NH TherAguix

A Nanomedicine Company

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The Team

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KOLs- Early Followers

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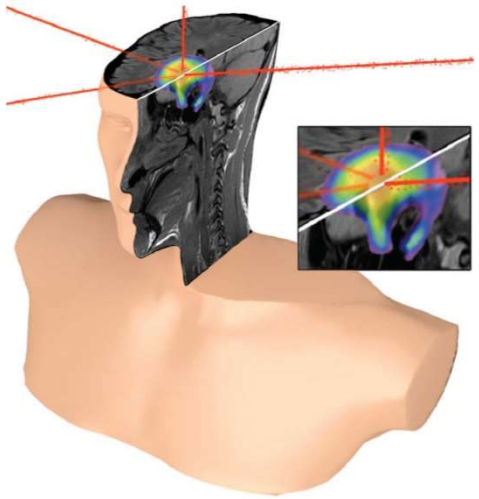
Pr. K. Price - Queens University
Dr. R. Berbeco - Harvard
Dr. G. Appelboom - Stanford

Advisory committee

B. Bigot	General Director CEA
Pr. J.F. Le Bas	Neuroradiologist
F. Mouthon	CEO Theranexus
P.Archinard	CEO Transgene

The Context



Taken from Institut Curie report

30% of people will have a **cancer**

60% of cancer patients will receive a **radiotherapy** (RT) as a treatment
(≈ 4 million people/year)

PROBLEMS:
- **30%** ***radioresistant*** *or* ***badly positioned*** *tumors*
- **70%** *secondary* ***adverse effects*** *of RT*

CONSEQUENCES:
- **full efficacy of RT constrained**
- **quality of life negatively impacted**

The AGuIX® solution: a theranostic solution

See What You Target & Target What You See

Targeting

Specific tumour accumulation

High precision

Unique administration

Intravenous (IV) injection

Imaging

Precise treatment contour

Patient selection

Personalized treatment

Treatment

Activatable drug

Cytotoxic under radiations

Local Radiation Booster

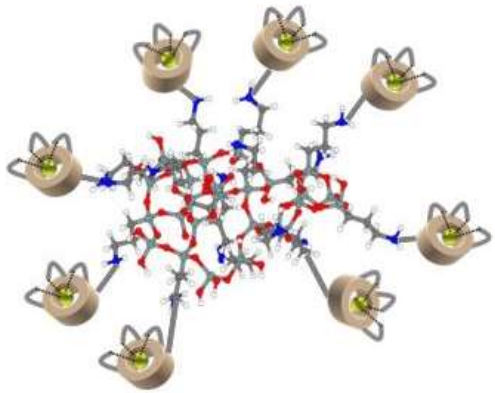
*AGuIX: « **A**ctivation and **Gu**idance of **I**rradiation by **X**-ray »*

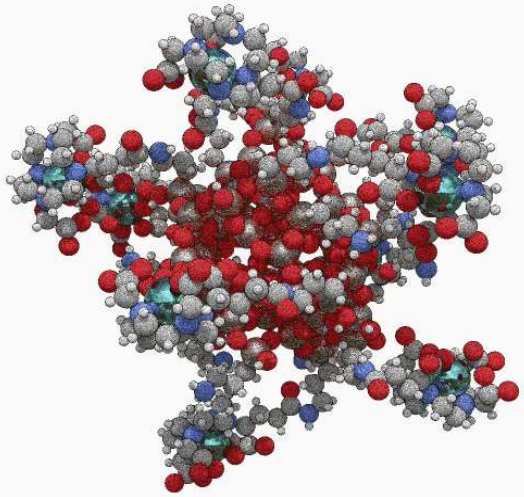
The AGuIX® Technology

no drug delivery, passive targeting

Structure and composition of AGuIX® (7 brevets et 1 FTO)

Polysiloxane + gadolinium cyclic chelates





Size 2-5 nm

Gadolinium

- high gadolinium content
- **paramagnetic** properties → **MRI**
- **radiosensitizing** effect → **radiotherapy** (RT)

