TME PHARMA ANNOUNCES FDA CLEARANCE OF INVESTIGATIONAL NEW DRUG (IND) APPLICATION FOR NOX-A12 PHASE 2 TRIAL IN BRAIN CANCER

- **Clinical trial protocol approved in the US to initiate Phase 2 study with NOX-A12 in glioblastoma providing a clear roadmap for clinical development to investors and potential partners**
- **FDA decision on Fast-Track Designation expected by end of March 2024**
- **US regulatory interactions supported by exceptional survival data demonstrated by NOX-A12 in GLORIA brain cancer trial**

Berlin, Germany, March 05, 2024, 08.00 a.m. CET – 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), announces that the US Food and Drug Administration (FDA) has cleared its Investigational New Drug (IND)[1] application for NOX-A12, *TME Pharma's* CXCL12 inhibitor, for use in the treatment of aggressive adult brain cancer, glioblastoma.

With the IND now open at the FDA, *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, chemotherapy-resistant glioblastoma patients having residual measurable tumor remaining after surgery. The study is expected to be initiated later this year, starting first in Europe, once the necessary resources and preparations are in place. Sufficient NOX-A12 clinical grade material has already been manufactured to initiate the study.

"Receiving approval of the FDA for the design of our Phase 2 clinical trial in glioblastoma provides a clear roadmap to potential industrial partners and investors on the next steps in clinical development. The discussions with the FDA have been constructive and have allowed us to design a robust Phase 2 that should provide us with solid evidence of the highly differentiated profile of NOX-A12 in combination with bevacizumab in newly diagnosed, chemotherapy-resistant glioblastoma patients. The open IND will also allow us to expand our clinical development into the US, where we expect to generate significant interest in the medical community," said **Aram Mangasarian, CEO of TME Pharma**. *"We also expect to receive the FDA's decision regarding Fast-Track Designation for NOX-A12 in glioblastoma in the next few weeks, which can further strengthen our regulatory position in the US and should help us in the search for industrial and financial partners who can assist TME Pharma in bringing NOX-A12 to patients in the quickest way possible."*

The study will address questions of dosing and contribution of components – NOX-A12 and bevacizumab – to overall efficacy of the combination therapy and will allow *TME Pharma* to optimize late phase development by testing multiple doses of NOX-A12 with bevacizumab in a patient

[1] Investigational New Drug (IND), the authorization from the FDA to administer an investigational drug or biological product to patients in the US as part of a clinical trial.

population that is also randomized to standard of care. Together with the IND submission *TME Pharma* has also submitted a Fast-Track Designation[2] request to the FDA to secure an expedited regulatory pathway for NOX-A12 in glioblastoma and the company expects to receive the FDA's decision before the end of March 2024.

Based on discussions with the FDA last year and further interaction during the IND application process, the FDA-approved 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)

TME Pharma's regulatory interactions were supported by recent survival data from the GLORIA Phase 1/2 study in which NOX-A12 demonstrated an unprecedented median Overall Survival (mOS) of 19.9 months in combination with bevacizumab and radiotherapy in glioblastoma patients with measurable chemotherapy-resistant residual tumors after surgery. This survival rate compares very favorably to a matched standard of care reference cohort, which achieved an mOS of approx. 10 months, and exceeds what *TME Pharma* believes to be all relevant competitor therapy trials in newly diagnosed glioblastoma patients resistant to standard chemotherapy.[3]

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[2] Fast track is a process designed by the FDA to facilitate the development, and expedite the review of drugs to treat serious conditions and fill an unmet medical need.
[3] See annex to the *TME Pharma* press release published on 13 September 2023.

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, and improved survival. 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, 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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