

# How drug delivery is enabling a clinical trial for Glioblastoma

With Christian Jones, CCO at Nanoform &  
João Seixas, PhD, CEO at TargTex

Featured partnership talk at PODD 2022

October 25th, 2022, 10am EDT



# Disclaimer

## Forward-Looking Statements

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# Executive Summary

## TargTex and Nanoform Present Tumour Eradication in Rodents from a Nanoformed Glioblastoma drug

TargTex CEO Dr João Seixas and Nanoform CCO Christian Jones presented on October 25<sup>th</sup> highly promising *in-vivo* data, enabled by a nanoformed drug product for the treatment of **glioblastoma multiforme (GBM)**, at the PODD Conference (Partnerships and Opportunities in Drug Delivery), in Boston USA. The data was generated for a planned Phase 1/2a clinical trial, due to commence in early 2024. Nanoform delivers GMP grade nanoformed material to TargTex for the clinical trial.

Nanoform is an innovative nanoparticle medicine enabling company and TargTex is a European biotech company and a customer to Nanoform.

The drug is a selective Ca<sup>2+</sup> channel blocker\* delivered by implantation at the site of the resected tumor in the brain. Nanoform and TargTex have collaborated in the optimization of a **hydrogel formulation enabled by nanoformulation of the drug**. Other 'technology and approach'-providers previously failed to deliver the necessary performance.

The study was conducted in a rat model for GBM in which GBM tumor cells are injected into the brain. After 2-3 weeks, the nanoformulated hydrogel was delivered locally in the brain of the animal, on top of the tumor.

**The study results showed long term survival of 40% of the treated animals and no microscopic tumor cells were detected in these animals at sacrifice.** The nanoformed drug product provided a controlled release and deep drug diffusion across the brain parenchyma. The data showed no systemic exposure and the drug was not toxic at maximum loading concentration.

The study was performed at a sub-therapeutic dose that can be increased by at least 2-fold. Future studies are planned to be performed at increased drug concentrations with the goal to further improve long term survival.

Small is a powerful ingredient in formulations and provides hope for patients, businesses, and drugs. The data further validates Nanoform's potential to enable new therapies by combining capabilities across its service offering: Starmap®, nanoforming, and nanoformulations.



# Introduction to Nanoform



# Nanoform in a snapshot

## The Share

- Listed June 4<sup>th</sup>, 2020, on Nasdaq First North Premier Growth Market in Helsinki and Stockholm
- Tickers: NANOFH and NANOFS
- Significant Nordic, European and US institutional ownership
- All press releases: <https://nanoform.com/en/section/media/press-releases/>

## Nanoform

- Global experts in nanotechnology and drug particle engineering
- ~140 employees, ~30 nationalities, ~40 with PhD degree
- Headquartered in Finland with additional senior staff and board members in Denmark, France, Portugal, Sweden, UK, and US
- >3000m<sup>2</sup> manufacturing site in Helsinki for nanoforming API's
- Strong balance sheet, more than EUR 80m in cash, no debt

## Platform Technology

- CESS® technology for small molecules (chemical compounds) discovered in 2012
- Technology for large molecules (biological compounds) launched in 2020
- Nanoform's clinical results confirm value proposition to the pharma industry





**We were delighted to gather the entire Nanoform team for the unveiling of our new patient statue.**

Embodying our dedication to improving patient lives, it has taken pride of place in our Helsinki headquarters, and it will continue to inspire the Nanoform team to expand the possibilities for patients worldwide.

