TME PHARMA PUBLISHES 2024 FINANCIAL RESULTS AND PROVIDES OPERATING UPDATE

- **Total €7.6 million raised through multiple transactions**
- **All convertible debt instruments removed from balance sheet during 2024**
- **Commitment to lean cost structure while focusing on completing strategic goals**
- **Next clinical development steps for NOX-A12 validated by regulators**
- **Pursuit of several transaction structures in parallel for the company's drug candidates**

Berlin, Germany, April 25, 2025, 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 today its financial results for the fiscal year ending December 31, 2024, and provides a business update.

The Annual Report 2024, as approved by the management and supervisory boards on April 24, 2025, is available on *TME Pharma's* website (www.tmepharma.com).

*"*TME Pharma *achieved a number of significant clinical and regulatory milestones in 2024 and, as 2025 progresses, we remain committed to advancing the key initiatives that make up our strategic roadmap,"* said **Aram Mangasarian, CEO of TME Pharma.** *"While strategic partnerships cannot be precisely timed, some of our discussions with potential partners and investors regarding strategic transactions for both NOX-A12 and NOX-E36 have been constructive. The regulatory validation of NOX-A12's Phase 2 randomized, controlled study design in glioblastoma by authorities in the US and Germany represented a key step in defining the clinical development pathway. Additionally, we have made important progress on getting NOX-E36 ready for clinical development in ophthalmic indications supported by promising preclinical data. While we pursue these clinical and strategic goals, we are also proactively preparing for contingencies to ensure operational continuity. Should strategic transactions not materialize by mid-2025, we will be ready to transition to a fully virtual and outsourced organizational structure, which would allow us to minimize costs while continuing to engage with industrial partners and investors to advance our clinical programs. By leveraging this flexible setup, we aim to preserve value for our shareholders."*

Business and Clinical Highlights for 2024 and 2025 Year-to-Date

Brain Cancer (Glioblastoma) – Unprecedented Clinical Benefit

Glioblastoma is a highly aggressive and deadly form of brain cancer in which *TME Pharma's* lead asset NOX-A12 has generated unprecedented clinical benefit in the GLORIA Phase 1/2 study. Newly diagnosed patients with glioblastoma tumors resistant to standard of care chemotherapy (MGMT unmethylated) and that are not amenable to complete surgical removal face a devastating prognosis of median overall survival (mOS) of approx. 10 months on standard of care. The development of effective treatments for these patients – *TME Pharma's* target population in the GLORIA trial – is particularly challenging since these tumors tend to be more aggressive and less responsive to current

therapies. Despite these unfavorable factors for the patients, *TME Pharma's* development program of its lead asset, the CXCL12 inhibitor NOX-A12, suggests a strong signal of clinical benefit in this patient population.

In early March 2024, the Food and Drug Administration (FDA) cleared *TME Pharma's* Investigational New Drug (IND) application on the basis of the protocol for its upcoming randomized Phase 2 trial in glioblastoma. Furthermore, in early April 2024, the company announced that the US FDA had granted Fast Track Designation for NOX-A12, in combination with radiotherapy and bevacizumab for newly diagnosed glioblastoma patients with chemotherapy-resistant disease and measurable tumor remaining after surgery.

Near-final efficacy data on glioblastoma patients treated with NOX-A12 combined with anti-VEGF and radiotherapy were presented by the lead investigator of the clinical trial, Dr. Frank Giordano, at a high-profile international cancer conference – the European Society for Medical Oncology (ESMO) Congress in September 2024 – revealing statistically significant improvement in survival for this triple combination over a standard of care reference cohort as well as NOX-A12 + radiotherapy alone (without anti-VEGF). The final median overall survival of the GLORIA 1/2 trial of the arm combining NOX-A12 with radiotherapy and bevacizumab achieved a remarkable 19.9 months. This exceeds what the company believes to be all relevant competitor studies conducted in the US or EU involving newly diagnosed, chemotherapy-resistant (MGMT unmethylated) glioblastoma patients.

<u>Promising New Opportunities for NOX-E36 in Ophthalmology</u>

TME Pharma's second clinical stage asset, the CCL2 inhibitor NOX-E36, previously completed four clinical trials and has already been administered to 175 human subjects. While in an oncology setting NOX-E36 targets the tumor microenvironment by modifying the innate immune system, it has also demonstrated significant potential in addressing unmet medical need in ophthalmic diseases affected by scarring (fibrosis) and inflammation.

The anti-fibrotic mode of action of NOX-E36 has already been demonstrated in a relevant animal model, and the company believes that development in ophthalmological indications could be a promising opportunity to diversify its project portfolio. The company is pursuing resource-efficient possibilities to perform clinical studies such as investigator-initiated trials (IIT) funded and performed by research institutes, with *TME Pharma* supplying the drug. In parallel, *TME Pharma* is discussing with potential partners and venture capital firms the best way to develop NOX-E36 in the ophthalmology space with minimal or no financial contribution from *TME Pharma's* shareholders.

