TME PHARMA PUBLISHES 2023 FINANCIAL RESULTS AND PROVIDES OPERATING UPDATE

- **Financial highlights include successful public rights offering and the subsequent 2024 buyback of all convertible bonds, terminating the convertible bond program**
- **Cash consumption reduced by more than 50% in 2023 vs 2022 as the NOX-A12 GLORIA brain cancer trial nears completion with exceptional clinical data**
- **NOX-A12 in combination with bevacizumab and radiotherapy delivers very promising survival data vs standard of care reference cohort: 10-fold higher rate of survival at 21 months (50% vs 5%) and median overall survival near double (19.9 months vs 10.5 months)**
- **FDA clears Investigational New Drug (IND) applications for NOX-A12 Phase 2 trial in brain cancer and pancreatic cancer**
- **Fast Track Designation from FDA granted to NOX-A12 in brain cancer provides enhanced visibility on path to US market**

Berlin, Germany, April 25, 2024, 06.00 p.m. CEST – TME Pharma N.V. (Euronext Growth Paris: ALTME), a biotechnology company focused on developing novel therapies for treatment of cancer by targeting the tumor microenvironment (TME), announced today its financial results for the fiscal year ending December 31, 2023, and provides a business update.

The Annual Report 2023, as approved by the management and supervisory boards on April 24, 2024, is available on *TME Pharma's* website (www.tmepharma.com).

"*2023 has been a year of significant clinical achievements which we believe have laid the foundations for the next steps of NOX-A12's clinical development as well as delivering value for our shareholders,*" said **Aram Mangasarian, CEO of TME Pharma**. "*With the support of our shareholders, we have continued to progress in 2024, getting the green light from the FDA for NOX-A12 to embark on the next leg of clinical development with a Fast Track Designation allowing enhanced visibility on the path to market in the US. The coming months will be about securing our ability to generate robust Phase 2 data for NOX-A12 in glioblastoma in a multi-center, randomized, controlled clinical trial and to achieve this goal with as little dilution as possible for our shareholders*."

Business Highlights for 2023 and 2024 Year-to-Date

- **Clinical Highlights for 2023 and 2024 Year-to-Date**

Brain Cancer (Glioblastoma) – Complete Clinical and Regulatory Package

Glioblastoma is a highly aggressive and deadly form of brain cancer. Patients with glioblastoma that is resistant to standard of care chemotherapy (MGMT unmethylated) and whose tumors 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. *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.

TME Pharma advanced and delivered clinical and regulatory milestones in its lead clinical program GLORIA, a Phase 1/2 dose-escalation study of NOX-A12 in first-line brain cancer (glioblastoma) patients in combination with radiotherapy, or radiotherapy plus anti-VEGF therapy, bevacizumab, conducted at six sites in Germany. Data from the study were presented by the investigators of the clinical trial, Dr. Frank Giordano and Dr. Julian Layer, at three high-profile international cancer conferences: a) the American Society of Clinical Oncology (ASCO) Annual Meeting in June 2023 where they showcased tissue analysis of a biomarker with the ability to predict clinical responses of glioblastoma patients to NOX-A12 combined with radiotherapy, b) the European Society of Medical Oncology (ESMO) Congress in October 2023 where they highlighted an in-depth analysis of how the combination of NOX-A12 and radiotherapy remodels the immune tumor microenvironment, and c) the Society for Neuro-Oncology (SNO) Annual Meeting in November 2023 where they provided updated efficacy data from glioblastoma patients treated with NOX-A12 combined with anti-VEGF and radiotherapy.

In light of the encouraging data emerging from the GLORIA trial, the company discussed its plans for the development of NOX-A12 for glioblastoma with the US Food and Drug Administration (FDA) in a pre-IND advice meeting in December 2023. The informative discussion with the FDA enabled *TME Pharma* to prepare an Investigational New Drug (IND) application that fits with the requirements of the US regulator in areas where there has been recent evolution in recommendations by the FDA's Oncology Center of Excellence, such as the selection of the appropriate therapeutic dose of new oncology drugs.

