TME PHARMA

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NEWS – BUSINESS DEVELOPMENT FORECASTS

PROFILE OF THE « BEST PARTNER » FOR NOX-A12

Having obtained IND and Fast Track designation from the FDA for the GBM program, the main challenge for TME in the near future is to raise the funds needed to initiate its Phase II trial, potentially paving the way for accelerated approval. In our view, the ideal scenario is still to sign an agreement with an industrial partner. While there could many different paths, we have attempted in this note to draw up a short list of the most likely partners. At the top of the list is Roche, the developer of Avastin, the original version of the beva. Since losing exclusivity in 2019, sales of Avastin have fallen by almost 75%. A collaboration with TME could create a market opportunity for Roche, with a risk/reward ratio that we believe to be attractive, given the financial investment involved (less than €100m) vs a potential gain estimated at $2.5bn/year in peak sales.

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Next step: financing + partnership = what would be the ideal scenario?

Having achieved its objectives at the start of the year, TME Pharma now needs to score on the business development front. The company has successfully brought together the various regulatory elements needed to ensure that the next Phase II trial in glioblastoma (GBM) follows a clear, well-marked path.
Validating the protocol for the Phase II trial, and obtaining Fast Track approval so as to be able to move towards conditional registration at the end of the study without waiting for the results of Phase III, are all arguments that can be presented to an industrial partner to make the collaboration attractive.
The dossier also has very strong clinical advantages, with the combination of NOX-A12 with radiotherapy and bevacizumab in newly diagnosed patients with partially resected glioblastoma which are resistant to chemotherapy showed a very high response rate and an unprecedented improvement in median overall survival. However, while these results are extremely promising, they relate to a cohort of just 6 patients (n=6). The company therefore needs to conduct a larger trial (n=100) to achieve robust statistical power, test different therapeutic conditions (doses and combinations), and thus validate the best treatment regimen for the majority of patients. In this case, the 3 main limitations to the interpretation and extrapolation of the data obtained in the current Ph I trial are (i) the size of the cohort, (ii) the absence of a control arm and (iii) the fact that the trial is not randomized at this stage (randomization of patients helps to avoid potential bias and minimize statistical interference). The planned Phase II trial, which is due to be launched in H2 24 (subject to raising the necessary funds), has been designed to address these various limiting aspects, and thus make it possible to aim for robust and potentially 'conclusive' results from a regulatory point of view (conditional approval).

At this stage, TME Pharma's main objective is to strengthen its cash position in order to pursue its Business Development activities, with the short-term objective of identifying a partner and signing a contract to bear part or all of the costs of the Ph II study in GBM. Ideally, the presence of a partner should be sufficient to resolve TME Pharma's 2 priorities, as the upfront associated with the licensing agreement should enable TME Pharma to cover its ongoing expenses over several months, while the partner would bear the costs of the Ph II trial for which it would be granted a license.

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

in € / share	2023e	2024e	2025e
Adjusted EPS	-0,46	-0,26	-0,73
chg.	*n.s.*	*n.s.*	*n.s.*
estimates chg.	*n.s.*	*n.s.*	*n.s.*

au 31/12	2023e	2024e	2025e
PE	n.s.	n.s.	n.s.
EV/Sales	-23,0x	0,7x	135,1x
EV/Adjusted EBITD	n.s.	n.s.	n.s.
EV/Adjusted EBITA	n.s.	n.s.	n.s.
FCF yield*	n.s.	n.s.	n.s.
Div. yield (%)	n.s.	n.s.	633,7%

* After tax op. FCF before WCR

key points	
Closing share price 26/06/2024	0,16
Number of Shares (m)	41,5
Market cap. (€m)	7
Free float (€m)	6
ISIN	NL0015000YE1
Ticker	ALTME-FR
DJ Sector	Health Technology

	1m	3m	Ytd
Absolute perf.	-36,9%	-51,0%	-31,4%
Relative perf.	-30,2%	-47,7%	-30,3%

Source : Factset, Invest Securities estimates

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In fact, in our opinion, the best scenario would be the signature of a worldwide exclusive license agreement for NOX-A12 in the GBM with a BioPharma player present in the field of oncology and/or rare diseases, with proven M&A activity, a declared strategy towards external growth, and potentially the need to accelerate its growth to respond to a market loss challenge for flagship products (such as the end of patents on "star" products, or the entry onto the market of generic/biosimilar competitors).

Taking these various factors into account, we have identified 4 player profiles most likely to meet TME Pharma's criteria for its GBM program (the arguments are developed on the next page of this note):
1. Roche, owner of Avastin, the original version of bevacizumab
2. Generic manufacturers of bevacizumab
3. Ipsen
4. Servier

Estimated study cost of €50m: the last 'challenge' before reaching the market?

It should be remembered that the initiation of Ph II in GBM is subject to substantial funding, since we estimate the total cost of this study at nearly €50m on the basis of the design proposed by TME Pharma. The protocol for the FDA-approved Ph II study will comprise the following 5 arms, each of which will enroll around 20 patients :

- Arm 1: NOX-A12 - 200mg/week + radiotherapy and bevacizumab
- Arm 2: NOX-A12 - 400mg/week + radiotherapy and bevacizumab
- Arm 3: NOX-A12 - 600mg/week + radiotherapy and bevacizumab
- Arm 4: NOX-A12 - 600mg/week + radiotherapy
- Arm 5: Control of standard treatment (temozolomide + radiotherapy)

The excellent data from Ph I/II having demonstrated a mOS (median overall survival) of almost 20 months, we consider that one of the main criteria to be considered for the validation of the Ph II trial will be survival at 18 and 24 months. Taking into account the size of the study and the speed of recruitment, we estimate that a first readout at 24 months of treatment will be possible between 3.5 and 4 years after the start of the Phase II study. In Phase I/II (cohort of 6 patients), mOS was 19.9 months with the NOX-A12/radiotherapy/bevacizumab combination versus 10.5 months with standard treatment, representing a near doubling of overall survival, while mPFS (median progression-free survival) was 9 months versus 4 months, with an ORR (overall response rate) of 83% versus <10% achieved with reference treatments. If these results are confirmed in Phase II on a sufficient number of patients to achieve robust statistical power, and in the context of a randomised controlled trial (comparison with standard treatments), then it is very likely that the NOX-A12/RT/beva combination could become the new reference treatment for newly diagnosed patients with glioblastoma treated by surgery but with residual tumor resistant to chemotherapy (unmethylated MGMT).

Financial visibility recently extended to the end of 2024 vs. July previously

As mentioned above, TME Pharma's main challenge today is to raise the funds it needs to continue its activities. The cash position at the end of 2023 was €2.2m (compared with €4.6m at the end of 2022, bearing in mind that €4.8m was raised during 2023), having been strengthened by €2.55m in 2024 through the exercise of warrants (BSA) as part of a sequential financing operation initiated at the end of 2023, and by €2.35m recently through a capital increase secured from guarantor investors. After market, on Monday 17th of June, the Group announced the launch of a capital increase through the issue of new shares for a total amount of €2.2m, which could be increased to €2.59m if the portion reserved for retail investors is fully subscribed (+15% of the amount of the private offering). The following day, the success of the operation was announced, raising €2.35m with the issue of 13,088,158 new shares, of which €2.27m raised through private offering and €79k raised through the offer reserved for the public (PrimaryBid).

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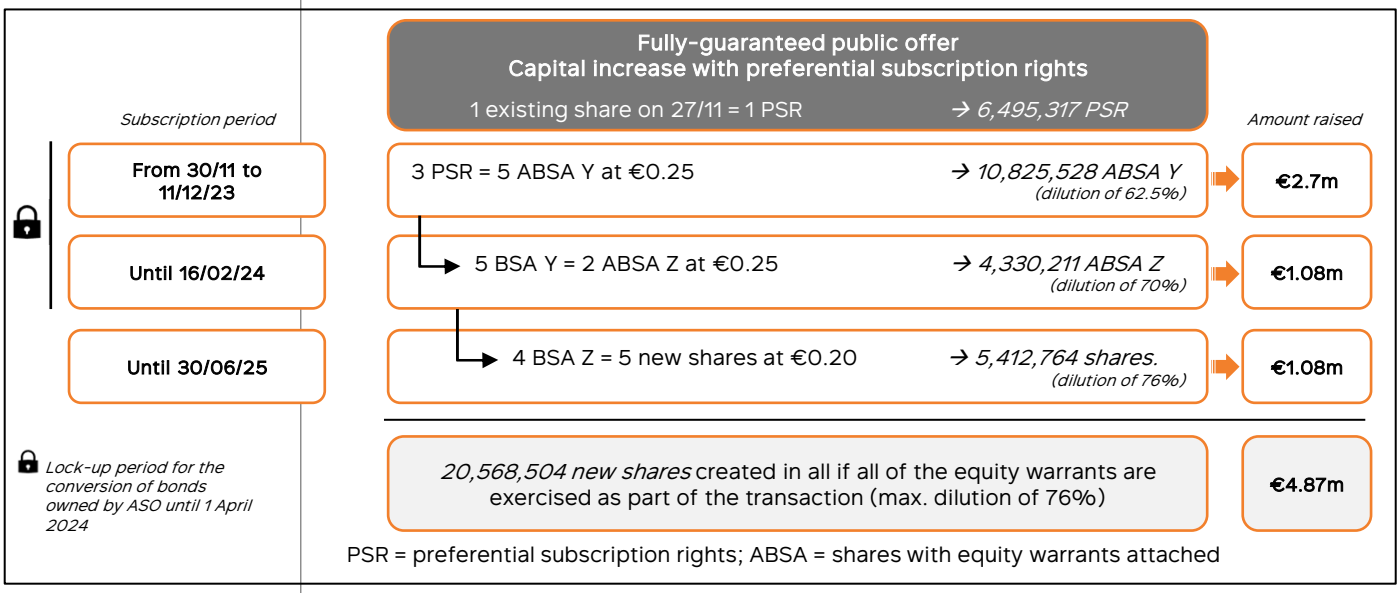
The subscription price was set at €0.1798, representing a 10% discount to the closing price on 17 June 2024, and a potential dilution of 31.5%. A guarantee agreement has been signed with professional investors for a minimum amount of €2.2m to be paid by the 28th of June 2024, which has made it possible to secure the transaction in its initial objective. As far as these investor-guarantors are concerned, it should be noted that this is not a concerted action in order to take control of the company. None of the investors exceeded the 50% ownership threshold on an individual basis following the transaction and the full exercise of the guarantee.
The net proceeds of the transaction will enable the company to extend its financial visibility to December 2024, compared with the previous July 2024, and to finance first and foremost :

- 30% of its R&D, in particular the Ph I/II trial in GBM (glioblastoma),
- 30% for business development,
- and for 40% of its general needs.

