TME PHARMA PUBLISHES AUDITED ANNUAL REPORT 2022

- **Financial visibility extended into December 2023**
- **Exceptional clinical results generated in brain cancer trial evaluating NOX-A12 in combination with radiotherapy and bevacizumab**
- **Survival data continue to improve with 83% of patients alive after one year**
- **15-month survival data expected in mid-2023**

Berlin, Germany, April 24, 2023, 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, 2022.

The Annual Report 2022, as approved by the management and supervisory boards on April 20, 2023, is available on *TME Pharma's* website (www.tmepharma.com).

"At TME Pharma *we are taking on one of the most difficult to treat and underserved cancer indications – the brain cancer called glioblastoma – and 2022 saw us make exceptional clinical progress in our brain cancer program,"* **said Aram Mangasarian, CEO of TME Pharma.** *"The data generated from the GLORIA study in newly diagnosed glioblastoma patients surpassed our expectations, in particular the interim results in the expansion arm evaluating the triple combination of NOX-A12, radiotherapy and bevacizumab that showed 83% of patients achieved durable partial responses. We recently reported encouraging survival data showing that after 12 months on study (median), 83% of patients were still alive. We are now keenly awaiting more mature survival data in mid-2023, that will allow us to initiate discussions with regulators and design the optimal regulatory path forward for NOX-A12. Our successful new financing transaction extends our cash runway into December 2023 and aligns with our commitment to reduce reliance on convertible debt and our strategy to bring new long-term investors on board and support the company through next clinical results. It will also enable us to maintain our focus on developing novel therapies for cancer patients where there is huge unmet medical need in a significant market that we estimate at $2.5 billion per year."*

Business Highlights for 2022 and 2023 Year-to-Date

Evolution to TME Pharma

To reflect its evolution and transition into an oncology biotech company focused on therapeutics targeting the tumor microenvironment, NOXXON Pharma changed its name to *TME Pharma* in July 2022. *TME Pharma* continues to work on the same clinical programs as NOXXON and aims to develop

and commercialize its proprietary class of drugs called Spiegelmers®[1], while keeping stakeholders' best interests as first priority and remaining committed to providing shareholders with long-term value.

Scientific Advisory Board

Two leading brain cancer experts from the US and Europe, Dr. Michael Lim and Prof. Monika Hegi, were appointed in May 2022 to the Scientific Advisory Board (SAB) chaired by Dr. Jose Saro, to provide strategic and scientific counsel on *TME Pharma*'s lead program NOX-A12 in brain cancer (glioblastoma). Prof. Monika Hegi is Head of the Laboratory of Brain Tumor Biology and Genetics, Department of Clinical Neurosciences, University Hospital Lausanne, Switzerland, and Dr. Michael Lim is Professor and Chair of the Department of Neurosurgery, Stanford University, California, USA.

Collaboration with US National Cancer Institute

In June 2022 *TME Pharma* entered into a collaboration with the US National Cancer Institute (NCI) of the US National Institutes of Health (NIH) to further explore the effects of *TME Pharma's* lead compounds, the CXCL12 inhibitor NOX-A12 and the CCL2 inhibitor NOX-E36, individually and combined, on brain tumors. The research program is led by Mark R. Gilbert, M.D., Chief of the Neuro-Oncology Branch at the NCI's Center for Cancer Research (NCI/CCR). Under the agreement, *TME Pharma* supplies NOX-A12 and mNOX-E36[2] to the NCI that is conducting preclinical testing in various combinations with immunomodulatory treatments, including immune checkpoint inhibitors.

Cash runway extended into December 2023

In April 2023 *TME Pharma* announced the successful closing of an innovatively structured €2 million financing with a group of new investors and Atlas Special Opportunities, LLC (ASO), extending the company's cash runway into December 2023. This is sufficient for *TME Pharma* to reach its next inflection points and to allow the further advancement of the ongoing GLORIA Phase 1/2 clinical study of NOX-A12 combination therapies in newly diagnosed glioblastoma patients. The company also announced it will not draw any further tranches from the ASO convertible bond vehicle and the company had terminated the agreement with ASO other than with regard to already issued convertible bonds. The termination of the ASO agreement represents the first step in *TME Pharma's* commitment to ending the company's reliance on convertible bond financing. A key aspect of the transaction is a soft lock-up of all new shares issued and lock-up of all outstanding convertible bonds for a 6-month period to align investors and support the company through the next round of clinical results.

