TME PHARMA ANNOUNCES POSTER PRESENTATION BY U.S. NATIONAL CANCER INSTITUTE ON CXCL12 INHIBITION BY NOX-A12 IN GLIOBLASTOMA AT 2024 SNO ANNUAL MEETING

- **Presentation highlights synergistic effect of combining NOX-A12's anti-CXCL12 activity with immune checkpoint inhibition in brain cancer models inducing a favorable tumor microenvironment (TME) for anti-tumor immune responses.**
- **Data support the different NOX-A12 combination strategies chosen by *TME Pharma* for brain and pancreas cancer**

Berlin, Germany, November 23, 2024, 09.00 a.m. CET – 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 the presentation of a poster featuring NOX-A12 data from preclinical studies performed at the U.S. National Cancer Institute (NCI) at the 2024 Society for Neuro-Oncology (SNO) Annual Meeting, taking place in Houston, Texas, USA, November 21-24, 2024.

The presentation showed that combining CXCL12 inhibition with anti-PD-1/CTLA4 immune checkpoint inhibition increases the presence of anti-cancer immune cells in tumor tissues both inside and outside the brain, including activated cytotoxic ("killer") T cells. Importantly, improved long-term survival and immunological protection from tumor recurrence were seen in models of tumors growing outside but not inside the brain. This suggests that while the combination with anti-PD-1/CTLA4 immune checkpoint inhibitors is a promising therapy for tumors outside the brain, it may not be an optimal approach for treating brain tumors.

These results support the different combination strategies pursued by *TME Pharma* in both brain and pancreas cancer. In pancreas cancer, a tumor originating outside the brain, NOX-A12 is combined with an anti-PD-1 immune checkpoint inhibitor and chemotherapy. In brain cancer (glioblastoma), *TME Pharma* pursues a different strategy combining NOX-A12 with anti-VEGF therapy and radiotherapy, which has already shown exceptional efficacy in animal models (100% complete response[1]) and in the GLORIA clinical trial where a statistically significant survival benefit over a matched standard of care cohort was shown with a doubling of median overall survival from 9.5 to 19.9 months[2].

"The presented results confirm the activity of NOX-A12 on the tumor microenvironment and support TME Pharma's *strategy to focus on combination with the VEGF inhibitor bevacizumab in brain cancer that has yielded excellent results in newly diagnosed chemotherapy-resistant patients with residual tumor remaining after surgery,"* said **Aram Mangasarian, CEO of TME Pharma.** *"The survival benefit shown at the SNO conference for the NOX-A12 combination with anti-PD1/CTLA4 immune checkpoint inhibitors suggests potential to treat multiple tumor types outside the central nervous system and supports our plans to combine NOX-A12 with the anti-PD-1 immune checkpoint inhibitor pembrolizumab and chemotherapy in the OPTIMUS pancreatic cancer study."*

[1] Liu 2014, Neuro-Oncology 16:21.
[2] Giordano (2024) ESMO Annual Meeting Oral Presentation, September 15, 2024.

The research was conducted at the NCI, part of the National Institutes of Health, under the material transfer agreement established with *TME Pharma* in June 2022 to explore the effects of *TME Pharma's* CXCL12 inhibitor NOX-A12 in brain tumors.[3]

Details of the poster presentation at the 2024 SNO Annual Meeting are as follows:

Title: *Potentiating the efficacy of immune check-point inhibitors in glioblastoma by inhibition of CXCL12*
Presenter: Dr. Chen Cam-El Makranz, Neuro-Oncology Research Fellow, National Cancer Institute, National Institutes of Health
Session: Poster Session, Poster number EXTH12
Time and Date: 7.30-9.30 p.m. CST, Friday, November 22, 2024

The abstract and poster presentation are available on 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 (olaptesed pegol, an anti-CXCL12 L-RNA aptamer) 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

[3] *TME Pharma* Press Release on June 13, 2022.

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 (emapticap pegol, L-RNA aptamer inhibiting CCL2 and related chemokines), showing potential to address fibrosis and inflammation is evaluated in ophthalmic diseases with a high need for well-tolerated therapies with anti-fibrotic effect. 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 in the expansion arm in which NOX-A12 is combined with radiotherapy and bevacizumab.

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

Translations of any press release into languages other than English are intended solely as a convenience to the non-English-reading audience. The company has attempted to provide an accurate translation of the original text in English, but due to the nuances in translating into another language, slight differences may exist. This press release includes certain disclosures that contain "forward-looking statements." Forward-looking statements are based on *TME Pharma's* current expectations and are subject to inherent uncertainties, risks and assumptions that are difficult to predict. Factors that could cause actual results to differ include, but are not limited to, the risks inherent in oncology 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.