BSA Z warrants can still be exercised until the 20th of June 2025, and if the remaining outstanding warrants are exercised in full, this could represent nearly €830k, or around 2 months of additional financial visibility. The full amount of the BSA Z warrants could generate up to €951k. An initial exercise period running from the 26th of February to the 22th of March 2024 raised €120k (479,624 BSA exercised, i.e. around 12.6% of the total number of BSA Z). This first exercise of BSA Z led to the issue of nearly 600k new shares, representing gross proceeds of nearly €120k and dilution of 2.11%. To date, therefore, there are 3,326,104 BSA Z outstanding, representing a potential amount of €831.5k, bearing in mind that the second exercise period is underway and should close in the next few days (from the 27th of May to the 28th of June). This amount could extend the company's financial visibility in Q1 25 by almost 2 months.

Reminder of the terms and conditions of the offer



Source: Invest Securities, TME Pharma

TME Pharma's main objective is to sign a license agreement during the course of the year to pursue developments in glioblastoma as a priority. Given the financial visibility afforded by the recent capital increase, if a partnership is signed, it should enable TME Pharma to secure the continuation of its activities. However, if an agreement is not reached before December, the company will have to prepare to raise funds to ensure business continuity and give itself additional time to attract a potential partner. We had predicted a fund-raising of between €2.5m and €3.5m to provide a further 6 months of visibility, given the current cash burn (estimated at €400k/month).

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Funding, the main short-term issue identified : what options available ?

With an IND and a Fast Track granted by the FDA, and on the basis of the clinical data obtained in Phase I/II, we believe that TME Pharma has solid arguments to convince an industrial and/or financial partner to support the continuation of the program. In parallel with these business development discussions, which are aimed at obtaining government or charitable grants, the company is looking at other non-dilutive financial levers to continue the program's development. In addition, TME Pharma is considering public subsidies and is studying the eligibility of NOX-A12 in GBM as a compassionate treatment. However, for the latter, it will be necessary to demonstrate robust clinical data with satisfactory clinical efficacy and treatment safety before considering submitting a dossier to obtain the green light from the health agencies. Given the procedure involved, this is unlikely to happen for several years, even in a blue sky scenario, and the revenues generated in such a context will not be able to contribute to TME Pharma's immediate financing needs.

To generate revenues, TME Pharma is also considering monetizing its NOX-E36 asset, developed at this stage to address fibrosis and ocular diseases, via a spin-out. NOX-E36 has been evaluated in Phase I and Phase II clinical trials, demonstrating its ability to target macrophages in a dose-dependent manner, and establishing its safety and tolerability profile in over 100 subjects. In addition to its anti-inflammatory effect on fibrosis, NOX-E36 has shown encouraging preclinical results in oncology, particularly in solid tumor models, notably pancreatic and liver cancer. TME Pharma plans to sell the rights to this asset in order to generate revenues to be reallocated to the development of NOX-A12 in triple therapy for GBM.

Apart from these options, there are still non-dilutive solutions such as debt (BEI, Bpifrance, or other lenders), as the company has committed to ending its convertible bonds financing program. Several programs exist with Bpifrance to finance the biotech company at all stages of development, depending on the company's profile. As far as the EIB is concerned, loans with warrants in several tranches, the drawdown of which is subject to a number of covenants, are also possible if the application is deemed eligible by the bank. These covenants often include clauses that require:

- a minimum amount tied up in cash,
- a time-to-market of just a few months/years, and a flagship study that is relatively mature in terms of R&D,
- the contribution of additional funds concomitant with each drawdown.

In view of TME Pharma's situation, it seems unlikely to us that it could be considered eligible by the EIB to obtain significant financing outside the scenario of a structuring partnership based on a licensing agreement.

After reviewing the various options available to TME Pharma, a partnership appears to be the ideal solution for a company with TME Pharma's profile :

- a small-cap company,
- the need of funds to support its developments,
- mid-stage program in terms of maturity, offering an attractive BD opportunity,
- promising initial clinical data,
- a paradigm shift in the management of resistant GBM,
- takeover possible if the company succeeds the Ph II trial.

License or license option: ideal solution for accelerating R&D on NOX-A12

As already mentioned, in the range of possible solutions for TME Pharma, a collaboration with an industrial player through a licensing agreement or a licensing option remains in our view the best configuration, given TME Pharma's need for funds and its current situation. We believe that a tie-up would make even more sense with a recognized player in oncology, or a player with the strategy of building a franchise in this field with the intention of distinguishing itself by :

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- a niche indication,
- a significant unmet medical need,
- a combination with unprotected standard treatments,
- a highly significant therapeutic effect (PFS and OS),
- a time-to-market of 5 years in a favorable scenario,
- a measured financial risk: study costs of around €50m to reach the market,
- demonstrated biological rationale (biomarkers and imaging).

While Roche appears to be the ideal partner, since it is the developer of Avastin, the original version of bevacizumab (beva), other less "obvious" players could also meet the criteria for a "B-to-B association" with TME Pharma. In particular, we have identified 2 other companies in the French environment that we believe could be of interest to TME Pharma's GBM program, as well as a less "conventional" type of player that could also fit the profile sought by TME Pharma.
On the basis of these considerations, here are the 4 avenues, in order of relevance, that we identify as the most likely and structuring in the context of a rapprochement with TME Pharma:

1. **Roche**: the most natural partner as developer of Avastin, the original version of bevacizumab,
2. **Generic beva manufacturers**, which could be interested in gaining new market share in the beva segment,
3. **Ipsen** for its positioning in oncology, rare diseases, its strategy focused on external growth, and the need to renew its drug pipeline to compensate for the loss of revenues following the loss of exclusivity of its flagship drug Somatuline (entry into the generic version market),
4. **Servier** to strengthen its oncology franchise initiated in 2018 with the acquisition of Shire, and to meet its external growth strategy.

1. Roche: the opportunity to relaunch an exclusivity cycle for Avastin !

Avastin was Roche's flagship drug for the treatment of cancer and inflammatory diseases. The product has received multiple approvals as an anti-cancer treatment for adult patients with cancers such as :

- cancer of the colon (large intestine) or rectum,
- metastatic breast cancer
- advanced non-small-cell lung cancer,
- advanced or metastatic kidney cancer,
- cervical cancer (cervix),
- epithelial ovarian cancer, in combination with other anti-cancer drugs.

Before its patent fell into the public domain, Avastin was Roche's leading blockbuster. In 2019, Avastin generated nearly $7.12 billion, the last year before the arrival of the first biosimilar competitors. Avastin revenue growth stagnated in 2019 (almost flat growth of just 1.7% between 2018 and 2019), this slowdown having been partly caused by the approval of Pfizer's biosimilar Zirabev in June 2019, after a 1st approval in the US of Amgen's biosimilar Mvasi. Since then, Avastin revenues have been declining, despite some attempts by Roche to resist biosimilars, notably through treatment combinations. In June 2020, the FDA gave its approval for a combination of Tecentriq and Avastin (Roche's anti-PD-L1 and anti-VEGF) in the first-line treatment of newly diagnosed liver cancer (HCC).

Thanks to this combination, Roche has generated nearly CHF 3.1 billion in revenues in 2021, which represents a loss of nearly - 37% compared with 2020, as this new positioning has not been able to offset the losses generated by the introduction of biosimilars, especially in the US (from 2019, and from 2022 in Europe).

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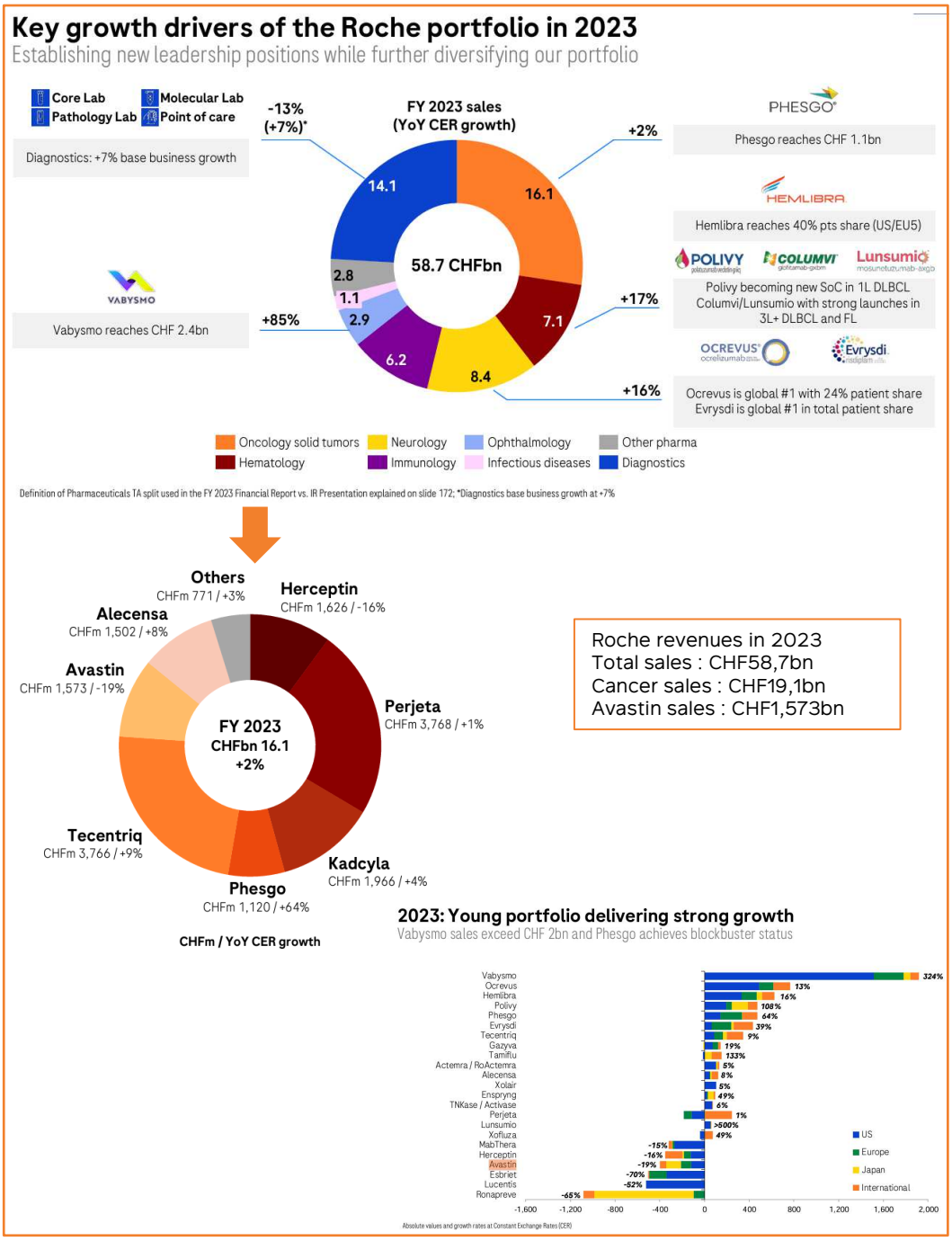
In 2023, the group recorded sales of CHF 58.716 billion ($68.2B), of which CHF 19.087 billion ($21.3B) was generated by the Oncology franchise (and CHF 16.1 billions for solid cancers). Avastin generated CHF 1.573 billion ($1.83B) in 2023, underlining the YoY decline faced by the product despite the company's attempts to halt the erosion of sales.



