NOX-A12 COMBINATION REGIMEN WITH BEVACIZUMAB: 17-MONTH SURVIVAL RATE EXCEEDS ALL RELEVANT COMPETITOR TREATMENTS AGAINST MOST SEVERE FORM OF ADULT BRAIN CANCER

- **NOX-A12, in combination with radiotherapy and bevacizumab, outperforms all relevant competing benchmark therapies in development in Overall Response Rate and median Overall Survival for chemotherapy resistant patients**
- **67% of GLORIA patients remain alive at the 17-month mark, so the median Overall Survival figure will continue to improve**

Berlin, Germany, September 13, 2023, 08.00 a.m. CEST – 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 median Overall Survival (mOS) and Overall Response Rate (ORR) for patients receiving NOX-A12 with the VEGF inhibitor bevacizumab and radiotherapy has now exceeded what *TME Pharma* believes to be all relevant competitor therapy trials in newly diagnosed glioblastoma patients resistant to standard chemotherapy.

After 17 months on study (median[1]), 67% of GLORIA expansion arm patients (4 of 6) are still alive. The median Overall Survival is expected to improve further as the remaining patients continue to receive treatment or follow-up care[2].

The milestone in survival at 17 months is a crucial landmark since it means the NOX-A12-based therapy has surpassed the survival rates achieved in what *TME Pharma* believes to be all the relevant competitor studies conducted in the US or EU involving newly diagnosed, chemotherapy-resistant (MGMT unmethylated) glioblastoma patients (see annex to this press release). In addition, the NOX-A12-based therapy achieved this result despite having a more difficult population to treat since only patients with residual detectable tumor after surgery were included the NOX-A12 trial, while competing trials included patients with complete removal of detectable tumor.

[1] The median is the middle value of a set of numbers. For the expansion arm testing NOX-A12 + radiotherapy + anti-VEGF with six patients, the median value will be the average of the 3rd and 4th longest surviving patients.
[2] In a clinical study, measuring the median Overall Survival (mOS) is one way to assess how well a new treatment works. The longer the patients remain alive, the longer it takes to reach mOS. mOS can only be calculated when more than half of patients in the study have deceased.

OS: 17 months (and increasing) for NOX-A12 + bevacizumab vs 13.4-16.9 months

With Overall Survival (OS) of 67% at 17 months demonstrated by NOX-A12 combined with radiotherapy and bevacizumab, the median Overall Survival (mOS) will continue to improve since more than 50% of patients are still alive. This compares favorably to the 13.4 to 16.5 months mOS in the chemotherapy resistant population demonstrated by relevant competing therapies in clinical development and to the 16.9 months demonstrated by the Tumor Treating Fields device that was approved by the US Food and Drug Administration (FDA) for newly-diagnosed glioblastoma in 2015.

ORR: 83% for NOX-A12 + bevacizumab vs 3-7.8%

NOX-A12 combined with radiotherapy and bevacizumab demonstrated a strong Overall Response Rate (ORR) of 83%, which compares favorably with much lower percentages of 3%, 7% and 7.8% demonstrated by paxalisib, enzastaurin and nivolumab, respectively.

"*This positive clinical update marks a significant step forward in our mission to transform the landscape of cancer treatment. The 17-month data and the exceptional survival rates in the GLORIA trial underscore the potential for NOX-A12 regimens to become the best available therapy for glioblastoma patients. We will need to confirm this potential in a larger, randomized trial,"* said **Aram Mangasarian, CEO of TME Pharma**. *"We are immensely proud of the dedicated team of researchers and clinicians who have contributed to this remarkable achievement; they will provide detailed clinical updates at the upcoming Society for Neuro-Oncology (SNO) conference in November. We believe that continued strong performance of NOX-A12 clearly supports further development of the NOX-A12 + anti-VEGF combination with radiotherapy and improves NOX-A12's profile for partnering and eligibility for accelerated regulatory pathways*."

Annex: Competing benchmark therapies against chemotherapy resistant glioblastoma in development in the US or EU

Experimental Agent (Company)	Surgical removal of detectable tumor (T=total; P=partial; B=biopsy only)	Patient number	Response criteria	Overall Response Rate (ORR)	Median Overall Survival (mOS) in months	Status	Reference
NOX-A12 + Radiotherapy + bevacizumab (TME Pharma)	0% T; 100% P	6	RANO	83%	>17 (67% OS at 17m)	Ph 1/2 ongoing	TME Pharma Internal Data
Tumor Treating Fields (TTF) + Radiotherapy + Temozolomide (Novocure)	53% T; 34% P; 13% B	209	Macdonald	n.a.	16.9	Approved	Stupp R (2017), JAMA
Val-083 after Radiotherapy + Temozolomide chemotherapy) (Kintara)	information not provided	36	RANO	n.a.	16.5	Fast Track Designation granted; Ph 2/3 GBM AGILE ongoing	O'Brien (2021), Society for Neuro-Oncology Annual Meeting
Paxalisib + Radiotherapy (Kazia)	77% T; 17% P; 10% B	30	RANO	3%	15.7	Failed pre-defined criteria for GBM AGILE trial Ph 3	Wen P (2022); J Clin Oncol.
Enzastaurin + Radiotherapy (Denova)	43.9% T; 40.4% P; 15.8 B	57	Macdonald	7%	15	Fast Track Designation granted; Ph 3 ongoing	Wick W (2013), Neuro Oncol.
Temozolomide chemotherapy + Radiotherapy + bevacizumab (Roche)	63% T; 34% P; 3% B #	215	Macdonald	n.a.	14.3	Failed in Ph 3	Gilbert MR (2014), NEJM
Nivolumab anti-PD-1 immunotherapy + Radiotherapy (BMS)	54% T; 46% P	280	RANO	7.8%	13.4	Failed in Ph 3	Omuro A (2022); Neuro Oncol.
Temozolomide chemotherapy + Radiotherapy	information not provided	60	n.a.	n.a.	12.7	Approved (current standard of care)	Hegi ME (2005) NEJM

For this study resection status applies to the total patient population (MGMT methylated + unmethylated)

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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, 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.

Disclaimer

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