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PRESS RELEASE

NH TherAguix Announces Completion of Enrollment in NANO-GBM Phase Ib/II Trial for Newly Diagnosed Glioblastoma and Publication of Positive Outcomes from Phase Ib in Clinical and Translational Radiation Oncology

- **NANO-GBM trial is a Phase Ib/II randomized clinical trial, conducted in collaboration with the Centre Jean Perrin (Clermont Ferrand – France), evaluating AGuIX® nanoparticles in combination with STUPP protocol (Standard of Care) in patients with non resected or partially resected newly diagnosed glioblastoma.**
- **AGuIX® displayed a good safety profile in combination with radiotherapy and temozolomide (Standard of Care).**
- **Pharmacokinetic data demonstrated that intravenous injection of AGuIX® exhibited mean Cmax increase in accordance with escalation of doses and confirmed the short plasmatic half-life of AGuIX®.**
- **Biodistribution data confirmed that after 4 injections, AGuIX® exhibited a signal of similar magnitude to the images acquired after the first injection in the region of glioblastoma.**

Paris, France, September 12th, 2024 – NH TherAguix (NHT), a phase II clinical-stage biotechnology company specializing in the development of novel nanomedicine solutions for precision radiotherapy in oncology, today announced the **completion of enrollment in NANO-GBM phase Ib/II trial,** evaluating the combination of AGuIX® nanoparticles with radiotherapy and temozolomide in the treatment of newly diagnosed glioblastoma **and the publication of the positive Phase Ib outcomes** and MRI-based biodistribution data from this trial in the journal Clinical and Translational Radiation Oncology under the title **"**NANO-GBM trial of AGuIX nanoparticles with radiotherapy and temozolomide in the treatment of newly diagnosed Glioblastoma: Phase Ib outcomes and MRI-based biodistribution**"**.

Glioblastoma progression occurs mainly within the tumor volume after treatment by radiotherapy. To address this challenge, a radiosensitization strategy with intravenous administration of AGuIX® nanoparticles is being explored in the NANO-GBM phase Ib/II trial (NCT04881032), which is the first-in-human use of these nanoparticles with radiotherapy and chemotherapy for the treatment of newly diagnosed glioblastoma.

Developed by NH TherAguix, AGuIX® is designed to improve tumor targeting and increase radiobiological damage to tumor tissue locally, thanks to its radiation signal amplification capabilities, in the purpose of expanding lifespan of cancer patients.

Enrollment completion

Nano-GBM is a multicentric, randomized, open-label and non-comparative Phase Ib/II trial. These patients with unresected or partially resected glioblastoma receive four injections of AGuIX® in combination with temozolomide (75 mg/m²/day) and radiotherapy (60 Gy in 30 fractions of 2 Gy), followed by adjuvant temozolomide according to Stupp protocol, as the standard of care.

The aim of the phase II study is to randomize patients within two arms: i) an experimental arm in which patients are treated with AGuIX® at a dose of 100 mg/kg in combination with radio chemotherapy (40 patients), and ii) a control arm in which patients are treated with radio chemotherapy alone (20 patients). To date, all patients of the phase II have been successfully enrolled.

The primary endpoint of this phase II study is progression-free survival at 6 months. Secondary endpoints include AGuIX® distribution in tumors, progression-free survival, overall survival, overall objective response rate and the safety profile of AGuIX® in combination with radiotherapy and temozolomide.

The Phase II final data are expected by mid-2026**.**

In May 2024, AGuIX® has received Fast Track designation from the U.S. Food and Drug Administration (FDA) as a next-generation radio-enhancer for the treatment of malignant gliomas, particularly glioblastoma (GBM). The Company has recently submitted a dossier for a PRIME designation from the European Medical Agency (EMA).

NH TherAguix is also preparing to launch a multicentric, randomized, double-blind pivotal trial in patients with recurrent glioblastoma in 2025.

Publication of the positive Phase Ib outcomes and MRI-based biodistribution

In the Phase Ib part of the NANO-GBM trial, eligible patients were aged 18 to 75 years with newly diagnosed and histologically confirmed glioblastoma with unresected or partially resected glioblastoma. A dose escalation approach was applied to assess 3 dose levels of AGuIX®: 50 mg/kg, 75 mg/kg and 100 mg/kg. Patients were treated with radiotherapy (60 Gy), and concomitant and adjuvant temozolomide. Four intravenous injections of AGuIX® were delivered during radiotherapy and concomitant temozolomide.