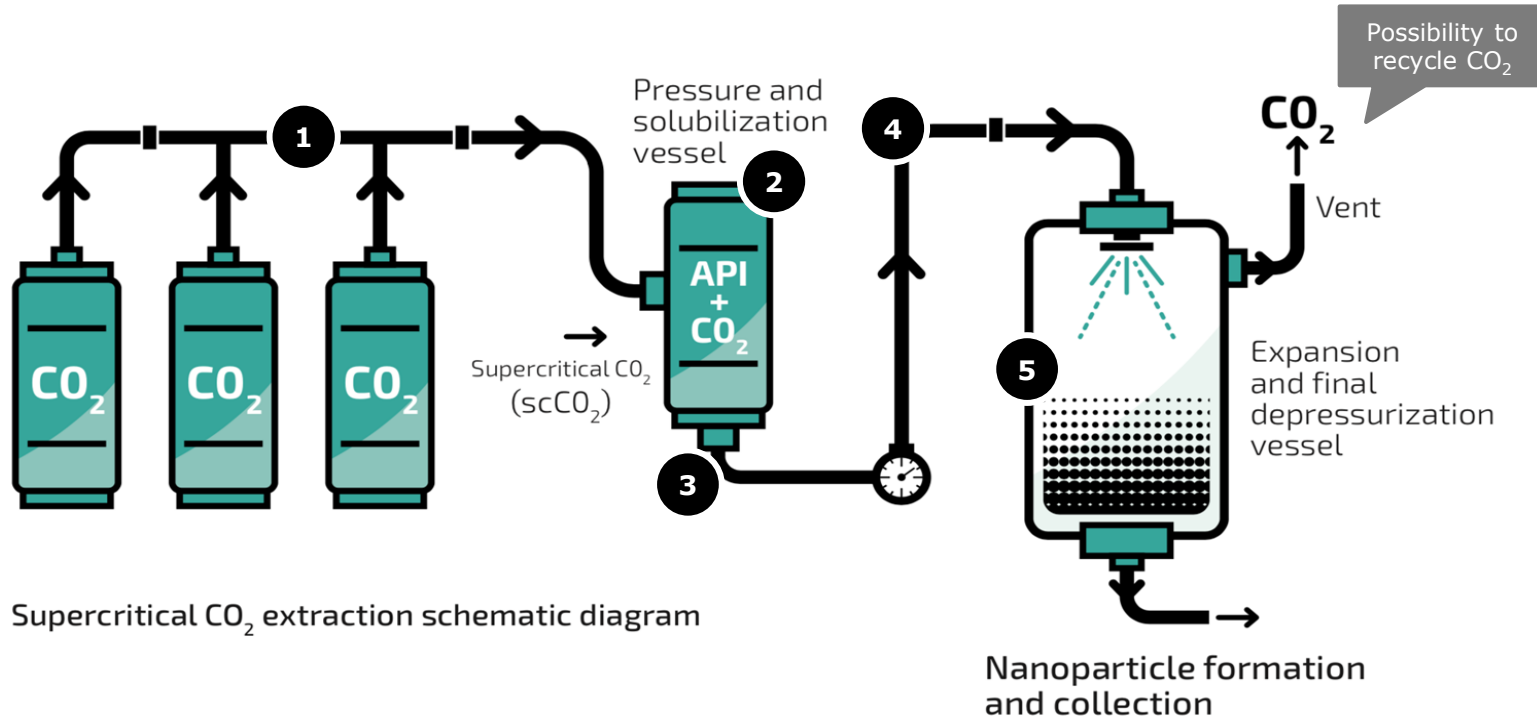


# Our nanoforming technologies



# Patented technology nanoforming API particles

## The Controlled Expansion of Supercritical Solutions - CESS®



> Relatively simple process developed through combining deep knowledge in physics, chemistry and pharma



# Small is a platform enabler across drug delivery

Rapid absorption of poorly soluble Piroxicam



Oral Tablet

Oral Buccal

Respiratory

Nasal &  
Oral

Ophthalmic

Co-Polymer  
Drug  
Delivery

Hydrogel

UK  
Respiratory Biotech  
Localized lung delivery

NPI-001 and NPI-002 enhanced  
ocular tissue penetration



Enhanced drug loading and release  
in hydrogel formulation for brain  
delivery (Glioblastoma)



