CEO MESSAGE H1 2024

Berlin, Germany, July 09, 2024, 06.00 p.m. CEST – TME Pharma N.V. (Euronext Growth Paris: ALTME), a clinical-stage biotechnology company focused on developing novel therapies for treatment of cancer by targeting the tumor microenvironment (TME), released today a message from Aram Mangasarian, CEO of *TME Pharma*, to its shareholders.

Dear Shareholders,

In the first half of 2024, we delivered a series of significant achievements, further strengthening the potential of our lead asset NOX-A12 and positioning *TME Pharma* as a pioneer in glioblastoma treatment, an urgent medical need.

I am pleased to write to you with an update on our progress during what has been a very busy and exciting start to the year, following a year of delivery on our promises including:

- Median survival nearly double, and 21-month survival 10-fold greater, than that of a standard-of-care reference cohort in brain cancer (glioblastoma) patients with chemotherapy-refractory residual tumor after surgery[1]
- Approval of our brain cancer Phase 2 clinical trial design by the US FDA[2]
- Fast Track designation granted by the US FDA for our lead asset, NOX-A12, in glioblastoma[3]
- Publication of NOX-A12 clinical data in the high-profile scientific journal *Nature Communications*[4]
- Complete elimination of convertible debt from the capital structure of the company[5]
- Recruitment of a new US-based board member with highly relevant partnering and M&A experience in the brain cancer space[6]

Constructive Engagement with Strategic Partners and Investors and a Clear Vision for the Future of *TME Pharma*

Based on the successful delivery of these objectives, we are now in discussions with strategic partners and investors interested in the potential of NOX-A12 program. Our goal is to finalize these discussions in the 4th quarter of 2024 before another capital increase is needed. This will allow us to progress towards our future vision for the company of having NOX-A12 approved for use in glioblastoma patients with *TME Pharma* in a strategic partnership with a pharmaceutical company and having support from governmental/charitable organizations and expert biotech investors. Once we can start the planned randomized, controlled Phase 2 clinical trial, we estimate that in approximately 3 years we will have sufficient data to launch a pivotal clinical trial that could lead to approval with positive results.

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[1] *TME Pharma* Press Release on February 2, 2024
[2] *TME Pharma* Press Release on March 5, 2024
[3] *TME Pharma* Press Release on April 2, 2024
[4] *TME Pharma* Press Release on June 17, 2024
[5] *TME Pharma* Press Release on February 9, 2024
[6] *TME Pharma* Press Release on June 27, 2024

Potential for Unprecedented Clinical Benefit in Glioblastoma

In our most significant clinical accomplishment to date, we announced survival data from our GLORIA study obtained in newly diagnosed glioblastoma patients with extremely poor prognosis: tumors resistant to standard chemotherapy plus incomplete surgical resection. The study achieved a remarkable 19.9-month median overall survival (mOS) rate for patients receiving NOX-A12 in combination with the VEGF inhibitor bevacizumab and radiotherapy. This nearly doubles the 10.5-month mOS rate demonstrated in the standard of care matched reference cohort. If this result is confirmed in a larger, randomized clinical trial, it would offer NOX-A12 a clear clinically and commercially relevant advantage over the current standard of care.

Moreover, the NOX-A12 survival results surpass those from what we believe are all relevant competitor therapy trials in newly diagnosed glioblastoma patients resistant to standard chemotherapy[7]. NOX-A12's effectiveness is even more impressive considering the NOX-A12 GLORIA trial enrolled patients with a worse prognosis than those in the competitor trials. The NOX-A12 trial only enrolled patients with residual detectable tumor after surgery whereas competitor trials also included patients with no detectable tumor after surgery, thereby giving the patients in these competitor trials a better expected average survival outcome.

This progress highlights the immense potential of NOX-A12 to transform the treatment of glioblastoma patients, who face a devastating prognosis from this highly aggressive form of brain cancer. With a median overall survival of 8 months, a staggering 93% of patients do not survive beyond five years and the current standard of care offers no cure and only limited survival benefit[8]. This huge unmet medical need demonstrates the importance of our goal to develop NOX-A12 to become part of the best glioblastoma therapy for newly diagnosed patients and make it available to them as fast as we can.

Constructive Interactions with US Regulator

We engaged in discussions with the US Food and Drug Administration (FDA) to establish a clear regulatory roadmap for the next stage of NOX-A12's clinical development and submitted an Investigational New Drug (IND) application for NOX-A12 in glioblastoma. This IND was approved by the FDA, paving the way for a new randomized, controlled Phase 2 clinical study. Randomized clinical trial data are a key benchmark for big pharmaceutical companies and later-stage cancer assets command higher valuations for milestone payments and in transactions, on average, so it is crucial for us to advance NOX-A12 into this Phase 2 evaluation.

Following the IND approval, NOX-A12 was also granted Fast Track designation by the US FDA. This designation, a second key regulatory milestone, aims to facilitate the development and expedite the review of drugs addressing serious conditions like glioblastoma. Fast Track designation allows for more frequent interactions with the FDA throughout the clinical development phase, enabling *TME Pharma* to optimize the design of the Phase 2 study and potentially accelerated timelines. It also means we have the potential to qualify for "accelerated approval" and "priority review" if NOX-A12 meets the relevant criteria.

We perceive the achievement of these two key regulatory milestones as the FDA's recognition not only of the urgent unmet medical need which glioblastoma represents, but also the potential of NOX-A12 to address it. This paves the way to accelerate NOX-A12's route to market and to de-risk its development, while providing investors and potential partners with a clear development pathway for NOX-A12. The open IND will allow us to expand our clinical development in the US, the most financially

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[7] *TME Pharma* Press Release on September 13, 2023

[8] Central Brain Tumor Registry of the United States (CBTRUS) Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2016-2020

important market for new pharmaceuticals[9], where we anticipate significant interest from the medical community.