Source: 2023 FY Financial Results, Roche

While the loss of market share for Avastin is undeniable and inevitable with the arrival of generic competition, Roche has nevertheless tried to defend its market share:

- by developing combinations of its cancer treatments. A first combination has been approved in liver cancer with its anti-PD-L1,

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- by taking legal action against certain biosimilars. Amgen/Allergan were the onl drugmakers that chose not to accept a deal with Roche to delay the launch date of their generic version of Avastin. In contrast, Mylan, Pfizer, Samsung Bioepis and the Teva Pharmaceutical-Celltrion team agreed to a deal with Roche to delay the launch of their products. In June 2020, its subsidiary Genentech sued Samsung Bioepis for patent infringement, with the aim of keeping the Samsung Biologics-Biogen version off the market.

That said, the Group has not undertaken any further research into Avastin. A search of ClinicalTrials.gov reveals no ongoing Roche-sponsored clinical programs involving Avastin. The group probably wants to prioritize its innovative programs that could generate ST/MT revenues that could exceed the current level of Avastin. However, we believe that Roche could be opportunistic if a relatively mature project enabled it to gain market share with its product. In terms of R&D spending, the company remains heavily invested in innovation, with almost CHF 13.24bn dedicated to R&D in 2023 ($15.9bn), of which CHF 11.6bn for the Pharma segment (CHF 1.6bn for the Diagnostics segment) vs CHF 13.95bn in 2022. These investments represent 22.5% of its revenues in 2023. In fact, a R&D investment that could represent less than €100m to support TME Pharma's promising work in GBM seems reasonable given the Group's capabilities and its positioning in oncology.

2023: Group operating performance

Core OP lower by -1% due to higher operating expenses and lower other revenue (Ultomiris base effect 2022)

	2023 CHFm	2023 abs. CER	2023 vs. 2022 CER growth
Sales	**58,716**	**+391**	1%
Other revenue	1,725	-664	-27%
Cost of sales	-15,251	+1,350	-8%
R&D	-13,237	-709	5%
SG&A	-13,518	-590	4%
OOI&E	805	+44	6%
Core operating profit	**19,240**	**-178**	-1%
Core OP in % of sales	*32.8%*		*-13% in CHF*
At CER	*34.4%*		
	(2022: 34.9%)		

CER=Constant Exchange Rates; OP=Operating Profit; R&D=Research & Development; SG&A=Selling, General & Administration; OOI&E=Other Operating Income & Expense

Source: 2023 FY Financial Results, Roche

This hypothesis makes all the more sense given that bevacizumab is used to treat GBM in certain cases. Avastin is approved to treat recurrent GBM in adults after a first line treatment. In this respect, Avastin has received accelerated approval from the FDA, whereas the EMA has not granted authorization for Avastin in brain tumours on the grounds that the reduction observed after treatment with Avastin was not a reduction in the tumor itself but a reduction in the size of the tumor environment. In newly diagnosed GBM, the work carried out did not demonstrate any improvement in overall survival (OS) despite a moderate effect on PFS (progression-free survival). As the clinical trial did not meet its primary endpoint, Avastin has not been approved for use in GBM newly diagnosed.

That said, this confirms Roche's initial interest in newly diagnosed GBM. Independently of TME Pharma's work. While Avastin alone failed to demonstrate significant improvement in OS, TME Pharma's results at this stage in newly diagnosed GBM are significantly different. The combination of bevacizumab with radiotherapy and NOXA12, based on initial results

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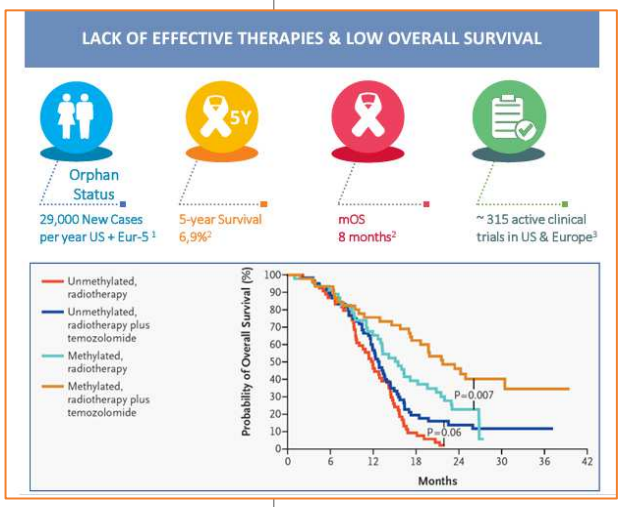
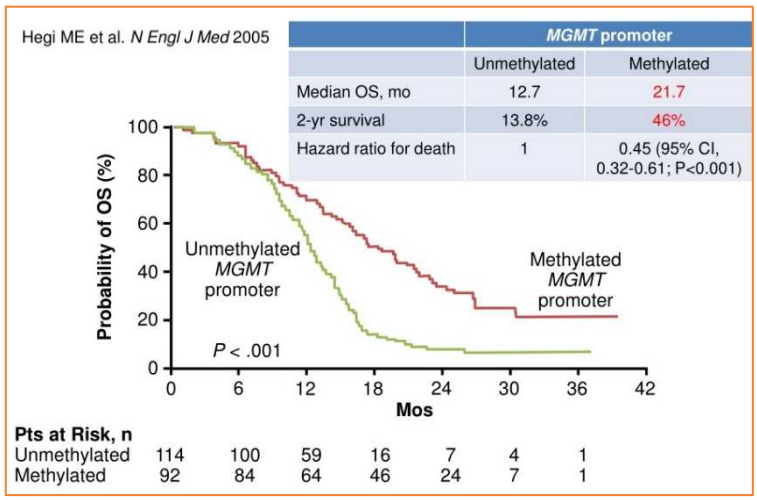
obtained from a small number of patients, shows significant efficacy and a major improvement in overall survival (19.9 months vs. 10.5 months for median OS, i.e. a gain of 9.4 months representing an improvement of +89.5%), which Avastin alone failed to demonstrate. Other clinical trials conducted by players other than Roche have confirmed the observations that bevacizumab is not effective as a single agent in newly diagnosed GBM. This tends to confirm that it is indeed the combination of the three NOX-A12/RT/beva treatments that induces the positive effect on OS.

While there are currently solutions for newly diagnosed GBM that respond to chemotherapy, there are still a number of patients who are considered difficult because they have no satisfactory therapeutic solution. It is precisely these patients that TME Pharma is targeting with its triple combination: newly diagnosed, surgically operated but with a residual tumor and a non-methylated MGMT profile known to be resistant to chemotherapy.





Source: TME Pharma

Glioblastomas occur at any age and often progress rapidly, within 2-3 months. In adults, GBMs are the most common brain tumors, with an incidence of around 1/33,330 per year, and an estimated prevalence of 1/100,000. Treatment is initially surgical, with as wide an excision as possible, bearing in mind that it is generally impossible to remove the entire tumor, which infiltrates the normal brain parenchyma. After surgery (where possible), the first-line treatment consists of targeted radiotherapy combined with chemotherapy. The benefit of these two treatments in terms of survival remains relatively modest, but has nonetheless been demonstrated. In the event of recurrence, second-line chemotherapy or even a repeat operation may be proposed. There is therefore a strong expectation that a new solution with greater therapeutic benefit will emerge if brain cancers are to be treated more effectively. This is all the more true for GBM in which the promoter of the MGMT gene is not methylated, due to a demonstrated correlation with chemoresistance.

With an incidence of 29k cases each year in the main regions (US and EU), this market could represent up to $2.5bn in first-line treatment of newly diagnosed GBM (where Avastin is currently absent due to failure to impact OS in a Roche trial). This estimate is based on pricing of $10k/month in the US and $5k in the EU, i.e. $120k and $60k in annual costs, in line with the prices of targeted antitumor therapies with a significant impact on OS.

In fact, a niche market that could represent close to $2.5 billion seems very attractive to Roche, especially if the first biological and clinical proofs are present, and if the financial investment to be made does not exceed €100m before a potential conditional market launch. We consider the risk/reward to be very attractive for a company such as Roche, which could see several advantages in doing so :

- seeking growth for Avastin, which currently generates less than $2bn, with a potentially

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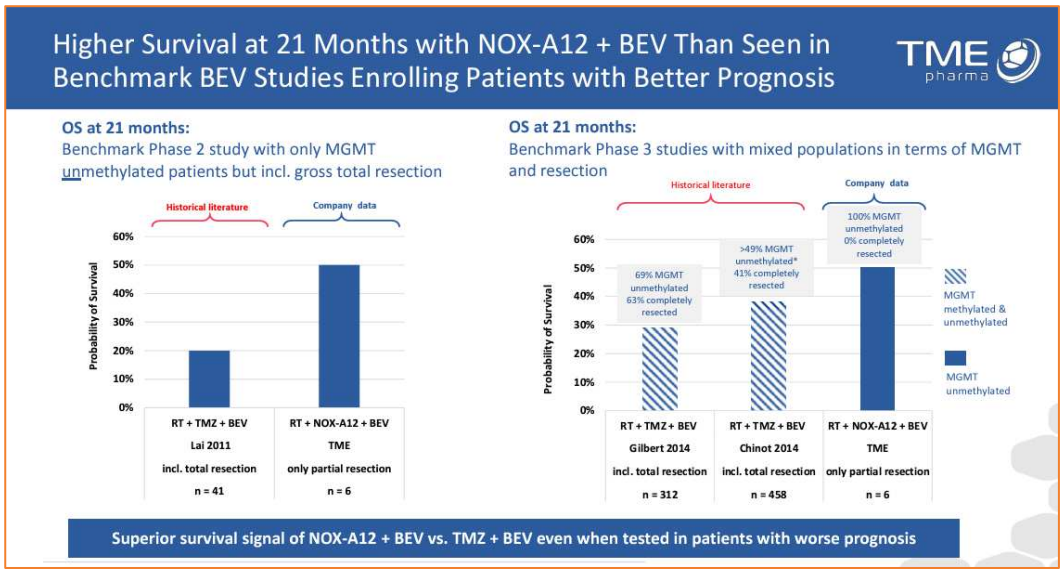
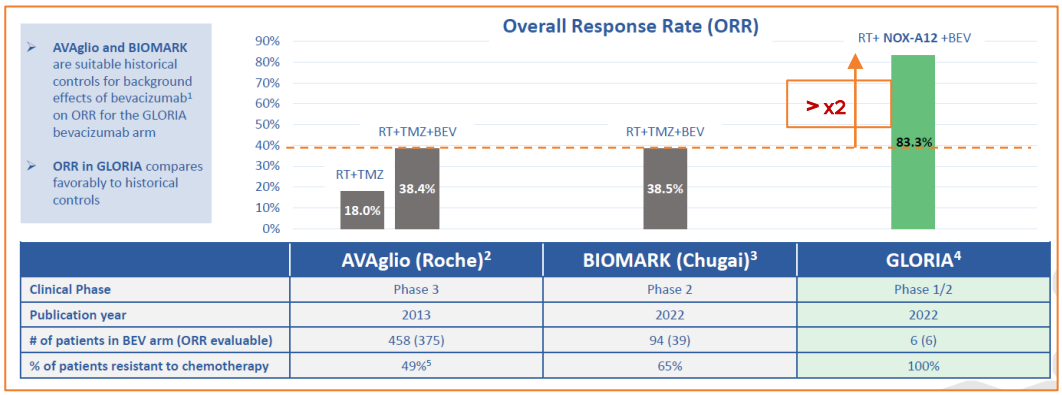
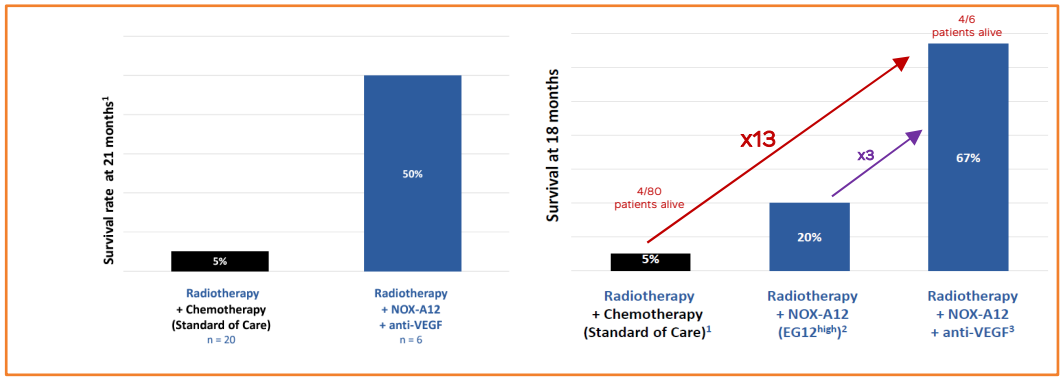
addressable market greater than current sales ($2.5bn in GBM could potentially be added to current revenues, which are in constant decline),

