



NH TherAguix announces the publication of promising preclinical results of AGuIX[®] in combination with targeted radioligand therapies (TRT) in <u>the Journal of Nuclear Medicine (October, 2023)</u>.

Paris, December 18th 2023 – NH TherAguix SA ("NHT"), a Phase II clinical stage biotechnology company developing AGuIX[®], a nanodrug to treat radiotherapy eligible tumours and metastases across oncology indications, announces the publication of new promising preclinical data of AGuIX[®] in combination with targeted radioligand therapies (TRT) in the Journal of Nuclear Medicine (October, 2023).

The paper depicts how AGulX[®], an already proven potent radioenhancer for external radiotherapy, can also potentiate internal radiotherapy, i.e. [177] Lutetium-labeled radiopharmaceutical compounds.

Key results of the publication in terms of efficacy are as follows:

✓ Of several protocols tested in a model of ovarian peritoneal carcinomatosis, the injection of 5 mg of AGulX[®] twice per day at 24h and 72h after 5 mBq of [177] Lu-DOTA-Trastuzumab was optimal for maximizing the therapeutic efficacy of the combination of AGulX[®] and TRT.

✓ The combination of AGulX[®] and TRT results in increased radioenhancement and therapeutic efficacy, while reducing the total activity injected.

✓ Compared to TRT alone (1/8 objective response, 3/8 progressive disease, 4/8 stable disease), mice treated with the combination AGuIX[®] and TRT showed a better objective response (5/8 objective responses, 3/8 stable disease, 0/8 progressive disease). In addition, median survival was significantly increased from 30-33 days for saline control animals and trastuzumab+AGuIX[®] control animals respectively (p < 0.0001), to 69 days (p <

0.016) for mice treated with TRT and 97 days (for AGulX^{\circ} combined with TRT (with 2 mice cured). The median survival of TRT alone was 69 days (p < 0,016).

The mechanisms of action are being deciphered but we have already demonstrated that:

✓ As previously shown in scientific publications, AGulX[®], colocalizes with lysosomes at the cellular level. Interaction with [177]Lu-mediated irradiation leads to lysosome disruption and production of iron mediated-reactive oxygen species leading to burst of oxidative stress and tumor cell death.

✓ Monte Carlo simulations showed that the presence of AGuIX[®] does not modify the total dose delivered by [177]Lu to tumors. The main modification was the increased production of Auger electrons (+13%) with a very localized energy deposit around the nanoparticle – while other radiations such as photon electric remained unchanged. Further studies are required to confirm the role of Auger electrons in lysosome disruption.

This research work has been driven by Garcia-Prada CD, Carmes L, Atis S, Parach A, Bertolet A, Jarlier M, Poty S, Garcia DS, Shin WG, Du Manoir S, Schuemann J, Tillement O, Lux F, Constanzo J, Pouget JP, among a collaboration including Institut de Recherche en Cancérologie de Montpellier (IRCM) as leader of the collaboration, Massachusetts General Hospital and Harvard Medical School (Boston, US), Institut Lumière Matière (Lyon) and NH TherAguix. This work was partially granted by Région Occitanie.

As said by Julie Constanzo and Jean-Pierre Pouget from IRCM "To our knowledge, this is the first study to demonstrate the beneficial effect of a TRT-AGUIX[®] combination. These results could not be taken for granted, as the radiobiological mechanisms of action involved in TRT differ from those of conventional external radiotherapy. This combination opens up new therapeutic prospects for patients with metastatic cancer."

"Although we could hypothesize from theory that such a combination between AGuIX[®] and a radiopharmaceutical could be beneficial, the work reported by Garcia-Prada CD *et al.* as a first preclinical proof of concept is extremely important for us. These preclinical results, associated to the current clinical development of AGuIX[®] (c.162 patients treated) pave the way for a translation into clinical development." said Géraldine Le Duc, CSO of NH TherAguix.

About NH TherAguix (<u>www.nhtheraguix.com</u>)

NH TherAguix is a Phase 2 biotech company developing AGuIX[®] to treat tumours and metastases in patients treated by radiotherapy. It is estimated that c.60% of cancer patients undergo radiotherapy treatment today. AGuIX[®] is currently assessed in 4 Phase II randomized trials 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) as well as in pancreatic and lung cancers (NANOSMART, Dana

Farber Brigham Cancer Center, Boston, USA). Results of the First in Human Phase I trial in brain metastases (NANORAD1, CHUGA, Grenoble, France) have confirmed AGuIX[®] safety and efficacy profile (Verry et al, Science Advances 2020, Verry et al. Radiotherapy & Oncology, 2021). AGuIX[®] has been extensively tested in various preclinical models and the results published more than 80 times in high impact publications. This innovation is protected by 18 patents families.

NH TherAguix was established in 2015 after 10 years of academic research that led to the invention of AGuIX[®] and the discovery of its radioenhancement effect. Altogether, NH TherAguix raised around €40M of dilutive and non-dilutive funds, including a €13M A series in 2019, led by Bpifrance with Arbevel, Omnes and Supernova.

NH THERAGUIX

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