TME Pharma has been collaborating with the Singapore Eye Research Institute (SERI) for several years and recent data from preclinical studies by SERI was selected for poster presentation at the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting in May 2025. The preclinical data show that mNOX-E36 offers a more favorable safety profile than standard of care mitomycin C (MMC), while demonstrating comparable efficacy in reducing post-operative inflammation and scarring (fibrosis) following glaucoma filtration surgery, a common procedure to reduce intraocular pressure. Unlike MMC, mNOX-E36 does not destroy blood vessels in the conjunctiva, potentially overcoming the substantial toxicity seen with MMC, which is a key limitation of this current standard treatment. Fibrosis and inflammation are also significant causes of treatment failure in back-of-the-eye indications, such as age-related macular degeneration and proliferative diabetic retinopathy. *TME Pharma* believes that anti-CCL2 therapy with NOX-E36 offers a novel therapeutic approach to address these issues and potential to access larger markets.

Due to these new findings and other unpublished data, *TME Pharma* and SERI have filed patent applications covering use of NOX-E36 in glaucoma filtration surgery and other ophthalmic diseases to support its development through a license to an industrial partner or the creation of a new corporate entity.

Post-Period Event – AI-Driven Drug Discovery

In January 2025, *TME Pharma* announced a partnership with *aimed analytics*, a cutting-edge data analytics company, to enhance *TME Pharma's* capabilities to leverage artificial intelligence (AI) in drug discovery and optimization. The goal of the collaboration is to use AI to create new and improved drug candidates with accelerated timelines and without the need for resource-intensive laboratory testing. The collaboration should also strengthen *TME Pharma's* corporate profile for strategic transactions and reinforce ongoing partnering discussions.

2024 Financial Summary

TME Pharma successfully strengthened its balance sheet by raising €7.6 million (gross) in 2024. Considering cash and cash equivalents of €3.2 million as of December 31, 2024, *TME Pharma* has financial visibility into June 2025.

As in prior years, *TME Pharma* has not generated any revenues. The Group – *TME Pharma N.V., TME Pharma AG* and *TME Pharma Inc.* – does not expect to generate any revenues from any product candidates that it develops until the Group either signs a licensing agreement or obtains regulatory approval and commercializes its products or enters into collaborative agreements with third parties and relies on dilutive and non-dilutive financing until it reaches profitability.

Research and development (R&D) expenses decreased 13% from K€ 2,652 in the fiscal year (FY) 2023 to K€ 2,296 in the FY 2024. The decrease in research and development expenses in 2024 compared to 2023 is primarily due to the clinical trial of NOX-A12 in brain cancer nearing completion, which required lower costs while at the same time generating more mature data. The pancreatic cancer clinical trial phase 2 protocol which has been approved by the FDA in the US has not been initiated, thereby keeping ongoing costs related to this clinical trial minimal. 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 decreased from K€ 2,989 in the FY 2023 to K€ 2,981 in the FY 2024. The decrease in G&A expenses in 2024 compared to 2023 is mainly driven by lower personnel expenses as well as lower public and investor relations expenses and other expenses, partly offset by higher legal, consulting and audit fees in connection with the financing transactions in 2024. Other general and administrative expenses comprise mainly of depreciation of rights of use assets and equipment, supervisory board remuneration, insurance premium, and ancillary leasing costs.

The finance income in the FY 2024 and 2023 was non-cash finance income. Finance income decreased from K€ 399 in the FY 2023 to K€ 32 in the FY 2024 as a result of ending the Atlas convertible bonds financing facility with Atlas Special Opportunities LLC (ASO). Finance income in 2024 mainly resulted from fair value adjustments of detachable warrants (ABSA Warrants) issued in connection with the

preferential rights issue. In 2023, finance income of K€ 237 resulted from the derecognition of conversion rights in connection with the ASO financing upon conversion and redemption of the bonds and of K€ 162 fair value adjustments of ABSA Warrants issued in connection with the preferential rights issue.

Finance cost decreased from K€ 1,518 in the FY 2023 to K€ 503 in the FY 2024 as a result of ending the Atlas convertible bonds financing facility with ASO. Finance cost in the FY 2024 and 2023 was non-cash finance cost, except for transaction costs of K€ 16 in 2024 and K€ 4 in 2023 borne by the company in conjunction with the exercise of ABSA Warrants (in 2024) and the issuance of Atlas convertible bonds (in 2023) as well as K€ 2 in 2024 and K€ 13 in 2023 relating to interest expense for lease liabilities. Finance cost in the FY 2024 of K€ 489 relate to the initial recognition of ABSA Warrants amounting to K€ 113 as well as losses of K€ 376 from exercises of such warrants. Finance cost in the FY 2023 of K€ 1,505 relate to the ASO facility (contractually entered into in 2020 and ended in 2023, except for outstanding convertible bonds that were fully redeemed in cash in the FY 2024) and comprise losses on initial recognition of convertible bonds, conversion losses, conversion right derivatives, interest in exchange for the lock-up of convertible bonds issued and outstanding as well as transaction costs.