- reinvest in an indication that had to be abandoned after clinical failure, on the strength of unique preliminary clinical results not achieved with bevacizumab alone or with other therapeutic approaches, and therefore with little risk of competition in the ST,
- provide an effective solution for patients suffering from a lack of satisfactory alternatives, at lower cost (€100m in costs vs. a potential gain of $2.5bn).





	AVAglio (Roche)[2]	BIOMARK (Chugai)[3]	GLORIA[4]
Clinical Phase	Phase 3	Phase 2	Phase 1/2
Publication year	2013	2022	2022
# of patients in BEV arm (ORR evaluable)	458 (375)	94 (39)	6 (6)
% of patients resistant to chemotherapy	49%[5]	65%	100%



Source: TME Pharma

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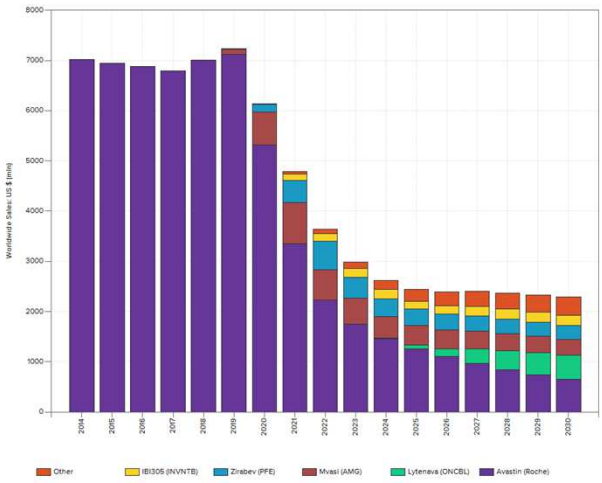
2. Avastin generic maker : market share and volume are the key words !

As previously mentioned, the Avastin patent expired in the US in July 2019, while the European patent expired in January 2022. Since then, several products have demonstrated the bioequivalence to Avastin required by health agencies to obtain marketing authorization. More than a dozen equivalent products have thus invaded the market for the same indications as those for which Avastin has received marketing authorization: treatment of carcinoma of the colon or rectum, breast cancer, non-small-cell lung cancer, kidney cancer, epithelial cancer of the ovary, fallopian tubes or primary peritoneum, and carcinoma of the cervix. Since 2019, annual sales of Avastin, at around $7 billion, have begun to fall sharply, and now stand below $2 billion in annual sales. Projections call for a 50:50 split between Avastin and its biosimilars by 2026, followed by a domination of biosimilars vs. Avastin from 2027 onwards. in potential of $2.5 billion).

Top 10 companies marketing bevacizumab

Companies	Products
Amgen	Mvasi
Biocon	Krabeva
Innovent Biologics	IBI305
Jiangsu Hengrui Parmaceuticals	BP102
Outlook Therapeutics	Lytenava
Pfizer	Zirabev
BeiGene	Avzivi
Organon	Aybintlo
Sino Biopharmaceutical	Bevacizumab injection
Viatris	Krabeva



Source: Evaluate Pharma

As a reminder, Avastin received its first FDA approval in 2004 for the treatment of colorectal cancer, and reached its peak sales in 2019 with record worldwide sales of $7.1 billion. As with all blockbuster drugs, Avastin's success has made it a prime target for biosimilar developers. Since the arrival of this competition on the market, bevacizumab biosimilars have enjoyed notable commercial success, with worldwide sales collectively exceeding $2.2 billion, roughly equivalent to Roche's Avastin sales today.

A more specific analysis of bevacizumab sales in the US, where the first biosimilar approvals were granted (see GlobalData chart), shows that it took at least two years for the introduction of biosimilars to have a significant impact on Avastin sales. GlobalData's forecasts estimate that Avastin sales will fall to just over $600m by 2029, while biosimilars will collectively exceed $2bn in sales by 2025 and remain at the same level until 2029, possibly holding close to 75% of the total market share of bevacizumab products. Given the lower price of biosimilars (between 77% and 87% of the price of original Avastin), the share of patients "captured" by biosimilars will according to these forecasts be greater than the share of patients on Avastin, meaning that over 80% of US patients treated with a bevacizumab antibody will be on a biosimilar by 2029. By 2022, it is estimated that over 60% of US patients and over 30% of EU patients will have switched to biosimilar bevacizumab.

The US remains the leading market for bevacizumab sales, followed by the EU and Japan. According to analyst consensus and GlobalData forecasts, Pfizer's prodrug Zirabev should be the first biosimilar to surpass the original Avastin in terms of worldwide sales by 2028.

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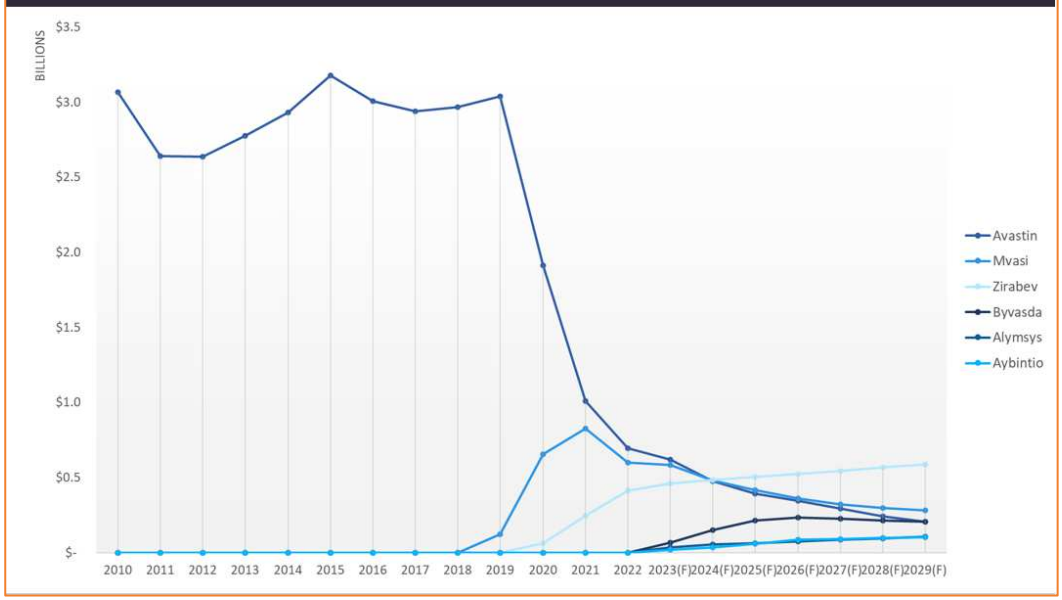
We note that among the players marketing Avastin biosimilars are Pharma companies, and that the Top 10 are not limited to generic pure players. According to GlobalData, the 2 biosimilars expected to gain the most market share in ST/MT are Pfizer and Amgen. Given the typology of these players, we believe it is entirely conceivable that one of them could be interested in an innovative positioning to differentiate itself from the rest of bevacizumab's competitors, with a view to growing sales and gaining market share. Furthermore, sales forecasts suggest that revenues will remain below $1 billion in the US by 2030, which makes positioning in TME Pharma's target market all the more attractive. Projections point to peak sales of $2.5 billion, i.e. more than 2x the estimated sales of bevacizumab in current markets by 2030.

Figure 1: Historical and future forecast sales for bevacizumab products in the US by year



Source: GlobalData

We consider that if Roche, the most natural partner for TME Pharma, did not seize the opportunity of the newly-diagnosed GBM market, one of the competitors before a beva biosimilar in its product portfolio could see the market opportunity to accompany TME Pharma in its developments to secure the GBM market in ST. According to the patent database, NOXA12 is protected until the end of 2029, with a possible 5-year extension to meet minimum market exclusivity guarantees. The initial submission for intellectual property protection concerned only the NOX-A12 product and not the combination with beva, which means that specific protection for the combination could probably guarantee a longer period of exclusivity for any partner deciding to sign an agreement with TME Pharma. Despite the existence of competing products for beva, the fact that NOX-A12 could only be supplied by the rights holder as part of a NOX-A12/beva combo, would guarantee this player a monopoly and exclusivity on the market for newly diagnosed, partially resected and chemotherapy-resistant GBM, i.e. a market estimated at $2.5 billion on the basis of relatively conservative pricing assumptions if the impact on overall survival is confirmed in the pivotal phase.

