TME PHARMA ANNOUNCES STRATEGIC PLAN TO EXTERNALIZE AND MONETIZE SECOND CLINICAL STAGE ASSET NOX-E36

- **NOX-E36 presents promising opportunity for development in eye diseases with a high need for well-tolerated therapies with anti-fibrotic effect**
- **Anti-fibrotic mode of action of NOX-E36 was demonstrated in preclinical eye disease model performed by leading Singapore Eye Research Institute**
- **Preclinical, clinical data and available drug supply lay optimal framework for rapid path to Phase 2 clinical proof-of-concept**
- ***TME Pharma* plans to enable separate corporate entity focused on NOX-E36 in ophthalmology to monetize the program and mobilize private investor support**

Berlin, Germany, July 22, 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), announces its plan to externalize and monetize the company's second clinical stage asset NOX-E36 – an L-stereoisomer RNA aptamer inhibiting the CCL2 chemokine. This decision leverages the compound's potential, as shown by clinical and preclinical data, to safely address significant unmet medical needs in ophthalmic diseases impacted by fibrosis.

The presence of the target of NOX-E36, CCL2, has been shown to predict early failure of glaucoma surgical intervention in patients and inhibition of the pathway targeted by NOX-E36 in preclinical models of glaucoma surgery prevents fibrosis thereby prolonging the success of the intervention[1]. NOX-E36 has already been administered to 175 clinical trial participants with an excellent safety and tolerability profile and showing activity on its target, already derisking a number of steps in early clinical development.

Fibrosis is a significant cause of treatment failure or increased severity in many clinically important eye diseases[2] with unmet needs such as diabetic retinopathy (9.6 million cases in the US, of which 1.84 million vision-threatening[3]), age-related macular degeneration (20 million cases in the US, of which 1.5 million vision-threatening[4]), and primary open angle glaucoma (>3 million cases in the US[5]).

"Our discussions with glaucoma clinicians revealed there is an unmet need for well-tolerated therapies with an anti-fibrotic effect to safely reduce scarring following eye surgery and provide patients with long-term benefit and that this indication could provide a rapid path to regulatory approval," said **Aram Mangasarian, CEO of TME Pharma**. *"We have already established NOX-E36's activity on its biological target and demonstrated its excellent safety and tolerability profile in patients, offering us a promising opportunity for rapid advancement in the ophthalmology space and an upside potential for the*

[1] Chong (2017) Invest Ophthalmol Vis Sci 58:3432 & Chong (2010) Ophthalmology 117:2353
[2] Sorenson (2024) Frontiers in Ophthalmology 2024 Vol. 4
[3] Lundeen (2023) JAMA Ophthalmol. 2023;141(8):747-754
[4] Rein (2022) JAMA Ophthalmol. 2022;140(12):1202-1208
[5] US National Eye Institute Glaucoma Tables, Link

company's valuation. Since we have sufficient drug supply for initial clinical trials, we are currently working with ophthalmology experts to lay the framework to generate proof-of-concept clinical data at limited cost for the company that could unlock significant business opportunities. Given the successful track record of two other RNA aptamers being approved for use in ophthalmology and the substantial partnerships formed in this space such as the $5.9 billion Astellas acquisition of Iveric primarily for the RNA aptamer now known as Izervay[6], we are confident in NOX-E36's potential to attract interest. While TME Pharma *will continue its focus on oncology, our goal is to create a new entity with full rights to develop NOX-E36 in ophthalmology supported by private investors. We expect to provide updates on these activities before the end of this year."*

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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

[6] Astellas press release July 11, 2023, Link

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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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.