Rapid absorption of poorly soluble,  
coupled with fast disintegrating ODT



Nasal delivery of CDNF  
for brain penetration and Oral  
delivery of HER096

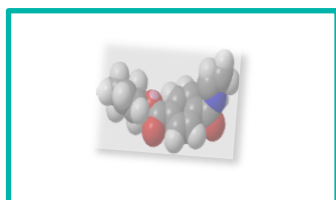
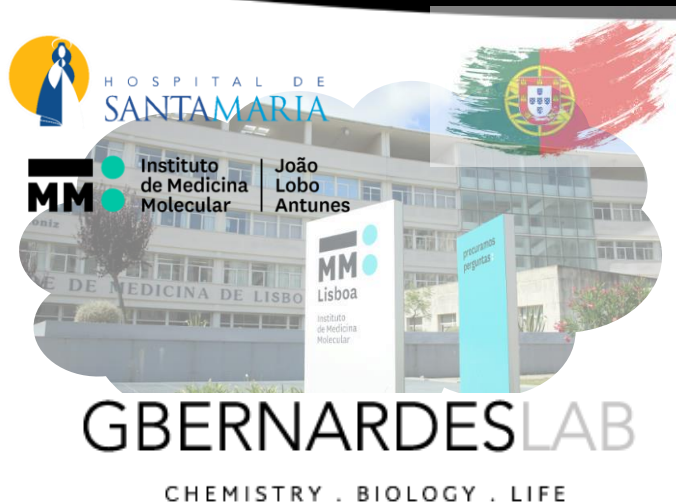


Sustained release delivery

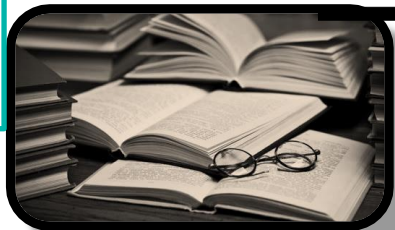
# Glioblastoma: history and progress



# History

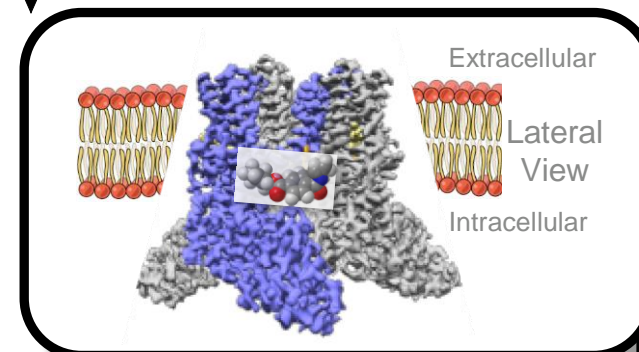


**Small Molecule (SM)** with  
Anticancer Properties Reported



**Machine Learning Algorithm**  
Infers a SM-Target Link

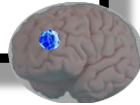
**Target:**  
**Calcium Channel Associated**  
**with Angiogenesis**



**Glioblastoma**  
**(GBM)**



# Glioblastoma (GBM)

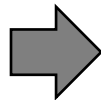
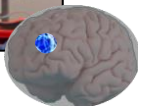


±200k yearly

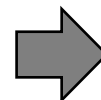
Most common and aggressive primary brain tumor

16 months life expectancy

1 FDA approved **drug** in the last 20 years



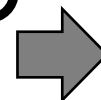
Craniotomy



CHEMOTHERAPY DRUG  
TOXIC

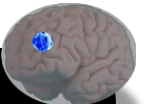


RADIO THERAPY



Blood-  
Brain  
Barrier

**Recurrence  
After ± 9m**



# Developing a solution



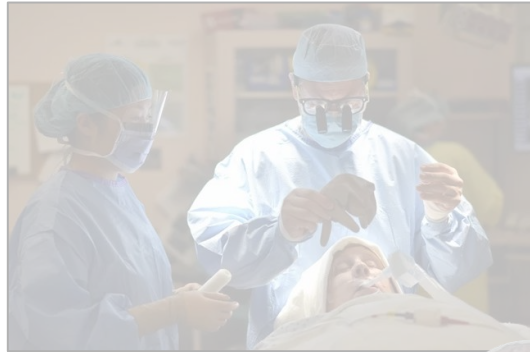
## Drug response in **primary patient** samples