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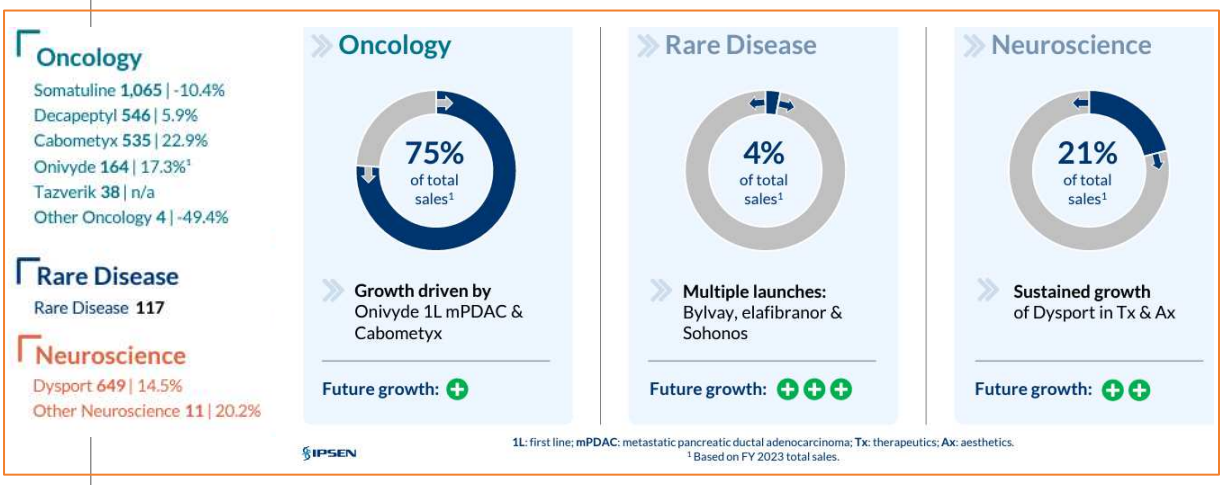
3. Ipsen: counter Somatuline losses through external growth

In addition to players with bevacizumab assets, we also selected Ipsen as a potential partner. Ipsen is making good progress in its 3 historical franchises: Oncology, Neuroscience and Rare Diseases.

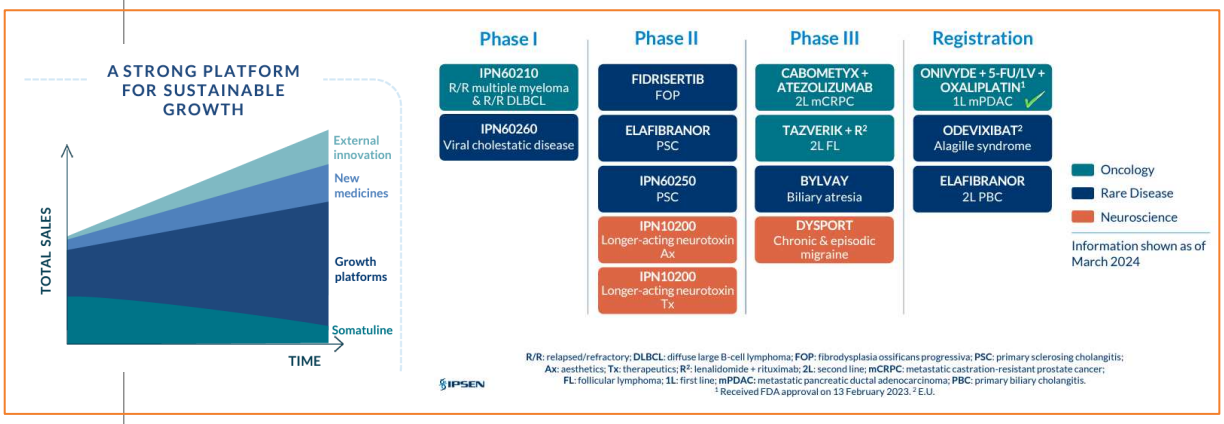
We see Ipsen as a potential partner for TME Pharma for 3 reasons:

- A strategy based on external growth that has been delivering results for several years,
- The need to accelerate growth to counter the loss of revenues linked to the arrival of generics of Somatuline (anticancer drug), which has had a significant impact on the product's sales since 2022. FY 23 sales came in at €3,127.5m vs. €3,233m, up +6.7% cc (+3.4% reported) despite the continued deceleration of Somatuline (-10.4% cc vs. 2022, i.e. €1,065.6m vs. €1,218m). Oncology remains the Group's main franchise (75% of total sales), although it grew by only +1.5% cc, while the Neuroscience franchise (21% of total sales) posted a solid performance of +14.6% cc.



Source: Ipsen

TME Pharma and NOX-A12 are at the crossroads of Ipsen's core franchises: oncology by virtue of its main positioning, but with a foot in the "Neuro" field because GBM is a brain cancer, and in the "Rare Disease" field because it is a niche market. Oncology remains a strong Ipsen franchise. By 2021, the Group has forged 7 partnerships and integrated 8 new assets. In 2022, the acquisition of Epizyme enabled it to extend its oncology portfolio to hematology, the group's stated objective being to add innovative new treatments to its R&D pipeline by 2025. We believe that NOX-A12 fits very well with Ipsen's strategy and could strengthen the pipeline in the Ph II Onco franchise, which currently has no oncology candidates.



Source: Ipsen

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4. Servier: strengthens oncology franchise with new mid-stage asset

The 4th player in our selection of "best partners" for TME Pharma is Servier, because of its major investment in oncology. According to a report published at the beginning of 2024 by the EPO (European Patent Office), Servier ranks 3rd in France in terms of national contributions to innovation in the fight against cancer between 2002 and 2021. This ranking takes into account patents filed in the period covered by the report, and highlights Servier's commitment to oncology, and the acceleration since 2018 with the acquisition of the oncology division of Irish laboratory Shire for $2.4bn, which has also enabled the group to penetrate the US market). On April 1, 2021, Servier completed the acquisition of the oncology division of Agios Pharmaceuticals. To date, the portfolio includes 7 drugs available to patients targeting cancers with a high unmet medical need, and a pipeline of 35 R&D projects in January 2024.

Servier's oncology strategy revolves around 3 points:

- Targeting difficult-to-treat cancers such as digestive cancers (gastric cancer, pancreatic cancer, cholangiocarcinoma or rare and aggressive biliary tract cancer), glioma or brain tumor, hematological cancers (acute myeloid leukemia, acute lymphoblastic leukemia, lymphomas) or pediatric cancers.
- Focus on promising, complementary therapeutic approaches, particularly in immuno-oncology and targeted therapies.
- Surround ourselves with multiple areas of expertise through collaborations in healthcare ecosystems at the cutting edge of innovation.

To meet this strategy, Servier allocates 70% of its current R&D budget to oncology. In the solid tumor pipeline, brain tumors stand out in several programs, particularly glioma. GBM is not yet an official priority for Servier, but we can imagine that the Group might be interested in a GBM asset to complement its portfolio of candidates. GBM thus meets the criteria of difficult-to-treat cancers, and NOX-A12 meets the targeted therapy approaches that the Group wishes to develop.

Oncology – solid tumors

Compound / MOA	Project	Therapeutic Area	Territory	Phase	Partner
Vorasidenib	S95032	Solid tumors	Worldwide	PCD 1 2 3	
Ivosidenib	S95031	Solid tumors (new indication)	Worldwide	PCD 1 2 3	
Anti-MET	S95027	Non small Cell Lung Cancer	Worldwide	PCD 1 2 3	
Vorasidenib + pembrolizumab	S95032	Solid tumors	Worldwide	PCD 1/2 3	
Ivosidenib combo	S95031	Solid tumors (new indication)	Worldwide	PCD 1/2 3	
Anti-TIM3 combo	S95018	Solid tumors	Worldwide	PCD 1/2 3	
Anti-CD73 combo	S95024	Solid tumors	Worldwide	PCD 1/2 3	
Anti-PD-L1/4-1BB	S95012	Solid tumors	Worldwide	PCD 1/2 3	pieris
Anti-NKG2A combo	S95029	Solid tumors	Worldwide	PCD 1/2 3	
MAT2A inhibitor	S95035	Solid tumors	Worldwide	PCD 1/2 3	
ND	S95043	Solid tumors	Worldwide	PCD 1 2 3	

Source: Servier

We also note 2 independent points that could play in favor of a Servier/TME Pharma merger:

- The need to move away from the Mediator scandal. In the pursuit of a strategy focused on Oncology, a collaboration with a player like TME Pharma should help renew the Group's image as a key player in the cancer field.
- As with the other 3 players/types of player, the risk/reward is attractive, all the more so for Servier, which is not listed on a stock market, thus limiting exposure to a negative impact on valuation in the event of a negative scenario.

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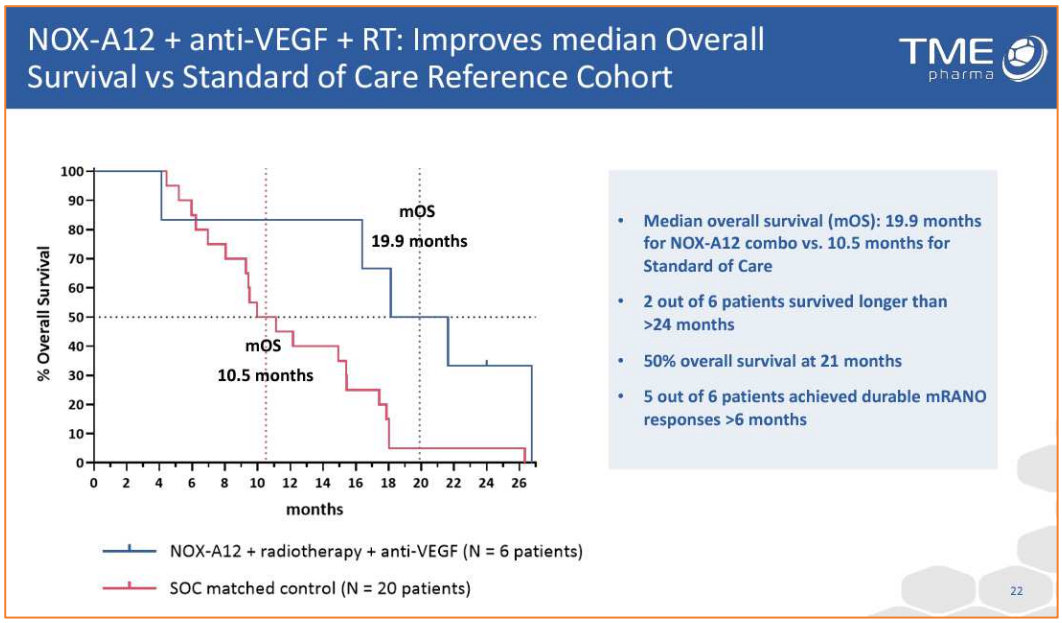
Very attractive package for a player willing to take measured risks

Very promising data at 24-month follow-up in a severe indication

The company announced that of the 6 patients in the cohort receiving the triple combination of NOX-A12/radiotherapy/bevacizumab treated for newly diagnosed and partially resected glioblastoma, 2 were still alive at 24 months' follow-up. This rate compares favorably with the literature with reference treatments showing a 2-year survival rate of only 5% vs. 33% in the TME Pharma trial. Although the figures for TME Pharma were obtained in a non-randomized, uncontrolled trial on a small cohort (n=6), this remains a good indicator of the trend for the triple combination evaluated, and this new result reinforces the data already known in terms of median overall survival (19.9 months vs. 10.5 months in the reference cohort), and in terms of response rate (83% vs. less than 10% with reference treatments). Following the FDA's validation of the protocol for the upcoming Ph II trial in glioblastoma, and the granting of the Fast Track label (enabling potential registration after the end of Ph II if results are positive), the company is now waiting to obtain the necessary funds (through a partnership or by raising funds) to initiate the Ph II trial this year.



