



NH THERAGUIX

announces the enrolment in Boston of the 2 first patients in its clinical trials NANOBRAINMETS Phase II targeting brain metastasis and NANOSMART Phase Ib/II targeting pancreatic cancer and cancerous lung lesions

Meylan (France) and Boston (US), October 1st, 2021

NH TherAguix (“NHT”), a French clinical stage company specialising in the development of innovative nano medicines for the radiotherapy treatment of cancer indications, announces today the enrolment of the 2 first patients in the NANOBRAINMETS Phase II trial targeting brain metastases and the NANOSMART Phase I/II trial targeting pancreatic cancer and cancerous lung lesions, sponsored by Dana-Farber Brigham Cancer Center and led by radiation oncologists Drs. Ayal Aizer and Jonathan E. Leeman, respectively.

These 2 randomized clinical trials will investigate the efficacy of the combination of AGuIX[®] intravenous injection with standard of care radiotherapy to increase survival and quality of life of patients.

NANOBRAINMETS is a double-blind, placebo-controlled randomized Phase II clinical trial of stereotactic radiation with or without AGuIX[®] gadolinium-based nanoparticles in the management of brain metastases at higher-risk of local recurrence with radiation alone. The objective is to test the hypothesis that, among 134 patients with brain metastases at higher-risk of local recurrence with radiation alone, AGuIX[®] gadolinium-based nanoparticles combined with brain-directed stereotactic radiation will improve local control, using Response Assessment in Neuro-Oncology – Brain Metastasis (RANO-BM) criteria, relative to brain-directed stereotactic radiation alone. This study follows the results already obtained by NH TherAguix through the NANORAD Phase I trial that demonstrated very promising results¹.

Dr. Ayal Aizer stated, “Increasingly, the mainstay of management for patients with brain metastases involves brain-directed stereotactic radiation. However, prior studies have identified subsets of patients with brain metastases for whom such radiation may be insufficient to achieve an efficient treatment. We have been searching for methods to safely and viably enhance radiation effect in these patients. Our study will provide insight as to whether AGuIX[®] is of potential benefit to patients with difficult to control brain metastases. We are enthusiastic about offering this study to patients managed at Dana-Farber Brigham Cancer Center.”

¹ Targeting brain metastases with ultras-small theranostic nanoparticles, a first-in-human trial from an MRI perspective. Verry C *et al.* **Science Advances**. 2020

Theranostic AGuIX nanoparticles as radiosensitizer: A phase I, dose-escalation study in patients with multiple brain metastases (NANO-RAD trial) Verry C. *et al.* **Radiotherapy & Oncology**, 2021


















NANOSMART is a Phase Ib/II clinical trial, with two treatment arms for patients diagnosed with either locally advanced pancreatic cancer or centrally located cancerous lung lesions. The radiotherapy will be performed using an MRI-Linac machine, allowing for the delivery of precise MRI-guided radiotherapy after intravenous AGuIX® injection.

During the Phase Ib part of the trial, patients will receive five fractions of stereotactic body radiation therapy in addition to one dose of AGuIX® nanoparticles seven days prior to radiation treatment and another one with the first fraction of radiation. Patients with cancerous lung lesions receiving radiation over a two-week period will be provided with an additional dose of AGuIX® along the fourth fraction of radiation. The Phase Ib part of the study will establish the dose of the drug used for each disease cohort during Phase II. At this point patients will be randomized to receive AGuIX® or not. NH TherAguix and Dana-Farber Brigham Cancer Center target an enrolment of 100 patients.

Dr. Jonathan E. Leeman stated, “There is a critical need to improve outcomes for patients with locally advanced unresectable pancreatic cancer or with centrally located lung tumors where effective treatments are limited. We believe this to be a very important study, which will evaluate the safety and benefits of AGuIX® gadolinium-based nanoparticles in combination with highly precise radiotherapy delivered using our MRI linear accelerator at the Dana-Farber Brigham Cancer Center. We greatly look forward to offering this opportunity to our patients.”

“The launching of these 2 clinical trials with Dana-Farber Brigham Cancer Center as the sponsor in the United States is a very important and significant step in our clinical development. This trial with Dana-Farber Brigham Cancer Center echoes with a historical and visionary collaboration initiated and pursued by Prof. Olivier Tillement and Dr. François Lux, co-founders of NH TherAguix (ILM, University of Lyon, France), and Dr. Ross Berbeco (Director of Medical Physics Research, Dana-Farber Brigham Cancer Center). Their drive for developing nanomedicine using AGuIX® started in 2010 and resulted in significant patents and scientific publications. This collaboration is still very active through an NIH grant of nearly \$3M awarded to NH TherAguix in 2020 for the AGuIX® second generation platform. We are very grateful and happy about this long-term relationship with our US colleagues,” **said Géraldine Le Duc as CEO of NH TherAguix.**

Following the enrolment of the 2 first patients in its clinical trials NANOBRAINMETS and NANOSMART, the clinical trials pipeline of NH TherAguix is as follows, with 4 clinical trials currently recruiting and 3 more expecting to be launched by the end of 2021:

Indications	Protocole	Location	Preclinical	Clinical Stage			Partners	Next Milestone
				Phase 1b	Phase 2	Phase 3		
Brain Metastases 	NANORAD 2 100 (50)			Trial finished and published	Ongoing 51 / 100			Interim report Q1-2022
	NANOBRAINMETS 136 (67)			Ongoing 1 / 136			Interim report Q3-2023	
Cervical Cancer 	NANOCOL 12 (12)			Ongoing 9 / 12			Phase 1 results Q2-2022	
Pancreatic / Lung Cancer 	NANOSMART 100 (60)			Ongoing 1 / 40			Phase 1 results S2-2022	
Glioblastoma 	NANO-GBM 66 (46)			Phase 1b-2 APPROVED			Phase 1 Launch Q4-2021	
Other Indications (Rectal, Head & Neck...)	NANOPRO 46 (46) NANORT-MSK 132 (66) NANOREC 34 (34)	 		NANOPRO : APPROVED Ph2 NANORT-MSK : APPROVED Ph2 NANOREC : PREPARATION Ph1b-2			Launch Q4-2021 Q4-2021 S1-2022	

Registrational trials to be launched in 2022

About AGuIX®:

AGuIX® is a bimodal nanomedicine, with a radiosensitizing effect and visible in MRI that has been extensively published (>70 papers). AGuIX® demonstrated a good post-injection safety, MRI contrast enhancement and early evidence of radiosensitization when combined with radiation therapy in patients with brain metastases (NANORAD 1 Phase Ib trial, Grenoble Alpes University Hospital, France). AGuIX® is currently also being tested through another Phase II trial in brain metastasis, using whole brain radiation therapy (NANORAD 2). In parallel, a Phase Ib trial for advanced cancer of the cervix (NANOCOL) is underway at the Gustave Roussy Institute in Paris.

About NH TherAguix (www.nhtheraguix.com):

NH TherAguix, headquartered in Meylan (France), is working on an innovation in nanomedicine, the drug candidate AGuIX®, whose potential clinical efficacy is based on nanometric structuring that allows its intravenous injection and the combination of three essential properties to fight tumors: targeting, imaging, and treating. The AGuIX® technology is therefore part of the concept of theranostics, which corresponds to a combination of therapy (radiosensitizing effect) and diagnosis (visible in MRI), and more widely in the personalized medicine of the future.

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