**Does not affect healthy cell** population  
in tumor microenvironment like SoC

Responds to **SoC resistant tumors**

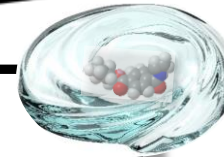
Equipotent against GBM **stem-like cells**





Craniotomy

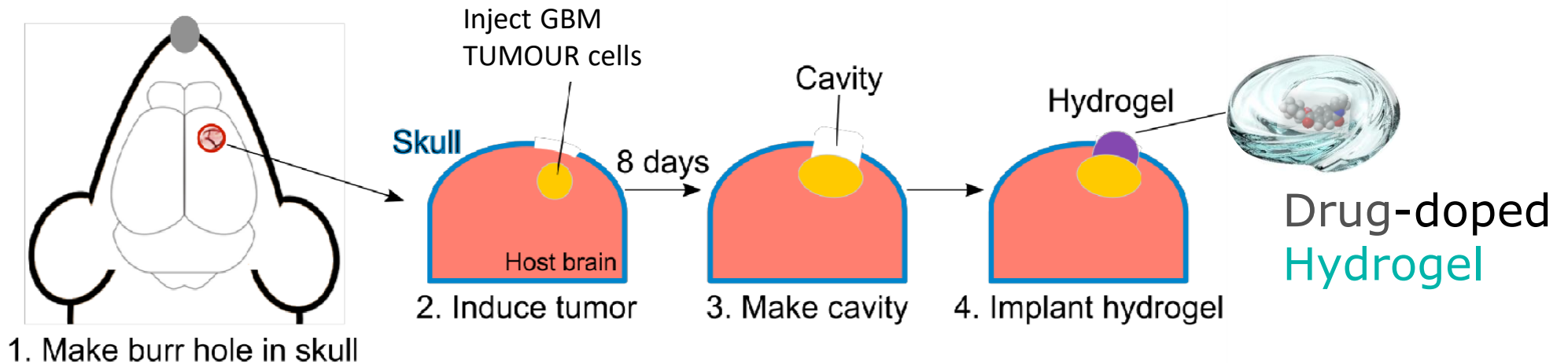
Local implantation of  
selective  $\text{Ca}^{2+}$  channel blocker  
in a hydrogel  
as adjunct to surgery