Source: TME Pharma

FDA Fast Track designation for NOX-A12 in GBM

Expected at the end of Q1 24, the FDA's decision on Fast Track designation was announced yesterday after market. The Agency has thus decided to grant Fast Track designation in the event of an application for marketing approval in the US based on clinical results to be obtained in the pivotal phase (Ph II or Ph III, depending on the quality of the data and medical need). Thanks to this designation, and given the clinical protocol chosen for Ph II (randomized, controlled study), a registration procedure could be initiated as soon as Ph II is completed, should the results be positive and superior to reference treatments.

The company has now achieved its 2 regulatory objectives: (i) validating the clinical protocol and obtaining the IND for Ph II, and (ii) obtaining Fast Track designation. The next step will be to continue discussions with potential partners, with a view to concluding a collaboration agreement with one of them..

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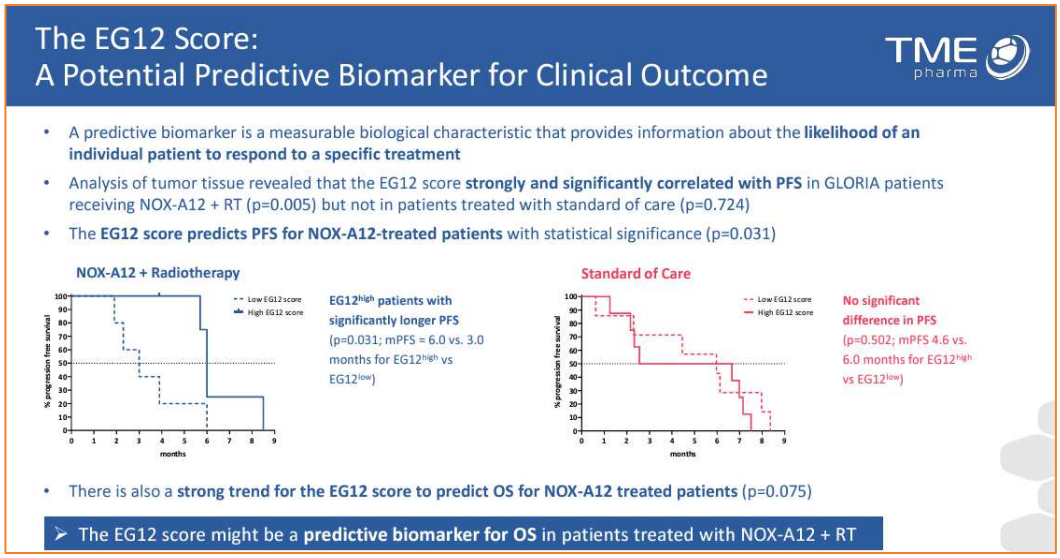
The amounts recently raised (and still to be raised) will primarily serve this business development objective. The company's objective is to present itself as soundly and attractively as possible in order to attract the interest of a potential partner:

- end of debt and convertible bonds financing program,
- obtaining an IND for a randomized, controlled Ph II trial (protocol validated by the FDA),
- Fast Track designation for an accelerated procedure and the possibility of submitting a registration application as soon as Ph II is completed,
- availability of sufficient clinical batches of NOX-A12 to conduct Ph II.

Biomarker development: better opportunities for patients

In parallel with the extremely promising clinical data obtained to date, particularly for the RT/NOX-A12/beva combo, a biological-related work has identified a potential biomarker that could predict the clinical response of brain cancer patients to NOX-A12 treatment. The presence of this specific biomarker is a considerable asset in the patient care pathway, as it should enable prescribers to better screen and select only those patients with a responder profile and who will therefore benefit most from the therapy. This should prevent patients who are unlikely to respond favorably to treatment from losing their chances of success and, ultimately, survival.

In addition, the presence of this predictive biomarker brings another advantage to TME Pharma, as it should encourage evaluators and payers to positively appreciate the availability of an effective therapy with a sensitive companion test, which in theory should increase NOX-A12's chances of regulatory approval and commercial success, while reducing the cost and duration of associated trials (thanks to better stratification and selection of target patients). At present, the company has financial visibility until September 2024. Discussions are underway on additional partnerships and financing options, which have recently been strengthened to ensure the future clinical development of NOX-A12 without recourse to convertible debt financing.



Source: TME Pharma

Beyond GBM: NOX-A12's potential may extend to other indications

Given NOX-A12's mechanism of action (see Appendix 3), its potential field of application in oncology extends beyond GBM. NOX-A12 targets the tumor microenvironment (MET) to overcome the escape strategies put in place by cancer (i) by making the MET permissive to the immune system and (ii) by blocking repair pathways that benefit tumor cells. In fact, NOX-A12 could prove effective in various types of cancer,

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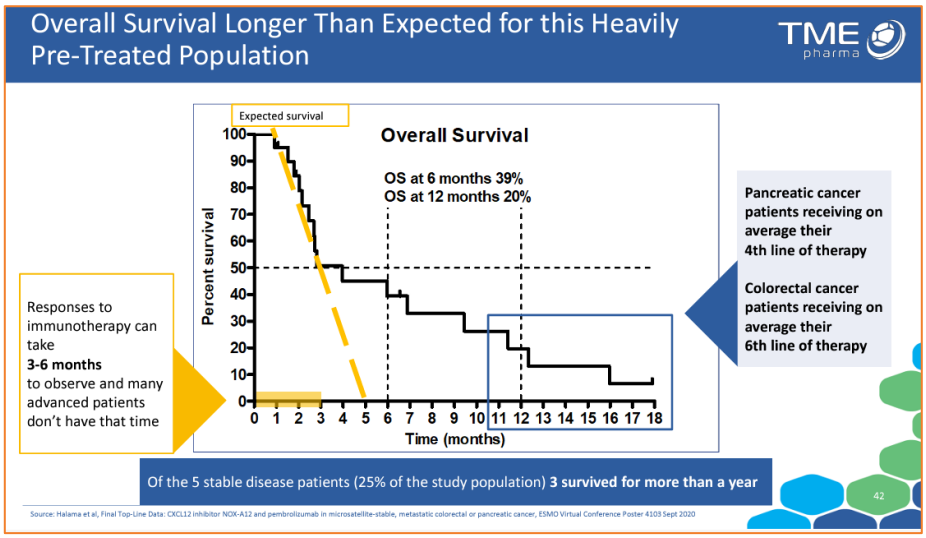
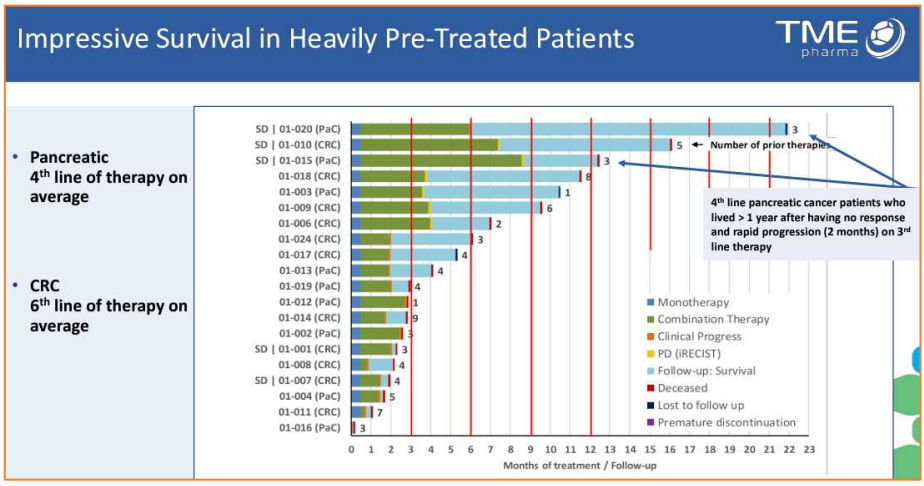
in particular those currently treated by radiotherapy, and also those which suffer from a high medical need because they are not sensitive to currently available solutions.

TME Pharma is exploring 2 other indications in addition to GBM:

- Pancreatic cancer, for which a Ph I/II study has already been successfully completed in combination with Keytruda (provided by Merck MSD). A Ph II trial has been designed to evaluate the combination of NOX-A12 with pembrolizumab +/- gemcitabine/Abraxane® or Onivyde®/5FU/LV in second-line pancreatic cancer. The protocol has been approved by regulators in France and Spain, and by the FDA. The company plans to conduct this trial in partnership, as its current resources do not allow it to consider developments on its own, and priority is currently given to the development of the GBM program in Ph II.
- The Ph I/II program which evaluated NOX-A12 + Keytruda included patients with metastatic colorectal cancer in 6th-line treatment. As these were heavily pre-treated patients with very advanced cancer, it is difficult to comment on the results.





Source: TME Pharma

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BUY opinion reiterated, TP €0.49

We are not changing our assumptions at this stage, as the purpose of this note is to gain a better understanding of the possible options open to TME Pharma in terms of business development.

Given the very promising results obtained with the NOX-A12 + radiotherapy + bevacizumab combination in newly diagnosed glioblastoma, an indication for which bevacizumab outside of a combo with NOX-A12 has failed to demonstrate an impact on OS (vs. near doubling of OS observed in TME Pharma's GLORIA trial), players who hold a bevacizumab antibody in their portfolios seem the most natural partners for TME Pharma.
Roche tops the list, of course, with Avastin, but other players who have developed a beva biosimilar could see this as an interesting market opportunity. We have highlighted a number of arguments in favor of a collaboration, including:

- time-to-market: 4-5 years from eventual commercialization,
- relatively low cost for a manufacturer,
- absence of real competition,
- blockbuster potential in the target GBM market,
- the possibility of extending to other oncology indications.

With financial visibility now extending to the end of 2024, TME Pharma needs to deliver on the BD plan and bring its discussions with various potential partners to a successful conclusion, in order to secure its developments. We believe that the company currently benefits from robust arguments to trigger the interest of a partner, although the clinical results obtained at this stage remain preliminary and "questionable" while awaiting confirmation in a randomized controlled trial. However, the risk/reward ratio remains very attractive, as Big Pharmas are well versed in clinical risk, sensitive to the issue of loss of exclusivity, and keen to achieve growth, especially in a potential blockbuster scenario. Very high amounts are very regularly raised for promising assets that are still in the early clinical or even pre-clinical stage, so the risk seems moderate to us for an asset in the Ph II-ready stage that has shown extremely promising initial efficacy signals, although these still need to be confirmed.