Clinical Highlights for 2022 and 2023 Year-to-Date

Brain Cancer (Glioblastoma) – Maturing Data with Promising Clinical Benefit

Glioblastoma is a highly aggressive and deadly form of brain cancer. Patients with glioblastoma that is resistant to standard-of-care chemotherapy and whose tumors are not amenable to complete surgical removal face a devastating prognosis of median overall survival (mOS) of 10 months on standard of care. The development of effective treatments for these patients – *TME Pharma's* target population in

[1] Spiegelmers – proprietary technology of synthetic target-binding oligonucleotides developed by TME Pharma – are a new class of therapeutics designed to combine the benefits of small chemical molecules and biologicals. Spiegelmers fold into distinct shapes that bind the targets of interest with high affinity and high selectivity. Furthermore, thanks to their mirror-image configuration, they are stable in the plasma and also do not trigger any immunological reaction.

[2] Since NOX-E36 is not active in rodents, the surrogate Spiegelmer mNOX-E36, which binds and inactivates mouse and rat CCL2, will be used for these experiments.

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 suggests significant clinical benefit could be achieved in this population with NOX-A12-containing regimens.

The company is advancing its lead 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, being conducted at six sites in Germany. Data were presented by the principal investigator of the clinical trial, Dr. Frank A. Giordano, at two high-profile cancer conferences in the US, the American Society of Clinical Oncology (ASCO) Annual Meeting in June 2022 and the Society for Neuro-Oncology (SNO) Annual Meeting in November 2022.

The results presented at the ASCO Annual Meeting focused on cohorts investigating the use of NOX-A12 and radiotherapy in first-line brain cancer (glioblastoma) patients and showed that 90% of patients who received NOX-A12 and radiotherapy achieved tumor size reductions compared to 25% of patients who received standard of care. Additionally, 40% of patients who received NOX-A12 and radiotherapy achieved radiographic partial response (defined as tumor size reduction of more than 50%) compared to only 10% in the standard of care group. The combination of NOX-A12 and radiotherapy was also safe and well-tolerated, with only 4% of adverse events being solely NOX-A12-related. Tumor tissue of patients who had repeat surgery while on NOX-A12 therapy showed an increase in the infiltration of the tumor by activated cytotoxic T-cells and M1-like macrophages. This suggests that NOX-A12 and radiotherapy can enhance the immune system's ability to infiltrate tumors, making them more susceptible to destruction. The median overall survival of 12.7 months was later reported for patients treated with this combination.

The results presented at the SNO Annual Meeting focused on interim data from an expansion arm of the GLORIA clinical study testing NOX-A12 in combination with radiotherapy and an anti-VEGF antibody, bevacizumab. This data showed that 100% of targeted tumor lesions treated with the triple combination were reduced by more than 50%, and 83% of patients achieved durable partial responses by mRANO[3] criteria. Two out of six patients achieved almost complete (>99%) tumor size reduction where contrast enhancing lesions were detectable but too small to be measured. The mean best tumor response was a 74.9% reduction, and the triple combination was well-tolerated and safe, with no dose-limiting toxicities observed. One patient experienced progressive disease and subsequently died due to distant metastases while shrinkage of the targeted tumor mass was maintained.

As of March 2023, with a median follow-up of 12 months, five of six patients (83%) were still alive in the NOX-A12 + radiotherapy + bevacizumab arm of the trial. The 12-month timepoint is an important landmark for assessment since it exceeds the expected survival for patients with MGMT unmethylated tumors and incomplete resection (Source: Kreth, 2013). The median overall survival (mOS) is the point at which more than half of the patients have died. The company expects the patients in the NOX-A12 + radiotherapy + bevacizumab expansion arm to have better mOS than those who received NOX A12 + radiotherapy only, where the mOS was 12.7 months. The company will provide updates on survival as the data matures, with the next update expected around the 15-month timepoint in mid-2023.

<u>Pancreatic Cancer – Regulatory Progress for Phase 2 in Combination with Keytruda</u>

The protocol of the planned Phase 2 OPTIMUS trial of NOX-A12 in second-line pancreatic cancer has been fully approved by regulators in France and Spain and is under discussion with the regulatory

[3] mRANO stands for Modified radiographic Response Assessment in Neuro-Oncology (mRANO) and uses both the medical imaging of the tumor and the patients' clinical condition to assess response to therapy.

authorities in the US. Preparations have been made so that the trial could be initiated rapidly when the required financial resources become available.