The goal of the phase Ib was to determine the recommended phase II dose (RP2D) by the evaluation of the occurrence of dose-limiting toxicity (DLT), and to evaluate pharmacokinetic and AGuIX® biodistribution in glioblastoma on MRI based images.

Eight patients were enrolled and have successfully received four intravenous injections of AGuIX®: at 50 mg/kg (1 patient), 75 mg/kg (1 patient), and 100 mg/kg (6 patients). No AGuIX®-related DLTs were observed, leading to the determination of the RP2D of AGuIX® as 100mg/kg for continuation in the ongoing phase II multicenter randomized trial.

Moreover, the pharmacokinetic data confirmed previous results obtained in the Nanorad study, with AGuIX® mean AUC increasing with dose and a mean plasmatic half-life ranging from 0.84 to 1.41 h.

The quantification assessment confirmed the precise and specific biodistribution of AGuIX® within the glioblastoma allowing to identify regions with different AGuIX® concentration levels, ranging from: moderate (36-123 µM) to high (123-291 µM) and very high (> 291 µM) concentration. These values are in agreement with range of concentration high enough for inducing a radiosensitization effect according to NH TherAguix knowledge and experience.

These results confirm the good safety profile of AGuIX® (with no occurrence of severe AGuIX®-related toxicity) and the widespread dispersion of nanoparticles throughout glioblastoma. Those outcomes support progression to the multicenter and randomized phase II, utilizing an RP2D of AGuIX® of 100mg/kg (4 injections).

Pr. Julian Biau, MD, Radiation Oncologist at Centre Jean Perrin (Clermont Ferrand, France), principal investigator of the NANO-GBM study said: *"We are very pleased to announce the lack of toxicity related to AGuIX® and the extensive dispersion of nanoparticles throughout the glioblastoma, as promising in the perspective of the upcoming Phase 2 results. We believe that AGuIX® nanoparticles represent a very promising option to demonstrate a radiosensitizing effect and are happy to continue this cutting-edge clinical trial to hopefully demonstrate clinical benefit for those patients with poor prognosis factor".*

Dr. Olivier de Beaumont, CMO of NH TherAguix said: "*We sincerely thank Pr. Biau and his team at the Centre Jean Perrin for their constant and fruitful collaboration. This study could lead to the development of a new standard of treatment for these devastating cancers, addressing a significant medical need today."*

Vincent Carrère, CEO of NH TherAguix, added: *"This publication in a high-impact journal like Clinical and Translational Radiation Oncology is a significant milestone, confirming the strong safety profile of AGuIX®, its robust EPR effect, and its biodistribution in glioblastoma tumors. These findings bolster our high expectations for potential clinical benefits in patients with glioblastoma. We are also pleased to have completed enrollment ahead of schedule, bringing us closer to final results by mid-2026, which may demonstrate AGuIX®'s efficacy in combating this deadly disease. These results will be pivotal for the further clinical development and eventual commercial approval of AGuIX® to address this critical medical need."*

About NH TherAguix: www.nhtheraguix.com

NH TherAguix is a Phase 2 biotech company developing AGuIX®, an innovative nano drug to treat tumors and metastases in patients undergoing radiotherapy. It is estimated that approximately 60% of cancer patients receive radiotherapy.

AGuIX® concentrates a high number of gadolinium atoms (~15) in an ultrasmall size object (~5 nanometers). Its pharmacological properties and its mode of action by bio-distribution allow it to enhance the precision and effectiveness of the radiotherapy directly in the heart of tumours and confer it a pan-cancer potential.

AGuIX® is currently being evaluated in multiple Phase 2 randomized trials across various cancer types:

- in brain metastases using either whole brain radiation therapy (NANORAD2, CHUGA, Grenoble, France) or stereo-radiosurgery (NANOBRAINMETS, Dana Farber Brigham Cancer Center, Boston, USA),
- in glioblastoma (NANOGBM, multicentric, Clermont Ferrand, France),
- in pancreatic and lung cancers (NANOSMART, Dana Farber Brigham Cancer Center, Boston, USA).

To date, over 200 patients have been treated with AGuIX® with an excellent safety profile and promising preliminary clinical results.

The innovation and technology behind the development of AGuIX® are protected by 18 patent families and have been extensively tested in various preclinical models, with results published in more than 80 high-impact, peer reviewed scientific publications.

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