of the cancer into the cerebrospinal fluid) is well above the literature data (range **3 – 7.8%**). So, if the current momentum of the expansion trial continues, we could see median overall survival reach values well beyond the 18 or 19 months.

...and 50% of patients have a complete response...

...thus one patient whose previous best response was 89.9% continued to progress and showed **a virtually complete reduction in tumor size**, which was **no longer detectable by MRI**. In fact, the independent central MRI reader of the GLORIA study and its expansion arm considered that this patient had **a complete response (CR)** to the RT+NOX-A12 combination. This means that **a third patient/6** has achieved a complete or near-complete (>99% reduction) response (CR) to treatment, bringing the total to 50%. According to Inca (Institut National du Cancer) " *The term complete response applies when all signs of the disease have disappeared after treatment. This is also known as complete remission. A remission may be complete even if there is a residual mass that has not progressed...* "

The current data are impressive. Indeed, if 100% of patients showed a **partial radiographic response** (tumor reduction > 50%) to treatment, the level of complete response would be of the order of 50%. The significance of these data, which remain to be confirmed in a larger sample of patients, is that the combination of RT+NOX-A12+BEV is 100% effective in treating glioblastoma tumors that are imperfectly resected or not resected at all. In addition, in three (3) patients out of 6, i.e. 50% of patients in the expansion arm, imaging data showed that their tumors were at levels that could not be measured, enabling them to be classified as patients in complete response. This complete reduction of their tumor on imaging therefore confirms the efficacy of the treatment for patients with newly diagnosed glioblastoma and **unmethylated MGMT promoter (therefore resistant to standard chemotherapy: temozolomide)**.

...and reinforces our positive view of the stock.

These new data from TME Pharma are particularly exciting because they indicate two things. Firstly, that the combination of RT+NOX-A12+BEV acts on the tumors of these patients, providing them with a proven therapeutic benefit:

- Tumor shrinkage on imaging in 100% of cases: **it works**.
- Almost total reduction of tumors in three (3) patients/6, i.e. **50% complete response**.
- Improved **median survival (>17 months)** for these patients, most of whom had reached a therapeutic dead end and whose prognosis was only **9 months with the current standard of care**. (Survival X2).

In our opinion, the quality of these survival results in the GLORIA extension places this RT+NOX-A12+BEV combination at the **forefront** of compounds in development for this indication of newly diagnosed glioblastoma with an unmethylated MGMT promoter. Given **the significance of these latest data**, it seems clear to us that several GBM players should approach TME Pharma as soon as possible after the SNO annual meeting (where more data could be communicated) and perhaps even before. **We are therefore maintaining our Strong Buy rating, with an updated price of €4.28 per share**.

Important Disclosure

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In Extenso Finance Equity Research stock market recommendations reflect the absolute change expected in the share price from a six to twelve-month perspective (in local currencies).

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% and -10 %
4. Sell	The absolute share price performance is expected to be comprised between -10% and -25 %
5. Strong Sell	The absolute share price performance is expected to be at least -25 %

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Detection of potential conflicts of interest

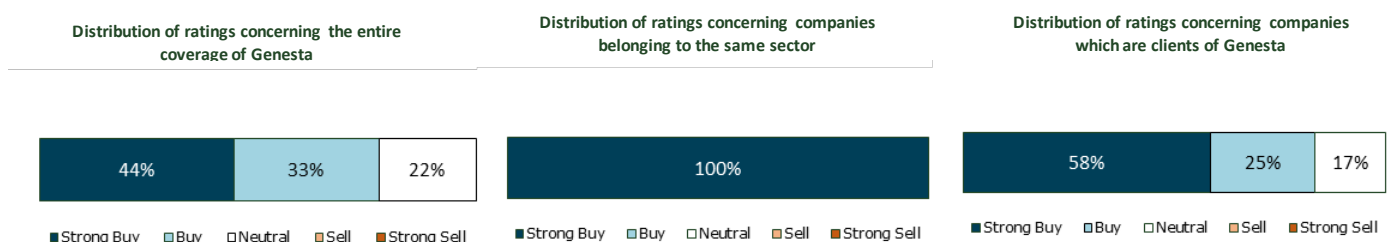
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No	No	No	No	Yes	No	Yes

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Rating and target price evolution throughout the last 12 months

Date of 1 st publication	Rating	Target Price
26 th September 2023	Equity Flash Strong Buy	€ 4.28
5 th July 2023	Semi-Annual Note Strong Buy	€ 3.52
16 th March 2023	Equity Flash Strong Buy	€ 2.70
15 th November 2022	Equity Flash Strong Buy	€ 5.24
30 th June 2022	Equity Flash Strong Buy	€ 5.24

Ratings distribution



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