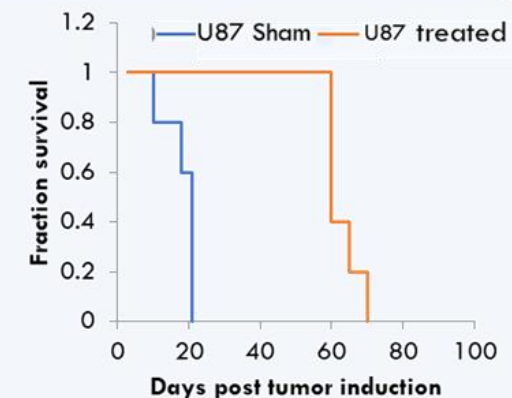
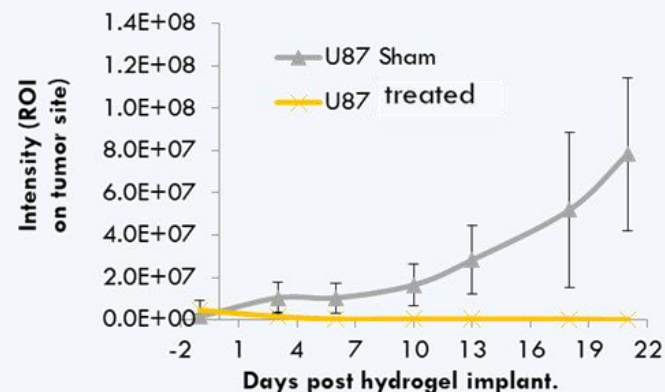
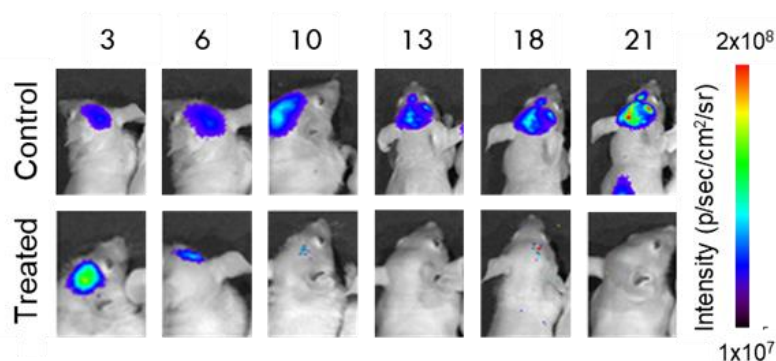
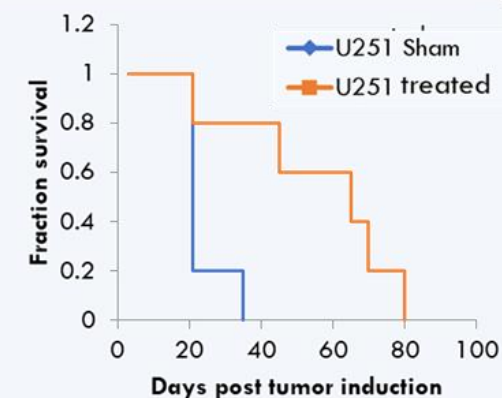
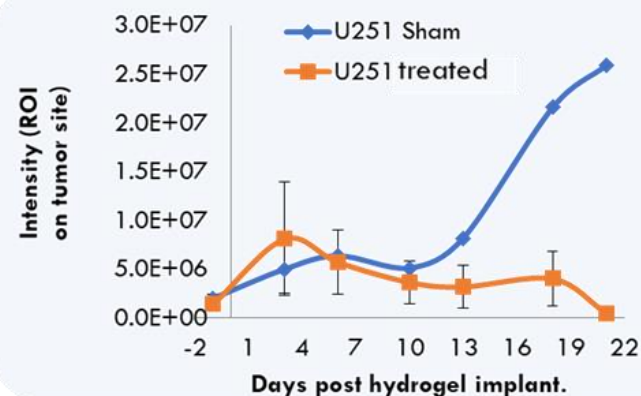
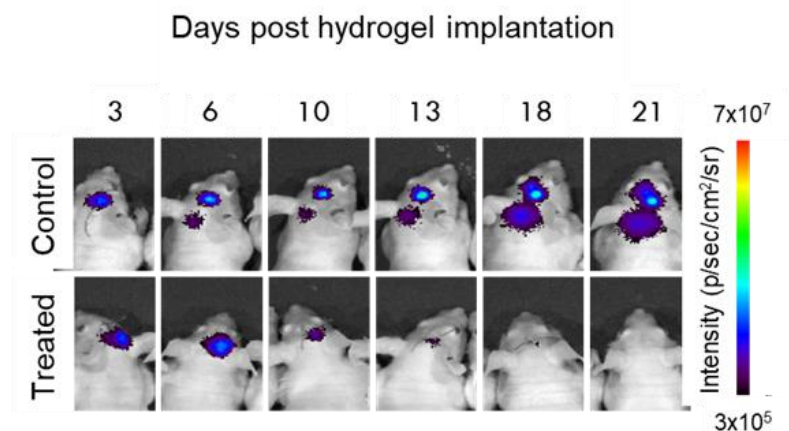
**Avoid  
Recurrence**



