TME PHARMA REPORTS H1 2024 FINANCIAL RESULTS AND PROVIDES BUSINESS AND CLINICAL UPDATE

- **Statistically significant survival benefit of NOX-A12 + bevacizumab + radiotherapy for glioblastoma patients compared to both standard of care and NOX-A12 + radiotherapy demonstrated by latest NOX-A12 clinical data analysis presented at ESMO 2024**
- **Active discussions with potential strategic industrial partners and governmental institutions to out-license NOX-A12 and secure non-dilutive support for the upcoming clinical trial**
- **Ongoing activities to externalize development of NOX-E36 with high potential in numerous ophthalmologic indications**
- **Financial visibility for the company extended by one month into January 2025**

Berlin, Germany, October 18, 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), announces its financial results for the six months ending June 30, 2024, and provides business and clinical highlights and an outlook for the rest of the year.

Aram Mangasarian, CEO of TME Pharma commented: *"2024 has been a highly productive year for* TME Pharma *marked by a series of important clinical, regulatory and financial achievements, that fully demonstrate our capabilities and potential to investors. The latest analysis of GLORIA clinical data showcased at this year's ESMO Congress highlighted the statistically significant benefit of NOX-A12 combined with bevacizumab and radiotherapy in glioblastoma patients when compared not only to the standard of care, but also to NOX-A12 combined with radiotherapy alone. Our extensive preclinical and clinical data package for NOX-A12 led to the FDA clearance of our IND application for a Phase 2 study and granting of Fast Track designation, substantially clarifying NOX-A12's path to market. Our Phase 2 preparations are underway, and we are in active discussions to secure the required funding. It is our firm belief that that further validation of NOX-A12's survival benefit through additional data will catalyze significant interest from the pharmaceutical industry, offering licensing and partnering opportunities and increasing value creation for our shareholders. Furthermore, we have made great progress in developing the spin-out opportunity for NOX-E36. We believe that its anti-fibrotic properties make it potentially applicable to a large number of ophthalmologic conditions, including glaucoma surgery, diabetic retinopathy, and both wet and dry forms of age-related macular, which offer a much larger market."*

Business and Clinical Highlights

Potential for Unprecedented Clinical Benefit in Glioblastoma

The GLORIA NOX-A12 clinical trial has achieved exceptional clinical results in newly diagnosed glioblastoma patients with extremely poor prognosis that have tumors resistant to standard chemotherapy plus incomplete surgical resection showing potential benefit as a therapy for glioblastoma.

- 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 doubles the 9.5-month mOS rate demonstrated in the standard of care matched reference cohort, as presented by Dr. Frank Giordano, the lead investigator of the clinical trial, at the European Society for Medical Oncology (ESMO) conference in September 2024. The ESMO presentation further revealed statistically significant improvement in survival for this triple combination (NOX-A12 + bevacizumab + radiotherapy) over standard of care reference cohort as well as NOX-A12 + radiotherapy alone.
- Analysis of the competitive landscape has shown that the NOX-A12 survival results surpass those from what *TME Pharma* believes are all relevant therapy trials in newly diagnosed glioblastoma patients resistant to standard chemotherapy. 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, i.e. patients that would be expected to have a better 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.

Clear Path for Phase 2 Clinical Development with Open IND and Fast Track Designation Awarded by US FDA, and Protocol Approved in Germany

TME Pharma engaged in discussions with the US Food and Drug Administration (FDA) in late 2023 to establish a clear regulatory roadmap for the next stage of NOX-A12's clinical development.

- The FDA cleared in March 2024 *TME Pharma*'s Investigational New Drug (IND) application on the basis of the protocol for a randomized, controlled Phase 2 clinical trial in glioblastoma, allowing the company to expand clinical development in the US. Subsequently, the Federal Institute for Drugs and Medical Devices (BfArM, *Bundesinstitut für Arzneimittel und Medizinprodukte*) has also approved the protocol, enabling the company to conduct Phase 2 study in Germany.
- NOX-A12 was also granted Fast Track designation by the US FDA. This designation aims to facilitate the development and expedite the review of drugs addressing serious conditions like glioblastoma. Companies whose programs are granted Fast Track Designation can benefit from more frequent interactions with the FDA during the clinical development process, and thus potentially accelerated timelines.

TME Pharma perceives 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 while providing investors and potential partners with a clear development pathway for NOX-A12.

Publication of Data from the GLORIA Study in Nature Communications

The research by Dr. Frank Giordano at the University Medical Center Mannheim and members of the five other centers in Germany led by a translational research team at the University of Bonn on a potential predictive biomarker, the "EG12 score", was published in the high-impact peer-reviewed journal, *Nature Communications*.

- The article highlights that the presence of NOX-A12's target in tumor tissue can be used as a biomarker to predict the success of treatment with NOX-A12 and radiotherapy in glioblastoma patients.
- The EG12 biomarker's predictive character provides robust evidence of NOX-A12's mechanism of action.

- Tumor tissue analysis revealed that patients with higher biomarker scores show superior clinical efficacy when treated with NOX-A12 + radiotherapy than patients with low biomarker scores.
- The EG12 score is calculated by analyzing the frequency of positivity for NOX-A12's target, CXCL12, on two key cell types in the glioblastoma tumor microenvironment: endothelial (E) and glioma (G) cells.

