TME PHARMA ANNOUNCES PUBLICATION IN NATURE COMMUNICATIONS OF BIOMARKER DATA FROM NOX-A12 GLORIA PHASE 1/2 TRIAL IN GLIOBLASTOMA

- **Publication in high-impact peer-reviewed journal highlights that the presence of NOX-A12's target in tumor tissue can be used as a biomarker to predict clinical efficacy in glioblastoma patients**
- **The EG12 biomarker's ability to predict clinical responses of glioblastoma patients to NOX-A12 + radiotherapy provides robust evidence of its 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**
- **Predictive biomarker could help de-risk NOX-A12 clinical development and could offer advantages in partnering and commercialization**

Berlin, Germany, June 17, 2024, 05.30 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 the publication of biomarker data from the GLORIA Phase 1/2 clinical trial of NOX-A12 in brain cancer (glioblastoma) in the peer-reviewed scientific journal *Nature Communications.*

The article by Dr. Frank A. 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, entitled *"L-RNA aptamer-based CXCL12 inhibition combined with radiotherapy in newly-diagnosed glioblastoma: dose escalation of the phase I/II GLORIA trial",* details a potential predictive biomarker known as the "EG12 score" for glioblastoma patients treated with NOX-A12 and radiotherapy.

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. The score significantly correlated with the clinical outcome, in terms of progression-free survival (PFS) for patients treated with NOX-A12 and radiotherapy ($r = 0.87$; $p = 0.005$), but not for a cohort of reference patients with comparable characteristics treated with standard of care ($r = 0.13$; $p = 0.56$). As such, the biomarker appears to be specific for response to NOX-A12-based therapies. When dividing the trial population into two groups in the middle by its EG12 score, GLORIA patients with higher EG12 scores had a significantly longer median PFS than those with lower scores (6.0 vs. 3.0 months; $p = 0.031$) and also a strong trend towards improved median overall survival (15.8 vs. 11.1 months; $p = 0.075$).

The research on the EG12 predictive biomarker published in *Nature Communications* builds on data first presented at the ASCO Annual Meeting in June 2023.

"The publication of this scientific article in the prestigious peer-reviewed journal Nature Communications is a validation of the groundbreaking biomarker data from our GLORIA trial in

aggressive adult brain cancer and builds on the earlier presentation of these findings at one of the world's top cancer conferences," said **Aram Mangasarian, CEO of TME Pharma**. *"A predictive biomarker has many potential advantages, not the least the ability to select patients who will most benefit from our NOX-A12-based therapies. This could help us identify target populations for future clinical trials, enhancing their statistical power and de-risking the further overall clinical development of NOX-A12. It also offers investors and potential partners peer-reviewed evidence of the potential of our glioblastoma program to bring benefit to patients suffering from this complex and underserved indication as we advance NOX-A12 toward Phase 2 evaluation."*

The full article is available online on *Nature Communications'* 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 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.

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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.