TME PHARMA CEO MESSAGE

Berlin, Germany, February 24, 2023, 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), released today a message from Aram Mangasarian, CEO of *TME Pharma*, to its shareholders with the following key highlights:

- Exceptional clinical results generated in brain cancer trial evaluating NOX-A12 in combination with radiotherapy and bevacizumab
- Maturing brain cancer survival data confirmed 83% of patients still alive at 10 months
- 12-month median follow-up survival data expected in early Q2 2023
- Intensified partnering and financing discussions to secure future clinical development of NOX-A12 without reliance on convertible debt financing
- Cash runway projected into September 2023

Dear Shareholders,

I would like to take a moment to both look back at 2022 and to look ahead to the 2023 catalysts that can move *TME Pharma* forward.

With the exceptional clinical results emerging from our brain cancer program throughout last year, it was time to make our transformation into an oncology biotech with a focus on therapeutics altering the tumor microenvironment – TME – visible with our new name. Our current strategy focuses all facets of our and collaborators' expertise on the development of our lead asset NOX-A12 in brain cancer as the opportunity with the fastest path to approval. Indeed, recent work has revealed a potential biomarker that may predict clinical response of brain cancer patients to NOX-A12-based therapy. Being able to select patients who will benefit most strongly from our therapy should increase chances of regulatory approval and commercial success while at the same time reducing cost and duration of associated trials.

At *TME Pharma* we pride ourselves on taking on one of the most difficult to treat and underserved cancer indications – brain cancer (glioblastoma multiforme, GBM). GBM is one of the most aggressive forms of brain cancer and the most common malignant central nervous system tumor in adults. Patients with this devastating orphan disease are faced with extremely poor prognosis and a staggering 95% of them will not survive beyond 5 years. There is a huge unmet medical need for an effective approach to treat GBM where the standard of care – a combination treatment including surgery, radiotherapy and chemotherapy – unfortunately is not curative, and provides only a minimal survival benefit despite its heavy toll on the last few months of the patients' and their families' lives. Moreover, not all patients will benefit clinically from the chemotherapy, which limits the efficacy of the treatment while adding side effects for patients. Our approach, built on research into the tumor microenvironment, has delivered a series of highly encouraging results in the clinic and demonstrates

that NOX-A12 combinations, granted orphan drug designation in the US and Europe, have the potential to considerably improve therapy of this disease.

Although we were confident that NOX-A12 could generate clinical benefit for patients, 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, the antibody also known as Avastin® from Roche. These results were reported in November at the Society for Neuro-Oncology (SNO) Annual Meeting in Tampa, US and showed that almost all patients responded to the NOX-A12 triple combination in an impressive manner: 100% of targeted lesions treated with the NOX-A12 combination shrank by more than 50% with 83% of patients achieving durable partial responses lasting longer than six months. Two of the six patients experienced tumor size reduction greater than 99%. These are exceptionally positive treatment outcomes for this patient group: a matched historical cohort treated with the standard of care showed only 25% of patients with tumor size reduction and 10% of patients with a reduction of 50% or more in tumor size.

The GLORIA study continues to generate important data, and we have not yet reached median overall survival (mOS). We recently reported that 83% of patients are still alive with the median time on study of 10 months. The 10-month timepoint is an important landmark for assessment since this is the expected median survival for our patient population with chemorefractory tumors and incomplete surgical removal. We are now keenly awaiting the 12-month median follow-up survival data which are due in early Q2 2023. More mature survival data will allow us to initiate discussions with the regulators and design the optimal regulatory path forward for NOX-A12.

As announced in June 2022, in response to the emerging positive data we have decided to focus our strategy so that our capabilities and resources advance the glioblastoma program. Over the last months we have been considering different options to maximize availability of mature data from the GLORIA brain cancer trial with available funds and we have now made the decision to pause the recruitment of additional patients in the other expansion arms. These changes provide additional cash runway with funding of *TME Pharma* projected into early September 2023. As such, to execute on its plans and meet its future financial obligations, the company will need to access additional financing in May 2023.

The goal of these actions is to enable us to deliver the datapoints needed to attract an industry partner or long-term investors. Throughout the last year, the *TME Pharma* team has participated in a range of industry events and conferences. Key clinical readouts were accepted for presentation at two of the most high-profile congresses related to novel cancer therapies, the American Society of Clinical Oncology (ASCO) and Society for Neuro-Oncology (SNO) annual meetings. This was a welcome validation of the importance of our research and development and contributed to raising awareness of the work we are doing in brain cancer among the wider scientific community. However, despite the recognition of our promising data, glioblastoma is generally perceived as one of the riskiest indications both by industrial partners and investors. Reluctance to invest in this particularly challenging indication has left patients without effective therapies for decades and made the pursuit for a new treatment so much more critical.

Advancing and financing of the glioblastoma program remains our priority for as long as data continues to show positive efficacy signals and generates interest among potential partners. In order to drive clinical development into the next phase we need long-term support from a strategic or financial

partner. Prospective partners and investors would like to wait though for more mature survival data and feedback from the regulatory agencies to advance the discussions.

The agreement put in place with Atlas Special Opportunities (ASO) in 2020 has served the company for more than 2.5 years as a predominant source of financing, however it is dilutive for our shareholders and puts downward pressure on the share price. It is our goal to bring long-term investors on board and to end reliance of the company on convertible debt financing. We are actively pursuing multiple alternatives to secure funding for *TME Pharma* and our clinical programs. We are optimistic that with more mature data and the potential to select patients that will respond to treatment with NOX-A12 we will be able to attract needed financial support to our program.

Although I am writing to you during a challenging time for the biotech industry, especially for a small company such as ours, I remain proud of our achievements at *TME Pharma* and convinced that investors and partners will ultimately see significant value in our NOX-A12 program. I would like to thank the entire *TME Pharma* team for their diligence and dedication. I know they share my excitement and expectations for the year ahead. I would also like to express my gratitude to our shareholders for their belief in the company and I look forward to updating you on our progress in 2023. We have entered 2023 with enthusiasm and determination for the busy time ahead of us, which contains a great promise for *TME Pharma*.

Yours sincerely,

Aram Mangasarian
CEO, TME Pharma
February 24, 2023

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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 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.

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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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