Ultrasmall size

- **IV** injection
- tumor **targeting**
- **renal clearance**

Safe composition

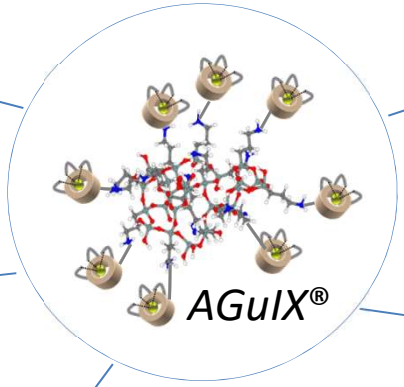
- **biocompatible** components

Preclinical Proof of Concept (PoC)

10 years of academic research

In vivo radiotherapy efficiency in 7 tumours models
brain, head&neck, pancreas, lung, melanoma

In vivo MRI contrast uptake in tumour models



Regulatory toxicity (rats/monkeys)
Scale-up and industrialization of the production

In vitro demonstration of radiosensitizing effects

- 10+ collaborations
(Harvard, MIT, Yale, IGR, Stanford)
- 50+ publications
- 4 patents (5 +)
- 9-12 PhD students
- POC in 7 in vivo tumour models

O Tillement designed the AGuIX®
G Le Duc discovered the radiosensitizing effect

***Le Duc G**, Miladi I, Alric C, Mowat P**,** Bräuer-Krisch E, Bouchet A, Khalil E, Billotey C, Janier M, Lux F, Epicier T, Perriat P, Roux S**, Tillement O.** ACS Nano. 2011 Dec 27;5(12):9566-74*

NANORAD Clinical Trial: A First-in-Human

Sponsor CHU Grenoble Alpes

PI Dr C. Verry , Radiotherapy Department
Head: Pr J. Balosso

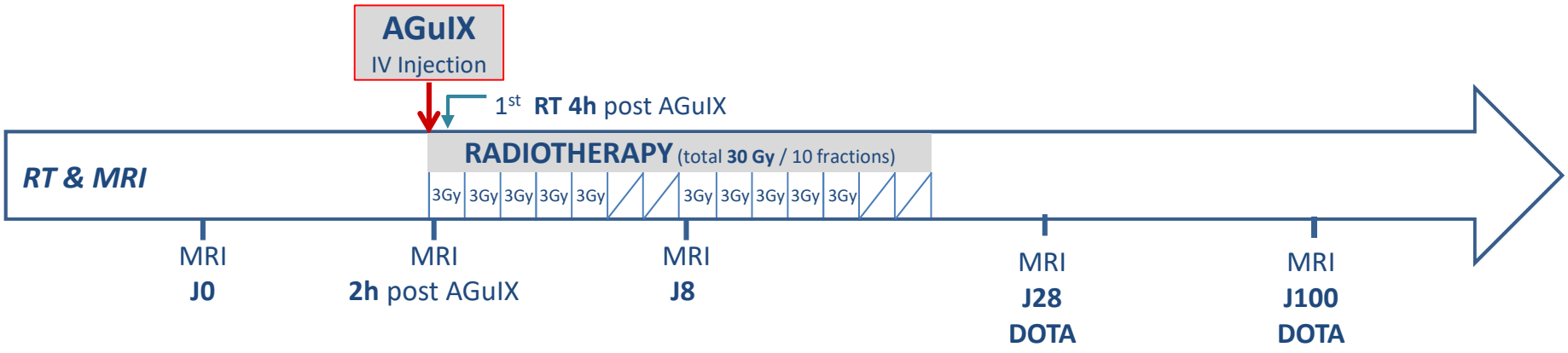
Dose-escalation 5 dose levels (n=3 patients)
15, 30, 50, 75 and 100 mg/kg