*In vivo*  
model

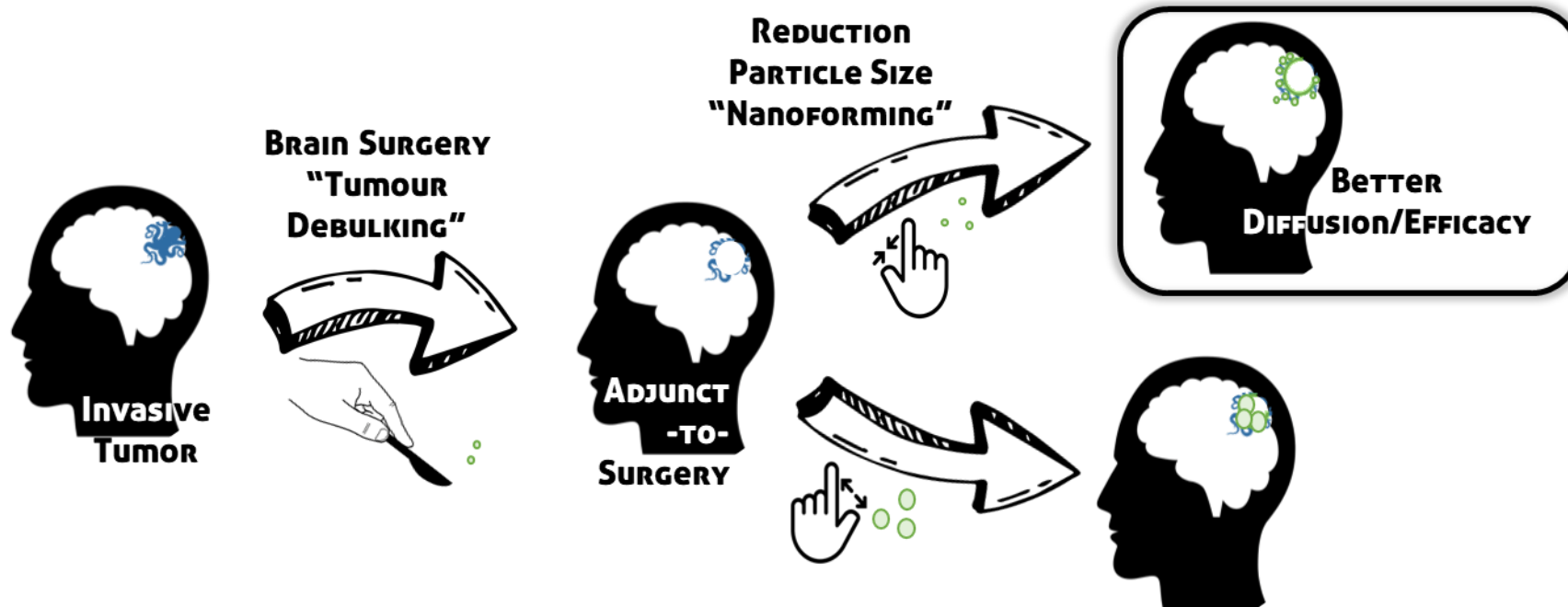


# Validation of localized therapy approach with first prototype hydrogel



Single dose administration of the drug@hydrogel formulation abolishes Primary GBM with safe histological profile

## Brain diffusion & penetration





## Drug Delivery Challenge

The first prototype hydrogel was effective for primary tumor eradication but did not stop tumor recurrence. This formulation also had limited dosing possibility.

