NEWS RELEASE

TME Pharma Provides Positive Update on 18-Month Survival for NOX-A12 Combination Regimen in Brain Cancer and Provides Strategic Update Including Decision to Engage with US FDA

10/10/2023

- Percentage of patients alive 18 months after start of therapy 10-fold higher than standard of care reference cohort
- Median overall survival will exceed 18 months and will improve further with continued patient follow-up
- Based on the mature 18-month survival data – key catalyst for TME Pharma – the company, in consultation with the board and its scientific advisors, has made the decision to request formal US Food and Drug Administration (FDA) advice in October 2023 – the first of several regulatory steps in the coming months
- TME Pharma's target is to have an FDA approved clinical trial protocol in glioblastoma as well as access to an expedited regulatory pathway by the end of Q1 2024

BERLIN, Germany--(BUSINESS WIRE)-- Regulatory News:

Fig. Overall Survival at 18 months: NOX-A12 Combinations Improve Survival in Chemotherapy-Resistant Incompletely Resected Glioblastoma Patients (Graphic: Business Wire)

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 a positive update on survival at 18 months for patients receiving NOX-A12 with the VEGF inhibitor bevacizumab and radiotherapy, and provides an overview on upcoming clinical development plans for NOX-A12 in the aggressive adult brain cancer, glioblastoma.

The percentage of patients who were alive 18 months after start of therapy of NOX-A12 with the VEGF inhibitor bevacizumab and radiotherapy is currently 50% (with the possibility to increase to 67% with the next patient reaching 18 months) which exceeds by 10-fold the 18-month survival of 5% observed in the matched group of patients receiving standard of care1. Since neither bevacizumab (anti-VEGF) alone, nor bevacizumab plus radiotherapy have previously shown to extend survival, the strong increase in survival can be attributed to the complementary mechanism of action of NOX-A12 with bevacizumab and radiotherapy2. The survival rate of the NOX-A12 triple combination also exceeds the 18-month survival of 20% seen in the patients with high levels of the NOX-A12 predictive biomarker EG12 receiving NOX-A12 + radiotherapy alone3, which further supports NOX-A12's potential to synergize with VEGF inhibition in glioblastoma (see figure below).

The median overall survival has now reached 18 months and is expected to improve further as the remaining patients continue to receive treatment or follow-up care4. Two of the three living patients are clinically stable despite radiographic tumor progression at last report from treating clinicians, including the patient who achieved complete response, now completing 22 months therapy. As a reminder, the matched standard of care reference cohort achieved a median overall survival of 10.5 months.

The NOX-A12-based therapy has now delivered median overall survival exceeding all the relevant competitor studies conducted in the US or EU involving newly diagnosed, chemotherapy-resistant (MGMT unmethylated) glioblastoma patients despite recruiting more difficult to treat patients whose tumors could not be fully removed by surgery5. NOX-A12 in combination with bevacizumab and radiotherapy continues to show an excellent safety and tolerability profile similar to that noted in previous publications.

In the upcoming 6 months the key regulatory steps for NOX-A12 program in brain cancer will include the following:

- Q4 2023 – Request advice in October from US Food and Drug Administration (FDA) on next trial design and eligibility for expedited regulatory pathways, such as Fast-Track Designation. Feedback expected in late December.
- Q1 2024 – Submit IND6 application for glioblastoma with the US FDA along with expedited regulatory pathway access request. Successful IND filing and feedback targeted by end of Q1 2024.

TME Pharma plans to keep the market updated on the progress of these regulatory discussions. The goal is to have an FDA approved clinical trial protocol in glioblastoma with an expedited regulatory path by the beginning of April 2024 in order to secure the funding for the necessary clinical trial via partnership, investment or other strategic transaction types.

"We believe that survival data from the NOX-A12 bevacizumab expansion arm is now sufficiently mature and have made the decision to request advice from the US regulatory authority in the coming weeks. Once we have feedback

from the FDA, we plan to submit an IND and request access to an expedited pathway for approval. We believe that having a clear path to marketing approval in brain cancer, validated by FDA, will significantly increase the attractiveness of NOX-A12 to investors and potential partners." said Aram Mangasarian, CEO of TME Pharma. "While we believe that the FDA will request a randomized clinical trial examining two doses of NOX-A12 combined with bevacizumab and radiotherapy and to compare these two dose regimens against standard of care as a next step, they may also request that these two doses of NOX-A12 be tested only with radiotherapy (without bevacizumab) in order to quantify precisely the benefit of the combination with NOX-A12 and bevacizumab, which would add two additional arms to the clinical trial. We anticipate that an additional trial or an expansion of the upcoming trial would be required for full approval."

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, TMEPharma'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. TMEPharma is considering several solid tumors for further clinical development. Further information can be found at: **www.tmepharma.com**.

Keytruda® is a registered trademark of Merck Sharp & Dohme Corp.

Visit TMEPharma on **LinkedIn** and **Twitter**.

About the GLORIA Study

GLORIA (NCT04121455) is TMEPharma'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 TMEPharma'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 TMEPharma'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.

1 Matched reference cohort of 20 patients from Giordano et al (2022 SNO Poster),
2 Chinot et al (2014) New England Journal of Medicine, Gilbert et al (2014) New England Journal of Medicine, Herrlinger et al (2016) J Clin Oncology
3 NOX-A12 + radiotherapy survival data from Giordano et al (2023 ASCO Poster)
4 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.

5 See TME Pharma's **Press Release dated 13 September 2023** for a competing benchmark therapies against chemotherapy resistant glioblastoma in development in the US or EU.

6**Investigational New Drug** (IND), the authorization from the FDA to administer an investigational drug or biological product to patients in the US.

For more information, please contact:

TME Pharma N.V.

Aram Mangasarian, Ph.D., CEO

Tel. +49 (0) 30 726247 0

investors@tmepharma.com

Investor and Media Relations:

LifeSci Advisors

Guillaume van Renterghem

Tel. +41 (0) 76 735 01 31

gvanrenterghem@lifesciadvisors.com

NewCap

Arthur Rouillé

Tel. +33 (0) 1 44 71 00 15

arouille@newcap.fr

Source: TME Pharma N.V.