Inclusion criteria

Multiple BM ineligible for local treatment by surgery or stereotactic radiation

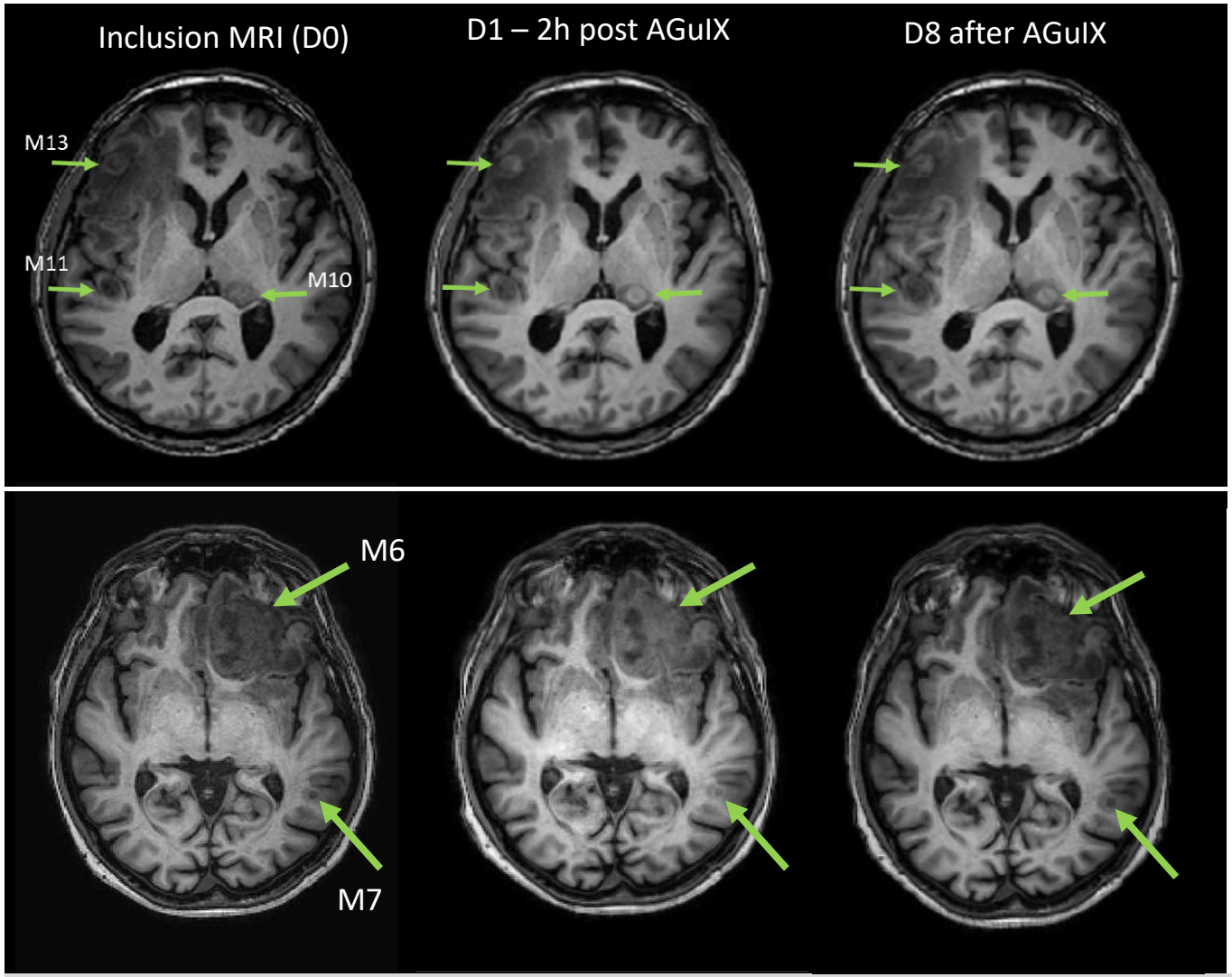
Primary cancer : Melanoma, Lung , Breast, Colon