## Hydrogel Optimization

- Thermo-responsive hydrogel
- Sterilizable, non-toxic, biocompatible, biodegradable...
- FDA approved excipients
- Controlled drug release
- Increased drug loading

# Development of tailored formulation

## Hydrogel Optimization



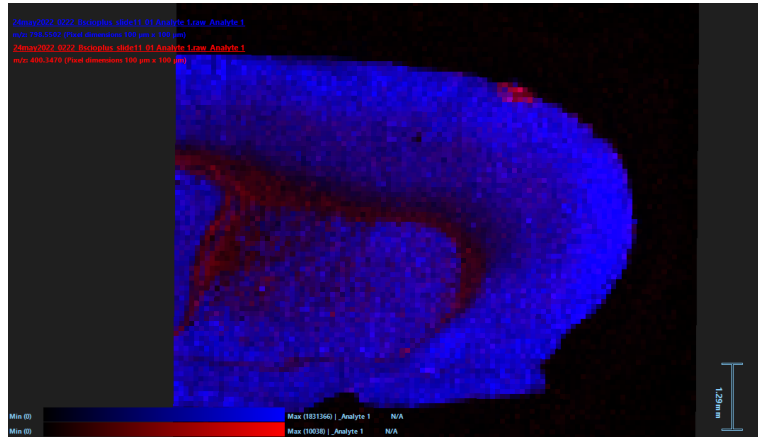
	Excipients Screening	Nanomilling	Nanoformed material
Solubility			
Tuning of release kinetics			
Particle size control			
% API incorporation			
Need for stabilizers and/or additives			
Storage stability			
GMP-scale up			

# Results





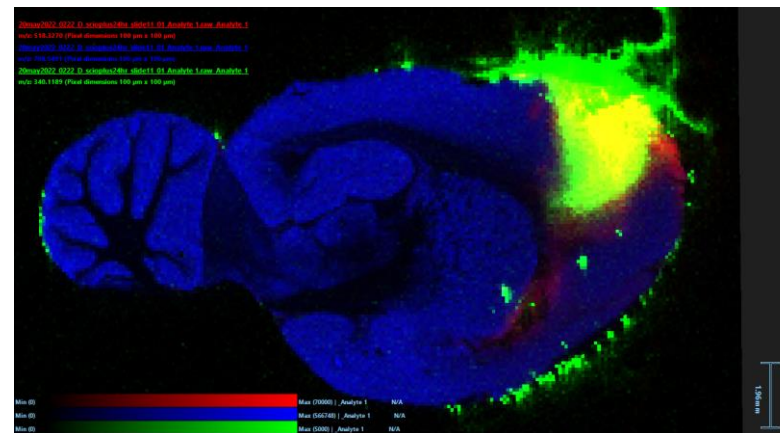
# Development – Results: Nanoformed hydrogel diffusion



Untreated rat brain

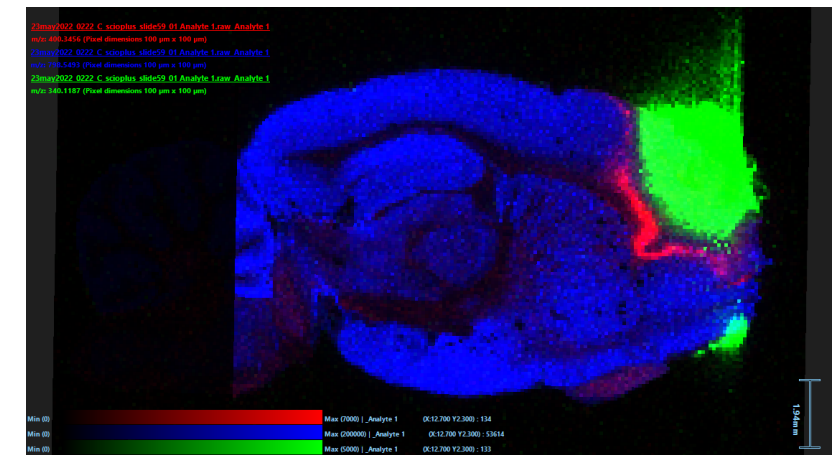
Nanoformed particles enable deep drug diffusion across the brain parenchyma.