Subsequent to the reporting period, the final median overall survival of the GLORIA Phase 1/2 trial of the arm combining NOX-A12 with radiotherapy and anti-VEGF bevacizumab reached 19.9 months and was announced in February 2024. 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. In addition, the NOX-A12-based therapy achieved this result despite having a more difficult population to treat since only patients with residual detectable tumor after surgery were included in the NOX-A12 trial, whereas competing trials also included patients with complete removal of detectable tumor who benefit from a longer expected survival. In terms of survival rate at 21 months, patients receiving the NOX-A12 combination with radiotherapy and bevacizumab demonstrated a 10-fold improvement compared to a reference cohort of matched patients receiving standard of care (50% vs 5%). Furthermore, as reported in April 2024, two out of the six patients achieved survival of 24 months or more (OS-24 of 33%) since the start of therapy, which continues to compare favorably with matched reference patients at this timepoint (OS-24 of 5%).

In early March 2024, the FDA cleared *TME Pharma*'s IND application on the basis of the protocol for its upcoming randomized Phase 2 trial in glioblastoma. 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 (MGMT unmethylated) and measurable tumor remaining after surgery. The FDA's Fast Track Designation aims to bring important new drugs to patients more quickly, facilitating the development and expediting the review of therapies intended to treat serious conditions and address unmet medical needs. Companies whose programs are granted Fast Track Designation can benefit from more frequent interactions with the FDA during the clinical development process.

Pancreatic Cancer – Regulatory Progress for Phase 2 in Combination with Keytruda

Following encouraging top-line results reported in the OPERA Phase 1/2 clinical trial, *TME Pharma* is planning the OPTIMUS Phase 2 trial to further evaluate NOX-A12 in pancreatic cancer. With the IND application cleared by the FDA in May 2023 and approval by regulatory authorities in France and Spain, *TME Pharma* is planning to initiate the trial in second-line pancreatic cancer patients to determine the best chemotherapy combination to pursue in a pivotal trial when appropriate financing and drug supply are available beyond that needed for development of NOX-A12 in brain cancer.

- **2023 Financial Summary**

TME Pharma successfully strengthened its balance sheet by raising €4.8 million (gross) in 2023. Considering cash and cash equivalents of €2.2 million as of December 31, 2023, and the additional €2.55 million (gross) raised in 2024 year-to-date, *TME Pharma* has financial visibility into July 2024.

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 67% from K€ 8,148 in the FY 2022 to K€ 2,652 in the FY 2023. The significant decrease in R&D expenses in 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 process to bring the pancreatic cancer clinical trial Phase 2 protocol to FDA approval in the US was also successfully completed in the first six months of 2023, reducing ongoing costs related to this clinical trial. 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.

General and administrative (G&A) expenses decreased 23% from K€ 3,882 in the FY 2022 to K€ 2,989 in the FY 2023. The decrease in G&A expenses in 2023 compared to 2022 is mainly driven by lower personnel expenses as well as lower legal, consulting and audit fees. In addition, public and investor relations expenses and other expenses decreased as well compared to 2022. 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 2023 and 2022 was entirely non-cash finance income. Finance income increased from K€ 303 in the FY 2022 to K€ 399 in the FY 2023. In 2023, finance income of K€ 237 resulted from the derecognition of conversion rights in connection with the Atlas Special Opportunities LLC (ASO) financing upon conversion and redemption of the bonds and of K€ 162 fair value adjustments of detachable warrants (Warrants Y) issued in connection with the preferential rights issue.

Finance cost decreased 55% from K€ 3,400 in the FY 2022 to K€ 1,518 in the FY 2023. Finance cost in the FY 2023 and 2022 was non-cash finance cost, except for transaction costs of K€ 4 in 2023 and K€ 122 in 2022 borne by the company in conjunction with its issuance of convertible bonds as well as K€ 13 in 2023 and K€ 11 in 2022 relating to interest expense for lease liabilities. Finance cost in the FY 2023 and 2022 of K€ 1,505 and K€ 3,350 relate to the ASO facility (contractually entered into in 2020

and ended in 2023, except for outstanding convertible bonds at the time) and reflect 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. Further, finance cost in the FY 2022 of K€ 39 relate to the exercise of warrants by Yorkville.