2022 Financial Summary

TME Pharma successfully strengthened its balance sheet by raising €7.3 million net cash under the Atlas Special Opportunities (ASO) facility in 2022. Considering cash and cash equivalents of €4.6 million as of December 31, 2022, and the additional €2.08 million (gross) raised in April 2023, *TME Pharma* has financial visibility into December 2023.

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.

Research and development (R&D) expenses accounted for 68% of total operating costs. The R&D expenses decreased from K€ 10,657 in 2021 to K€ 8,148 in 2022 due to lower costs associated with clinical trials, including costs for drug manufacturing, service fees and other costs related to clinical trials and preclinical testing, partly offset by increased patent costs and consulting services, personnel expenses and other expenses. The R&D expenses were primarily related to the ongoing GLORIA trial of NOX-A12 in brain cancer.

General and administrative (G&A) expenses increased from K€ 2,876 in the Fiscal Year 2021 (FY 2021) to K€ 3,882 in FY 2022 to support operational activities. The increase in G&A expenses in 2022 was mainly driven by higher personnel expenses as well as higher legal, consulting and audit fees. In addition, public and investor relations expenses and other expenses increased compared to 2021. In 2022, *TME Pharma* executed on several corporate actions concerning the reorganization of share capital and the company name change, also resulting in an increase in G&A expenses. The increase in personnel expenses was also driven by the addition of the CFO, who departed end of 2022.

The finance income in the FY 2022 and 2021 was entirely non-cash finance income. Finance income decreased from K€ 319 in the FY 2021 to K€ 303 in the FY 2022 and resulted predominantly from the derecognition of ASO conversion rights.

Finance cost amounted to K€ 3,400 in the FY 2022 (compared to K€ 1,504 in the FY 2021) and was non-cash expense, except for transaction costs resulting from issuance of convertible bonds (K€ 122 in 2022 and K€ 47 in 2021). Non-cash finance cost mainly reflected losses on initial recognition of ASO convertible bonds, conversion losses and conversion right derivatives.

As a result of these factors, *TME Pharma N.V.* reports a net loss for FY 2022 of K€ 15,133 compared to K€ 14,453 in the FY 2021. In 2022, the net loss from operations is K€ 12,029 and decreased compared to prior year by 9%. Net cash used in operating activities amounted to K€ 12,143 in FY 2022 compared to K€ 12,381 in FY 2021.

Outlook 2023

<u>NOX-A12-based Therapies in Bran Cancer</u>

It is believed in the scientific community that many future cancer treatments will rely on combination therapies that have a synergistic benefit for the patient by fighting the cancer via different pathways simultaneously (Source: Mahoney, 2015). *TME Pharma* works toward positioning its lead product

candidate NOX-A12 as a combination partner for a wide range of cancer treatments by leveraging its unique mechanism of action on the tumor microenvironment in combination with existing therapy classes, including immune checkpoint inhibitors and cell therapies, as well as standard therapies such as chemo- and radiotherapy.

Comparing the results from NOX-A12-containing treatment regimens with those achieved by standard of care (without NOX-A12) suggests that significant clinical benefit could be achieved for brain cancer patients treated with NOX-A12 combinations. In response to the emerging positive data and limited available resources the company has decided to focus its strategy, capabilities and resources on the advancement of the glioblastoma program.

Once mature data for survival are available, the company plans to discuss with regulators in the US and EU to determine the most efficient path to approval for NOX-A12. The company believes that the next study will need to be a randomized, controlled trial comparing one or more NOX-A12-containing regimens to standard of care.

Additionally, recent work suggests the possibility of identifying biomarkers with the potential to predict the clinical responses of brain cancer patients to NOX-A12-based therapy. Being able to select patients who will benefit most strongly from the therapy should increase the chances of regulatory approval and commercial success, while at the same time reducing the risk, cost and duration of associated trials. The company is evaluating emerging data and plans to disclose available results in mid-2023.

For more information, please contact:

TME Pharma N.V.
Aram Mangasarian, Ph.D., CEO
Tel. +49 (0) 30 726247 0
investors@tmepharma.com

Investor and Media Relations:

LifeSci Advisors
Guillaume van Renterghem
Tel. +41 (0) 76 735 01 31
gvanrenterghem@lifesciadvisors.com

NewCap
Arthur Rouillé
Tel. +33 (0) 1 44 71 00 15
arouille@newcap.fr

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 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. NOX-A12 in combination with radiotherapy has 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 and Spain and is in discussion with regulatory authorities in 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

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.