25 % of cancer patients, Life expectancy < 4 months

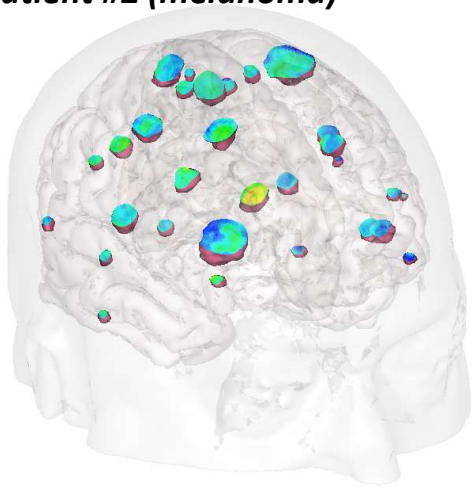


Tumor Targeting

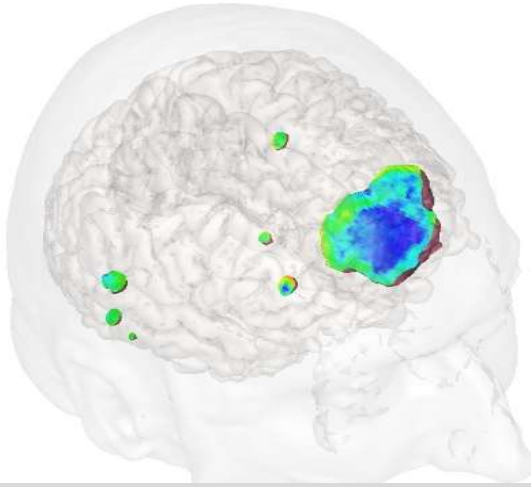
MRI T_1 enhancement of metastases (case of 15 mg/kg)



Patient #2 (melanoma)



Patient #3 (lung)



→ ***good AGuIX uptake****, i.e.* ***targeting****, for* ***every tumor type*** *even at the* ***lowest administrated dose***

→ ***persistent accumulation*** *of the AGuIX® product up to 1 week*

NANORAD Phase I on brain metastases
Intermediate results after 9 patients
(15 patients done – 12 evaluated)