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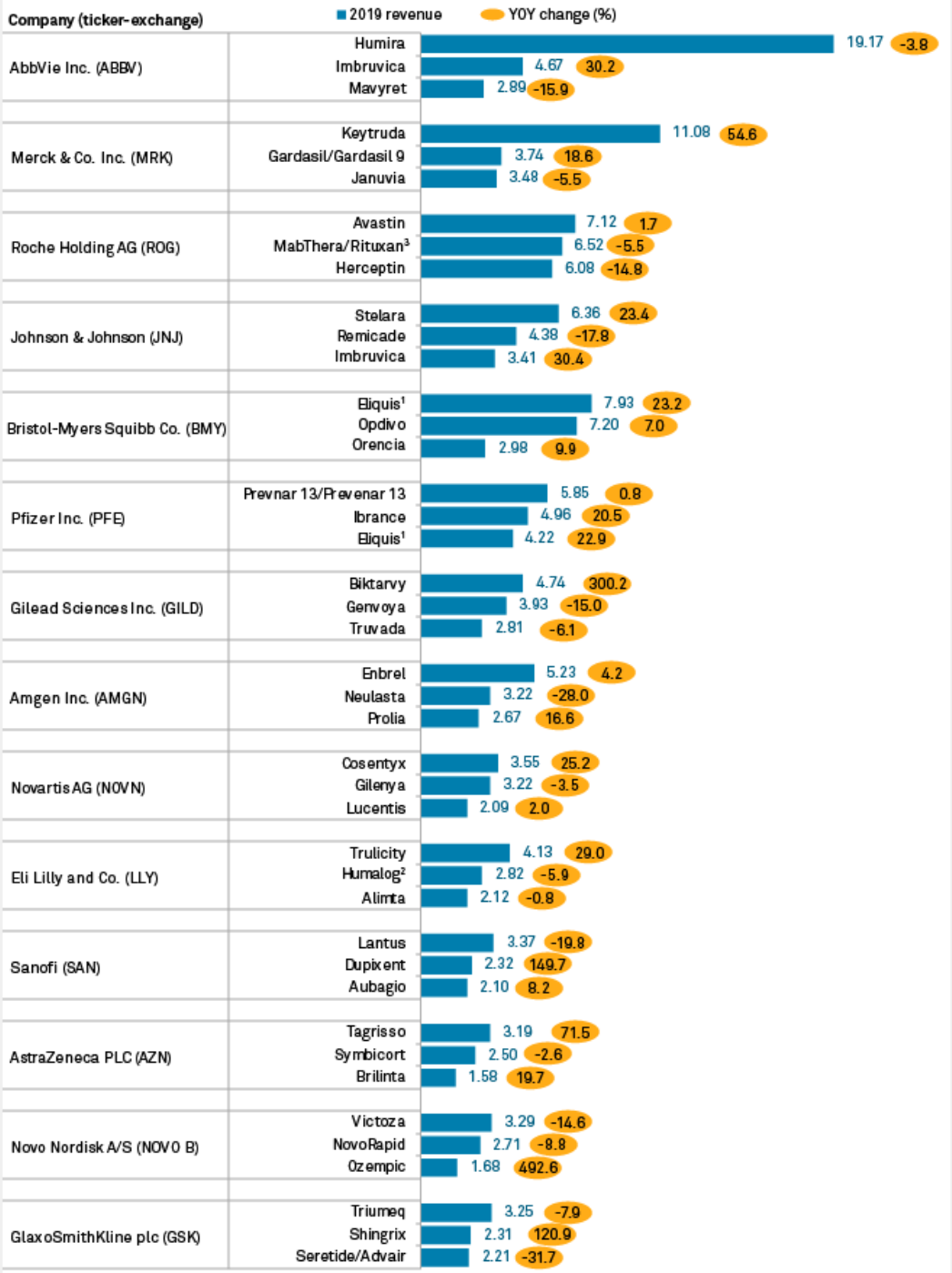
APPENDIX 1

Top three product sales of select pharmaceutical companies in 2019 ($B)



Data compiled March 11, 2020.
Based on SEC Form 10-k, earnings release or other annual reports as of Dec. 31, 2019.
Analysis limited to select large public biotechnology and pharmaceutical companies.
Reported sales not in U.S. dollars used the average exchange rate over the respective reporting period.
[1] Eliquis was jointly developed by Bristol-Myers Squibb Co. and Pfizer Inc., each company reported sales for the drug.
[2] Humalog revenue includes insulin lispro
[3] MabThera/Rituxan figures combine revenues for sales between oncology and immunology.
Source: S&P Global Market Intelligence

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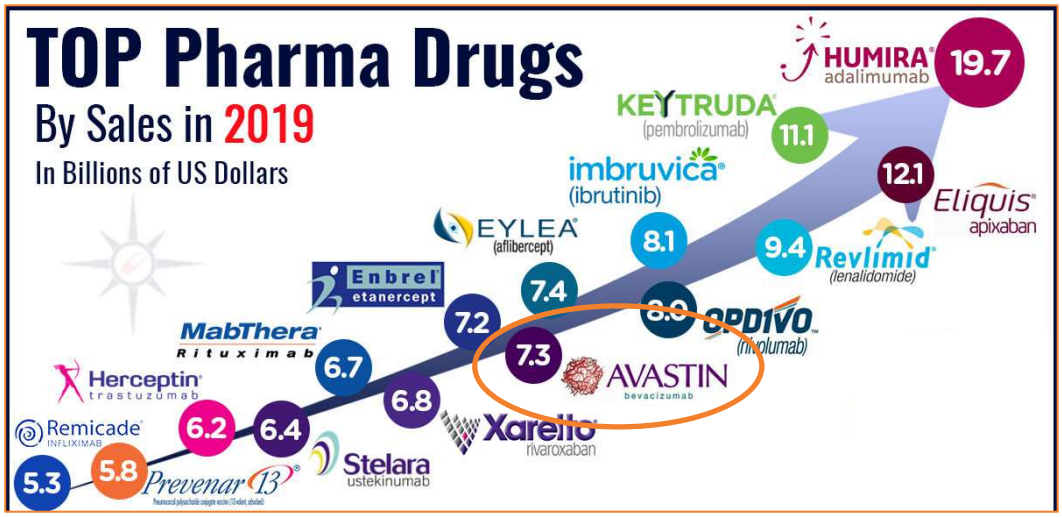
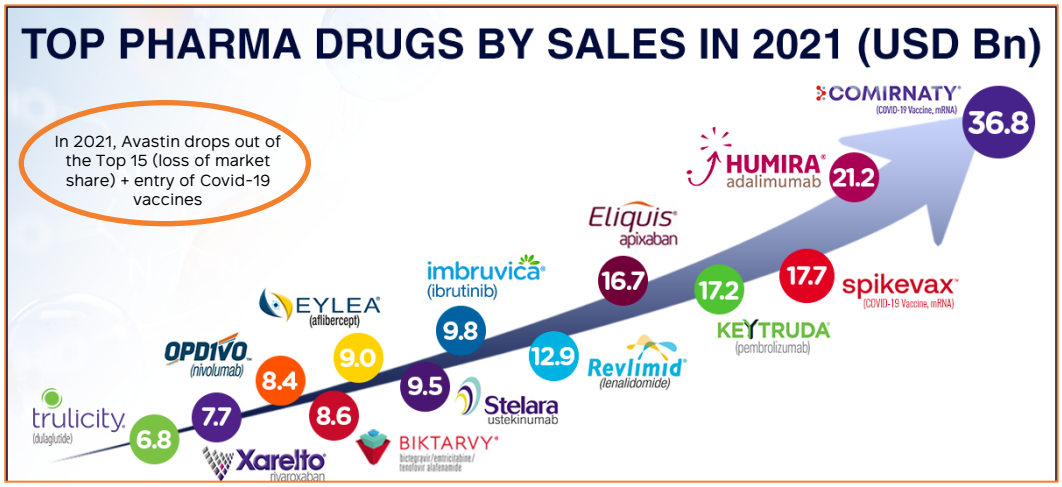
APPENDIX 2





Source: PharmaCompass

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APPENDIX 3

Mecanism of action of NOX-A12 via inhibition of the chemokine CXCL12

NOX-A12 targets CXCL12 (C-X-C Chemokine Ligand 12), a key protein in the chemokine family of intercellular signaling proteins. The role of chemokines is to direct the movement and displacement of cells. In cancer, CXCL12 acts as a communication bridge between tumor cells and their environment (MET = tumor microenvironment). It thus promotes tumor proliferation, the formation of new blood vessels and metastases, as well as inhibiting tumor apoptosis (programmed cell death).

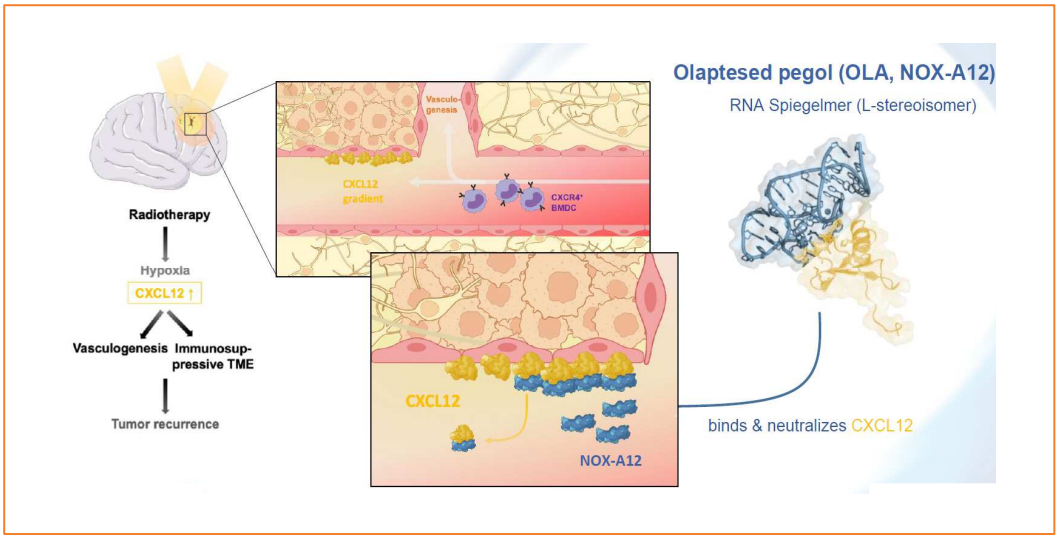
« The mechanism of action of NOX-A12 is to disrupt the activity of CXCL12 chemokines, a key factor in tumor proliferation, by binding to them and inducing their destruction. »

It has now been established that chemokines such as CXCL12 create a permissive MET for tumor growth and metastasis. In fact, they are an important signaling mechanism that enables cancer cells to evade detection by the immune system and anti-cancer treatments. NOXXON's drug candidate, NOX-A12, is unique in its ability to bind to two key sites of chemokine proteins: CXCR4 and CXCR7. The mechanism of action of NOX-A12 is to disrupt the activity of chemokines by binding to these proteins via 2 key sites, and tagging them to induce their destruction.

