TME PHARMA ANNOUNCES ORAL PRESENTATION AT ESMO CONGRESS 2024 WITH UPDATED RESULTS FROM NOX-A12 GLORIA PHASE 1/2 TRIAL IN GLIOBLASTOMA

- **Presentation highlights data from the combined inhibition of angiogenesis and vasculogenesis with NOX-A12 and bevacizumab in newly diagnosed glioblastoma patients**
- **Combination of NOX-A12 and bevacizumab resulted in significantly improved survival compared to matched standard of care cohort or NOX-A12 alone**
- **Marked decrease in tumor blood-flow supports the NOX-A12 combination's mode of action**

Berlin, Germany, September 16, 2024, 08.00 a.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), announced an oral presentation by Dr. Frank A. Giordano, lead investigator of the NOX-A12 GLORIA Phase 1/2 trial in first-line brain cancer (glioblastoma), taking place on Sunday, September 15, 2024, at the European Society for Medical Oncology (ESMO) Congress in Barcelona, Spain. The presentation provided the updated results and key conclusions from the combined therapy with NOX-A12 and bevacizumab in newly diagnosed glioblastoma patients resistant to standard chemotherapy (MGMT unmethylated) with residual detectable tumor after surgery.

In the presentation, Dr. Giordano highlighted that inhibition of two paths of brain tumor revascularization after radiation – vasculogenesis with NOX-A12 and angiogenesis with bevacizumab – resulted in deeper clinical responses, i.e. stronger shrinkage of tumor size compared to NOX-A12 therapy alone. The research showed a significant decrease in tumor perfusion which supports the suggested mode of action of the combination therapy. The presentation also reveals that the deeper responses to the combination therapy with NOX-A12 and bevacizumab translate to significantly longer median progression free survival (mPFS: 9.1 months, p=0.003) and median overall survival (mOS: 19.9 months, p=0.005) compared to a matched SOC reference cohort (mPFS: 4.0 months; mOS: 9.5 months) or to NOX-A12 alone (mPFS: 5.7 months; mOS: 12.7 months). Two out of the six glioblastoma patients in the NOX-A12 + bevacizumab arm of the GLORIA trial survived for more than 26 months since the start of therapy.

"The median OS of 19.9 months achieved in patients receiving combination therapy in the GLORIA study is especially exciting when considering the prognosis this chemotherapy-refractory patient population with residual detectable tumor after surgery would otherwise face on current standard of care, notably survival of approximately 10 months," said **Aram Mangasarian, CEO of TME Pharma.** *"What further strengthens our confidence in our dual inhibition approach is the tumor tissue analysis showing spatially distinct expression patterns of NOX-A12's target CXCL12 and VEGF. This indicates that the two different ways of growing blood vessels occur in different tumor structures: vasculogenesis driven by*

NOX-A12's target, and angiogenesis driven by bevacizumab's target. This helps explain why combined inhibition of both pathways is needed to effectively prevent tumor vasculature restoration after radiotherapy."

Details of the oral presentation at the ESMO Congress 2024 are as follows:

Title: *Dual inhibition of postradiogenic angio-vasculogenesis in glioblastoma: Results of the phase 1/2 GLORIA trial*
Presenter: Dr. Frank A. Giordano, Chair of the Department of Radiation Oncology, University Medical Center Mannheim, Germany
Session: Mini oral session: CNS tumors
Time and Date: 08.30-8.35 a.m. CEST, Sunday, September 15, 2024

The full presentation is available online via 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 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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