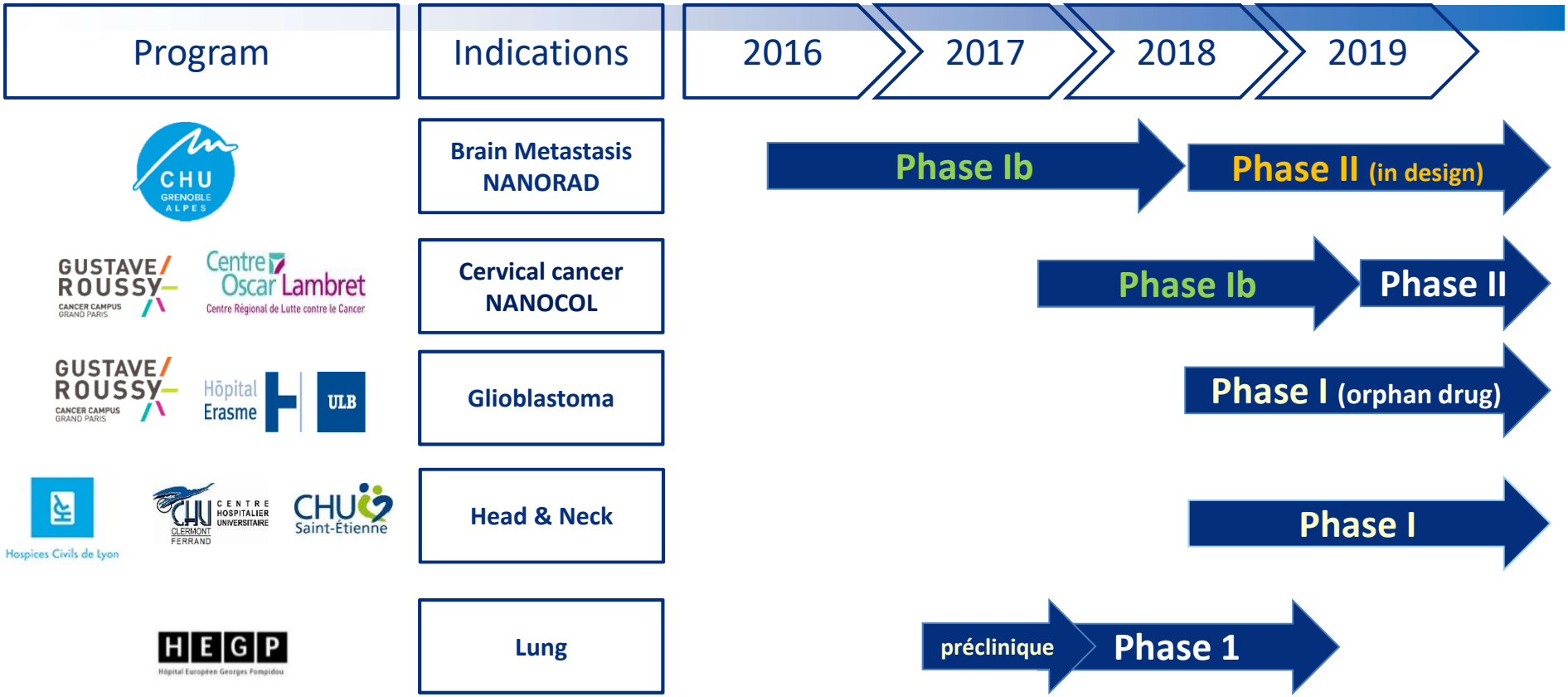
15 mg/kg	30 mg/kg	50 mg/kg	75 mg/kg	100 mg/kg
n=3	n=3	n= 3		

✓ **First proof of safety**
No adverse effects due to the injection of the drug (even minor)
Fast blood half life and renal elimination

✓ **First proof of contrast uptake**
Contrast uptake for 9/9 patients (15 - 30 – 50 - 75 mg/kg)
(melanoma, NSCLC, Colon carcinoma)
Remanence of the contrast enhancement 8 days after injection in tumour tissues

✓ **Therapeutic response**
Response to the treatment (WBRT + AGuIX)
Clinical benefit
Correlation between AGuIX contrast uptake and tumour response
Dose effect

Pipeline of clinical trials



Summary

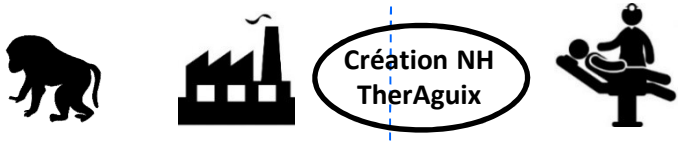
2005 2010 2015 2016 2017

Preclinical PoC - Academic institutions

- 10+ collaborations
- 50+ publications,
- 4 patents (2+)
- 9-12 PhD students

→ PoC 6 *in vivo* tumours models

~ 10 Millions € invested
academic



Scale-up

Regulatory toxicity

→ 1000 vials for clinical trials (Carbogen)

1,5 Millions € invested
academic

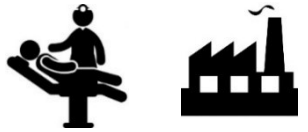
Clinical trials

- First In Man Nanorad

3 Trophies

- Tremplin-Senate
- France Biotech
- R2B Onco

Capital 100 k€
Sales 120 k€
BPI 200 k€
Fund Raising 600 k€



Clinical trials

- *Nanorad (12 pat/15)*
- *Nanocol trial accepted*
- *Nanorad Phase 2 in design*

Production of Batch 2

On going, for Phase 2

Fund raising 1,2 M€
Bank Loan BPI 200 k€
SATT Pulsalys 300 k €