As a result of these factors, *TME Pharma N.V.* reports a net loss for FY 2024 of K€ 5,722 compared to K€ 6,736 in the FY 2023, a decrease of 15%.

Outlook for 2025

TME Pharma's strategic focus for 2025 centers on maximizing the value of its clinical-stage assets, NOX-A12 and NOX-E36, through strategic partnerships, licensing agreements, and potential M&A. The company is pursuing these opportunities while maintaining a lean cost structure and actively preparing for a contingency plan involving a fully outsourced organizational structure, should targeted financing or strategic transactions not materialize by June 2025.

<u>NOX-A12 in Glioblastoma</u>

Given the unprecedented clinical data and clear regulatory pathway, *TME Pharma* has strategically prioritized the development of NOX-A12 in first-line, chemotherapy resistant glioblastoma since the company believes this indication offers the fastest path to regulatory approval for NOX-A12 in the solid tumor space.

The partnering package for NOX-A12 in glioblastoma is particularly attractive due to:

- **Significant Clinical Benefit**: Statistically significant improvement in survival for NOX-A12 with radiotherapy and anti-VEGF bevacizumab compared to both the standard of care reference cohort (p=0.003) and the cohort treated with NOX-A12 and radiotherapy alone (p=0.021).
- **Regulatory Validation:** A clear regulatory pathway with a Phase 2 design approved by the US FDA and the German BfArM and enhanced regulatory interactions with Fast-Track status granted by the FDA in the US and Orphan Drug Designations granted in the US and EU.
- **Commercial Protection:** Commercial protection provided by the Orphan Drug Designations and potentially also by the patent application filed in 2022 covering the NOX-A12, radiotherapy and bevacizumab combination, which would provide cover into the 2040s if granted.

- **Non-dilutive Funding:** Non-dilutive financial support of more than €7 million pledged for the approved Phase 2 trial once it is initiated, including a €2.4 million grant from the German federal government.
- **Trial Readiness:** Clinical trial grade (GMP) NOX-A12 sufficient to rapidly initiate the approved Phase 2 trial at the six centers already open in Germany.

NOX-E36 in Ophthalmology

TME Pharma recognizing NOX-E36 potential in ophthalmology has chosen to collaborate with the Singapore Eye Research Institute (SERI) to maximize efficiency and minimize required resources for further development of the asset.

The NOX-E36 program is poised for rapid advancement into the clinic on the basis of:

- **Strong Scientific Rationale:** Compelling preclinical proof-of-concept and clinical data supporting CCL2 as a valid target.
- **Funding Opportunities:** Funding for Phase 1b study potentially available through grants accessible to SERI
- **IP Protection:** Joint patent applications filed for the use of NOX-E36 in eye diseases in March 2025.
- **Drug Availability:** GMP drug supply manufactured and ready to use pending local ocular toxicity bridging for subconjunctival administration, ensuring a smooth transition to clinic.
- **Established Safety Profile:** Excellent systemic safety and tolerability and dose-dependent pharmacologic activity established in 175 human subjects across previous clinical trials.

As part of its most recent business planning *TME Pharma* is pursuing several transaction structures in parallel for its drug candidates:

- **Out-licensing NOX-A12:** Seeking an exclusive worldwide or regional out-licensing deal for NOX-A12 program to a pharmaceutical partner. The targeted transaction structure would bring in payments upon signature and significant regulatory and commercial milestones as well as providing for royalties on sales.
- **Out-licensing NOX-E36:** Seeking an exclusive worldwide out-licensing deal for NOX-E36 program both by *TME Pharma* and collaboration partner SERI to a newly formed company funded by venture capital partners.
- **Asset Sale:** Exploring the sale of the private operational subsidiary *TME Pharma AG* holding assets and intellectual property to a pharmaceutical partner or investor. This would result in *TME Pharma N.V.* holding either cash or shares of the acquiring entity.
- **Virtual Setup**: As a contingency plan in case none of the above can be realized by June 2025, *TME Pharma* is preparing to change its organizational structure to allow it to continue pursuing the goals of financing, licensing or M&A transactions focused on its clinical stage assets, NOX-A12 and NOX-E36 while minimizing costs by outsourcing essentially all functions to maintain and advance the programs and conduct industrial partner and investor outreach.

The outsourced staffing structure will likely be the most economically efficient option to manage collaborations and develop further transactions on NOX-A12 and NOX-E36 and so *TME Pharma* is actively preparing to transition to a fully outsourced staffing structure at the end of June 2025.

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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 (olaptesed pegol, an anti-CXCL12 L-RNA aptamer) 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 the United States. The company's second clinical-stage drug candidate, NOX-E36 (emapticap pegol, L-RNA aptamer inhibiting CCL2 and related chemokines), showing potential to address fibrosis and inflammation is evaluated in ophthalmic diseases with a high need for well-tolerated therapies with anti-fibrotic effect. Further information can be found at: www.tmepharma.com.

Keytruda® is a registered trademark of Merck Sharp & Dohme Corp.

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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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