As a result of these factors, *TME Pharma N.V.* reports a net loss for FY 2023 of K€ 6,736 compared to K€ 15,133 in the FY 2022 leading to cash consumption being reduced by more than 50%.

Termination of Convertible Bond Program:

In early 2023 *TME Pharma* announced its decision to stop the reliance on convertible debt financing and to clear up its balance sheet and to relieve the pressure of such financial instruments. This announcement was followed in April 2023 by a successful equity financing and an agreement between *TME Pharma* and ASO to significantly reduce the amount of convertible debt on *TME Pharma*'s balance sheet through a conversion in shares and a lock-up of all outstanding convertible bonds for a 6-month period. In November 2023, *TME Pharma* initiated a fully guaranteed public rights offering that offered to existing shareholders the opportunity to participate through preferential subscription rights and minimize their dilution. The transaction, concluded in December 2024, saw a strong demand from the shareholder base and enabled the company to eliminate nearly half of the remaining outstanding convertible debt on its balance sheet.

In February 2024, *TME Pharma* completed the redemption of all outstanding convertible debt, marking the end of the convertible bond program.

Outlook for 2024

NOX-A12 Development in Glioblastoma

In the light of the encouraging data emerging from the GLORIA trial and based on the discussions with the US FDA leading to the open IND, *TME Pharma* plans to proceed with the continued clinical development of NOX-A12 in a Phase 2 randomized controlled study in approximately 100 newly diagnosed glioblastoma patients with extremely poor prognosis – chemotherapy-resistant patients having residual measurable tumor remaining after surgery. The study is expected to be initiated later in 2024 provided appropriate funding is secured. The study design includes five arms, with 20 patients per arm:

- 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: Standard of Care control (temozolomide + radiotherapy)

The study will address questions of dosing and contribution of individual components – NOX-A12 and bevacizumab – to overall efficacy of the combination therapy and will allow *TME Pharma* to optimize late phase development by selecting the best performing arm against standard of care.

Status of NOX-A12 OPTIMUS Phase 2 clinical trial in Pancreatic Cancer

With the IND application cleared by the FDA in May 2023 and approval by regulatory authorities in France and Spain, *TME Pharma* is planning to initiate the OPTIMUS Phase 2 trial in second-line pancreatic cancer patients when appropriate financing and drug supply are available beyond that needed for development of NOX-A12 in brain cancer.

NOX-E36 Opportunity in Oncology and Ophthalmology

The company's second clinical stage asset, the CCL2 inhibitor NOX-E36, which was initially developed in diabetic nephropathy, completed four clinical trials (two Phase 1, one Phase 1/2 and a Phase 2 trial), has already been administered to 175 human subjects. In an oncology setting NOX-E36 targets the tumor microenvironment by modifying the innate immune system, specifically highly immunosuppressive cells that contribute to the cancer's ability to evade the immune system, and the animal data suggest a therapeutic potential in pancreatic and liver cancer. The company believes that NOX-E36 is significantly de-risked to embark on clinical development.

TME Pharma is also investigating the potential for the use of NOX-E36 in ophthalmology, where CCL2 contributes to excessive inflammation and fibrosis after glaucoma surgery. These postoperative processes impede long-term surgical success. The anti-fibrotic mode of action of NOX-E36 has already been confirmed 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 investigating possibilities to perform clinical studies in the form of investigator-initiated trials (IIT) funded and performed by research institutes that it would support with drug supply. In parallel, *TME Pharma* will evaluate ways to monetize the potential of NOX-E36 in the ophthalmology space.

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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 also 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 has also received orphan drug designation 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 Twitter.

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

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