NOX-A12 is designed to combat solid tumors by modulating MET in two distinct ways:
breaking tumor protection, by allowing immune cells such as effector T cells to penetrate the tumor and unleash the full potential of immuno-oncological approaches such as immune checkpoint inhibitors (ICIs).
inhibit tumor repair, by preventing the attraction of "repair cells" by tumors and the repair of blood vessels damaged by RT, and thus prevent the resumption of tumor growth post-RT.

« NOX-A12 has been designed to combat solid tumors by modulating MET in 2 ways: (i) allowing effector immune cells to reach the tumor, and (ii) preventing tumor cell repair.»

Preclinical studies have shown that CXCL12-mediated influx of highly angiogenic monocytes/macrophages is a key factor in revascularization and tumor growth after GBM RT. Thus, inhibition of CXCL12 by NOX-A12 should have an anti-tumor effect by blocking the pro-tumor effect induced by CXCL12.



Source: SNO 2021

The use of RT induces hypoxia by damaging blood vessels, which provokes a tumor response leading to an increase in CXCL12 levels within irradiated tissue, to promote revascularization and increase oxygen supply. This phenomenon also establishes an immunosuppressive MET that promotes tumor growth. The use of NOX-A12 in parallel with and following RT precisely counteracts these post-RT effects, and avoids the establishment of a MET impermeable to effector immune cells, which promotes the proliferation of cancerous tissue.

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FINANCIAL DATA

Share information	2017	2018	2019	2020	2021	2022	2023e	2024e	2025e
Published EPS (€)	-2,54	-2,70	-0,08	-0,32	-0,21	-6,33	-0,46	-0,26	-0,73
Adjusted EPS (€)	**-2,54**	**-2,70**	**-0,08**	**-0,32**	**-0,21**	**-6,33**	**-0,46**	**-0,26**	**-0,73**
Diff. I.S. vs Consensus	*n.s.*	*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	0,00	1,00	2,00

Valuation ratios	2017	2018	2019	2020	2021	2022	2023e	2024e	2025e
P/E	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
EV/Sales	144,40x	18,58x	24,21x	-21,48x	-27,42x	-47,29x	-22,99x	0,65x	135,12x
EV/Adjusted EBITDA	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
EV/Adjusted EBITA	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Op. FCF bef. WCR yield	n.s.	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.	n.s.
Div. yield (%)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	633,7%

NB : valuation based on annual average price for past exercise

Entreprise Value (€m)	2017	2018	2019	2020	2021	2022	2023e	2024e	2025e
Share price in €	*15,6*	*0,16*	*0,16*	*0,16*	*0,16*	*0,16*	*0,16*	*0,16*	*0,16*
Market cap.	36	7	7	7	7	7	7	7	7
Net Debt	*1,9*	*0,5*	*0,2*	*-9,7*	*-10,6*	*-13,5*	*-9,9*	*-8,5*	*9,3*
Minorities	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*1,0*	*2,0*
Provisions/ near-debt	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*
+/- Adjustments	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*0,0*	*1,0*	*2,0*
Entreprise Value (EV)	**38**	**7**	**7**	**-3**	**-4**	**-7**	**-3**	**0**	**20**

Income statement (€m)	2017	2018	2019	2020	2021	2022	2023e	2024e	2025e
Sales	0	0	0	0	0	0	0	0	0
chg.	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*	*n.s.*
Adjusted EBITDA	-5	-4	-4	-6	-10	-6	-7	-5	-16
adjusted EBITA	**-5**	**-4**	**-4**	**-6**	**-10**	**-6**	**-7**	**-5**	**-16**
chg.	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***
EBIT	-5	-4	-4	-6	-10	-6	-7	-5	-16
Financial result	-1	-6	3	-5	-5	-3	-1	-2	-2
Corp. tax	0	0	0	0	0	0	0	0	0
Minorities+affiliates	0	0	0	0	0	0	0	1	2
Net attributable profit	-5	-11	-1	-10	-15	-10	-8	-5	-16
Adjusted net att. profit	**-5**	**-11**	**-1**	**-10**	**-15**	**-10**	**-8**	**-5**	**-16**
chg.	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***	***n.s.***

Cash flow statement (€m)	2017	2018	2019	2020	2021	2022	2023e	2024e	2025e
EBITDA	-5	-4	-4	-6	-10	-6	-7	-5	-16
Theoretical Tax / EBITA	0	0	0	0	0	0	0	0	0
Capex	0	0	0	0	0	0	0	0	0
Operating FCF bef. WCR	**-5**	**-4**	**-4**	**-6**	**-10**	**-6**	**-7**	**-5**	**-16**
Change in WCR	0	0	0	0	0	0	0	0	0
Operating FCF	**-5**	**-4**	**-3**	**-6**	**-10**	**-6**	**-7**	**-5**	**-16**
Acquisitions/disposals	0	0	0	0	0	0	0	0	0
Capital increase/decrease	3	8	1	14	16	12	4	5	0
Dividends paid	0	0	0	0	0	0	0	0	0
Other adjustments	-1	-6	3	-5	-5	-3	-1	-2	-2
Published Cash-Flow	**-3**	**-3**	**1**	**3**	**1**	**3**	**-4**	**-2**	**-18**

Balance Sheet (€m)	2017	2018	2019	2020	2021	2022	2023e	2024e	2025e
Assets	0	0	0	0	0	0	0	0	0
Intangible assets/GW	0	0	0	0	0	0	0	0	0
WCR	-2	-2	-2	-2	-2	-2	-2	-2	-2
Group equity capital	-4	-3	-2	8	-2	1	-3	-4	-22
Minority shareholders	0	0	0	0	0	0	0	1	2
Provisions	0	0	0	0	0	0	0	0	0
Net financial debt	**2**	**0**	**0**	**-10**	**-11**	**-14**	**-10**	**-8**	**9**

Financial ratios	2017	2018	2019	2020	2021	2022	2023e	2024e	2025e
EBITDA margin	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
EBITA margin	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Adjusted Net Profit/Sales	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
ROCE	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
ROE adjusted	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Gearing	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
ND/EBITDA (in x)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.

Source : company, Invest Securities Estimates

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INVESTMENT CASE

TME PHARMA (ex-NOXXON) is a biotech company with an oncology-focused portfolio. The two products it has developed to date—NOX-A12 (glioblastoma, as well as metastatic pancreatic and colorectal cancer) and NOX-E36 (solid cancers)—are designed to break the tumor protection barrier and block tumor repair by neutralizing chemokines in the tumor microenvironment (TME). Its clinical approach is unique and can be used in combination with other therapeutic approaches, notably radiotherapy and immunotherapy, to weaken tumor defenses against the immune system and enable greater therapeutic impact.

SWOT ANALYSIS

STRENGTHS

- An innovative approach within the IO space
- Promising Ph I/II results in GBM
- Drugs that target indications with little competition

WEAKNESSES

- Relatively early-stage pipeline
- Need for additional financing

OPPORTUNITIES

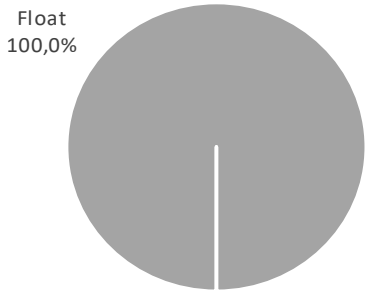
- Combination drug trials
- Possibility of new partnerships
- Significant M&A activity in the field

THREATS

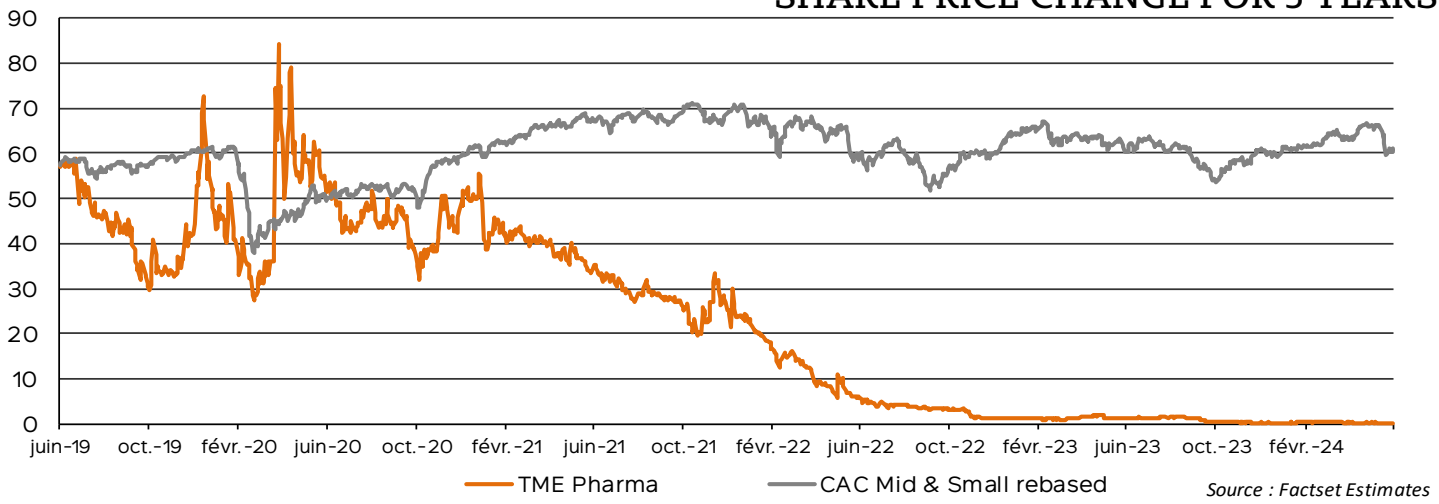
- Regulatory and clinical risks
- Legal risks
- Commercial risks

ADDITIONAL INFORMATION

Shareholders



SHARE PRICE CHANGE FOR 5 YEARS



Source : Factset Estimates

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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

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12-MONTH HISTORY OF OPINION

The table below reflects the history of price recommendation and target changes made by the financial analysis office of Invest Securities over the past 12 months.

Company Name	Main Author	Release Date	Rating	Target Price	Potential
TME PHARMA	Jamila El Bougrini	02-avr.-24	ACHAT	0,61	+94%
TME PHARMA	Jamila El Bougrini	26-févr.-24	ACHAT	0,62	+130%
TME PHARMA	Jamila El Bougrini	13-févr.-24	ACHAT	0,67	+101%
TME PHARMA	Jamila El Bougrini	27-nov.-23	ACHAT	0,4	+36%

DETECTION OF CONFLICTS OF INTEREST

	TME PHARMA
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.	Yes
Invest Securities and the issuer have signed a research service agreement.	Yes
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.

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