H1 2024 Financial Highlights

For the reporting period, the Group – *TME Pharma N.V.*, *TME Pharma AG* and *TME Pharma Inc.* – has not generated any revenues. The Group, like most pre-commercial biotech companies, does not expect any revenues to be generated from any product candidates that it develops until the Group either signs a licensing or collaboration agreement or obtains regulatory approval and commercializes its compounds.

Research and development (R&D) expenses decreased by 16% in H1 2024 over the same period last year. This reduction is primarily due to the GLORIA trial of NOX-A12 in brain cancer nearing completion, which required lower costs while at the same time generating more mature data. As a result, *TME Pharma* was able to decrease drug manufacturing costs, service fees and other costs related to the clinical trials and preclinical testing, in addition to lower personnel expenses, patent costs and consulting services, partly offset by higher other research and administrative expenses.

General and administrative (G&A) expenses increased by 12% in H1 2024, mainly driven by higher legal, consulting and audit fees in connection with the financing transactions in the first six months of 2024. The net loss for H1 2024 decreased by 11% compared to the prior year period.

Capital Raised in H1 2024

The company raised €5 million (gross) through multiple financial transactions in the first half of 2024.

- The successful €1.48 million (gross) private placement with a group of new investors closed in February 2024 was intended for buyback of outstanding convertible debt and allowed the company to redeem all of the outstanding convertible bonds held by Atlas Special Opportunities (ASO) at that time. The event marked the end of *TME Pharma*'s convertible bond financing program with ASO.
- *TME Pharma* successfully completed a capital raise in June 2024 for a total consideration of €2.35 million (gross) through a private placement with professional investors and a public offering to retail investors in France via the PrimaryBid platform.
- In addition, the company raised €1.2 million (gross) through Warrants Y and Z exercises during the first half-year 2024, resulting from the preferential rights issue launched in November 2023. Subsequent to the reporting period, the exercise of Warrants Z, settled in September 2024, resulted in the issuance of 1,940 new shares for gross proceeds of €0.4 thousand. Outstanding 2,811,080 Warrants Z have potential to raise an additional €0.7 million if exercised in full before the end of the final exercise period in June 2025.

TME Pharma has focused its financial resources on achieving its primary goal of generating mature overall survival data in the GLORIA trial of NOX-A12 in brain cancer and creating an attractive clinical and regulatory package to enable initiation of Phase 2 trial. With the trial now nearing completion, *TME Pharma* will assess how and where to deploy the Group's available financial resources to maximize the chances of NOX-A12 reaching the market.

Considering cash and cash equivalents of €2.7 million as of June 30, 2024, *TME Pharma* has financial visibility into January 2025.

Outlook for the Remainder of 2024 and for 2025

NOX-A12 Clinical Development Plans in Glioblastoma

TME Pharma has achieved significant regulatory milestones in advancing the NOX-A12 glioblastoma program to the next phase of clinical development, having received approval for the Phase 2 study protocol from both the FDA in the US and BfArM in Germany. *TME Pharma*'s next milestones in the clinical development of the NOX-A12 program are financing and initiation of the randomized, controlled Phase 2 clinical trial. With clinical trial preparations underway and sufficient supply of NOX-A12 available, the clinical trial can be launched rapidly upon closing of the funding gap. The company is actively engaged in discussions with potential strategic industrial partners and governmental institutions to out-license NOX-A12 and secure non-dilutive support for the upcoming clinical trial.

NCI's Presentation of NOX-A12 Pre-Clinical Research at SNO

The Society for Neuro-Oncology (SNO) Annual Meeting in November 2024 will feature a poster presentation highlighting data from preclinical studies conducted at the U.S. National Cancer Institute (NCI) exploring the effects of inhibition of CXCL12 by NOX-A12 in combination with immune checkpoint inhibition in glioblastoma models. The research was conducted at the NCI under the material transfer agreement established with *TME Pharma* in June 2022 to explore the effects of *TME Pharma*'s CXCL12 inhibitor NOX-A12 in brain tumors.

Clinical development plans for NOX-E36

While *TME Pharma* has largely focused its available resources on NOX-A12 during recent years, *TME Pharma* also has a second clinical-stage asset, NOX-E36. While limited resources have been employed behind NOX-E36 over the last two years, it presents a very promising opportunity for development in eye diseases with a high need for well-tolerated therapies with anti-fibrotic effect. The anti-fibrotic mode of action of NOX-E36 has already been demonstrated in a relevant animal model published by researchers at the Singapore Eye Research Institute (SERI), and *TME Pharma* believes that development in ophthalmological indications could be a promising opportunity to diversify its project portfolio. For these reasons, *TME Pharma* has engaged in discussions with multiple players and institutions specialized in ophthalmology to develop NOX-E36 in the clinic with minimal or no financial contribution from *TME Pharma*, yet leaving a potential commercial success as potential upside to *TME Pharma*'s investors.

The Group will carefully monitor its available cash and calibrate additional financings through available sources in order to ensure its ability to complete its ongoing trial and pursue financing of its future clinical development plans in brain cancer and, to the extent deemed appropriate, maintain a sufficient cash runway, yet minimize shareholder dilution whenever possible.

The Half-Year Financial Report 2024 can be downloaded from the *TME Pharma* website.

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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.

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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 in the expansion arm in which NOX-A12 is combined with radiotherapy and bevacizumab.

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

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