Funding Phase 2 Clinical Trial and Managerial Engagement
In our trial design and planning, we have been implementing strategies to optimize timelines and reduce costs of our glioblastoma program overall. Sufficient supply of NOX-A12 is available to initiate the trial quickly upon closing the funding gap. We continue discussions with engaged stakeholders and are pursuing funding options through a combination of non-dilutive grant funding, a strategic alliance and/or investment from expert institutional investors, with the objective to materialize these interactions in Q4-2024.

As we work to secure the Phase 2 trial financing, we have cleaned up our balance sheet removing all convertible debt instruments and recently announced a cash runway extension to year-end. To highlight my confidence in our mission, I personally invested in the company subscribing to more than 500,000 new shares since December 2023[10].

I would like to thank all of you, our shareholders, for your continued commitment and support of our efforts. After having achieved all our recent clinical, regulatory, and financial targets we remain focused on delivering our main mission: to bring NOX-A12 to market as quickly as possible to offer a solution to patients affected by a devastating disease, glioblastoma.

Yours sincerely,

Aram Mangasarian
CEO, TME Pharma
July 9th, 2024

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[9] European Federation of Pharmaceutical Industries and Associations: the-pharmaceutical-industry-in-figures-2024.pdf (efpia.eu)
[10] See Managers Transactions for A. Mangasarian from: December 5, 2023, and February 8 and 12, 2024.

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About TME Pharma

TME Pharma is a clinical-stage company focused on developing novel therapies for treatment of the most aggressive cancers. The company's oncology-focused pipeline is designed to act on the tumor microenvironment (TME) and the cancer immunity cycle by breaking tumor protection barriers against the immune system and blocking tumor repair. By neutralizing chemokines in the TME, *TME Pharma's* approach works in combination with other forms of treatment to weaken tumor defenses and enable greater therapeutic impact. In the GLORIA Phase 1/2 clinical trial, *TME Pharma* is studying its lead drug candidate NOX-A12 in newly diagnosed brain cancer patients who will not benefit clinically from standard chemotherapy. *TME Pharma* has delivered top-line data from the NOX-A12 three dose-escalation cohorts combined with radiotherapy of the GLORIA clinical trial, observing consistent tumor reductions and objective tumor responses. Additionally, GLORIA expansion arms evaluate safety and efficacy of NOX-A12 in other combinations where the interim results from the triple combination of NOX-A12, radiotherapy and bevacizumab suggest even deeper and more durable responses, and improved survival. US FDA has approved the design of a randomized Phase 2 trial in glioblastoma and *TME Pharma* was awarded fast track designation by the FDA for NOX-A12 in combination with radiotherapy and bevacizumab for use in the treatment of the aggressive adult brain cancer, glioblastoma. NOX-A12 in combination with radiotherapy had also previously received orphan drug designation (ODD) for glioblastoma in the United States and glioma in Europe. *TME Pharma* has delivered final top-line data with encouraging overall survival and safety profile from its NOX-A12 combination trial with Keytruda® in metastatic colorectal and pancreatic cancer patients, which was published in the Journal for ImmunoTherapy of Cancer in October 2021. The company has entered in its second collaboration with MSD/Merck for its Phase 2 study, OPTIMUS, to further evaluate safety and efficacy of NOX-A12 in combination with Merck's Keytruda® and two different chemotherapy regimens as second-line therapy in patients with metastatic pancreatic cancer. The design of the trial has been approved in France, Spain and the United States. The company's second clinical-stage drug candidate, NOX-E36, is designed to target the innate immune system. *TME Pharma* is considering several solid tumors for further clinical development. Further information can be found at: www.tmepharma.com.

Visit *TME Pharma* on LinkedIn and X.

About the GLORIA Study

GLORIA (NCT04121455) is *TME Pharma's* dose-escalation, Phase 1/2 study of NOX-A12 in combination with radiotherapy in first-line partially resected or unresected glioblastoma (brain cancer) patients with unmethylated MGMT promoter (resistant to standard chemotherapy). GLORIA further evaluates

safety and efficacy of NOX-A12 three additional arms combining NOX-A12 with: A. radiotherapy in patients with complete tumor resection; B. radiotherapy and bevacizumab; and C. radiotherapy and pembrolizumab.

About the OPTIMUS Study

OPTIMUS (NCT04901741) is *TME Pharma's* planned open-label two-arm Phase 2 study of NOX-A12 combined with pembrolizumab and nanoliposomal irinotecan/5-FU/leucovorin or gemcitabine/nab-paclitaxel in microsatellite-stable metastatic pancreatic cancer patients.

Disclaimer

Translations of any press release into languages other than English are intended solely as a convenience to the non-English-reading audience. The company has attempted to provide an accurate translation of the original text in English, but due to the nuances in translating into another language, slight differences may exist. This press release includes certain disclosures that contain "forward-looking statements." Forward-looking statements are based on *TME Pharma's* current expectations and are subject to inherent uncertainties, risks and assumptions that are difficult to predict. Factors that could cause actual results to differ include, but are not limited to, the risks inherent in oncology drug development, including clinical trials and the timing of and *TME Pharma's* ability to obtain regulatory approvals for NOX-A12 as well as any other drug candidates. Forward-looking statements contained in this announcement are made as of this date, and *TME Pharma* undertakes no duty to update such information except as required under applicable law.