24h post-dosing



Drug penetration through rat brain parenchyma (green & yellow)

72h post-dosing

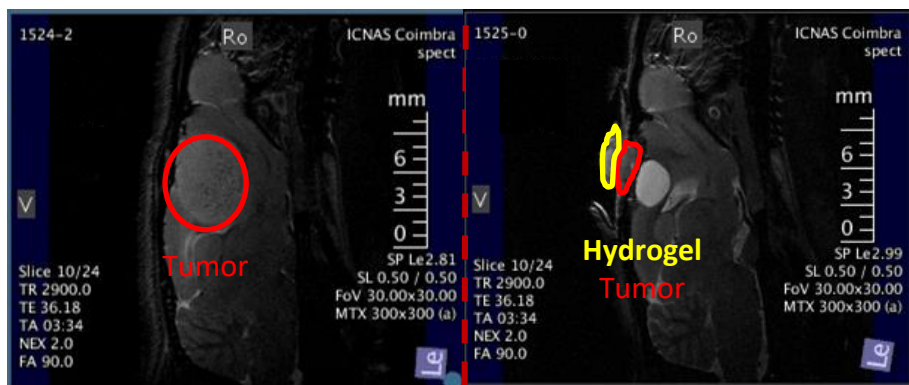


Drug penetration through rat brain parenchyma (green)

# Efficacy – Complete Tumor Eradication with Nanoformed hydrogel

## RNU-U87 xenograft rat model

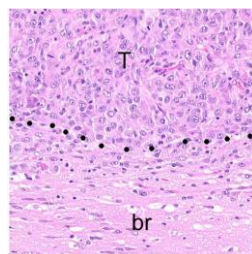
Day 12 post treatment



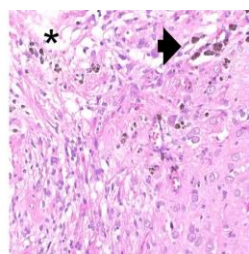
Untreated

Treated group

No microscopic tumor cells  
detected at LTS' time of  
sacrifice

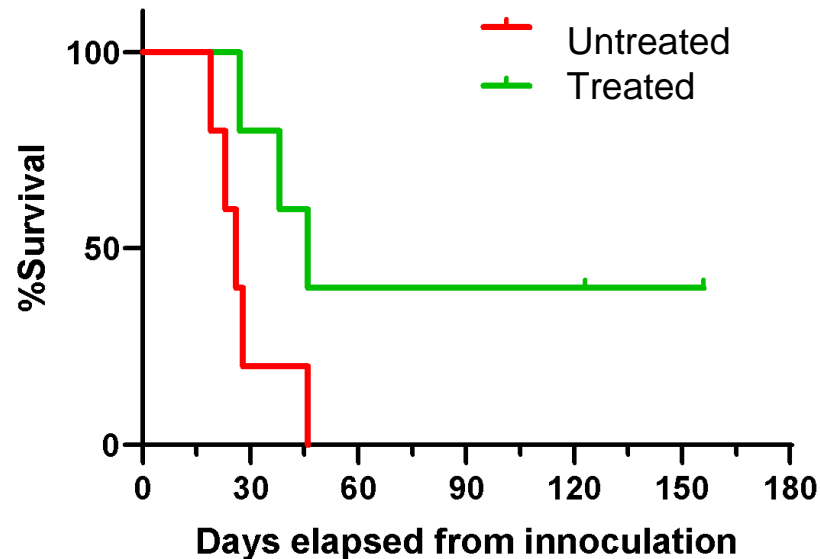


Untreated



Treated

T tumor  
br brain  
\* Focal  
necrosis  
residual  
inflammation



40% Long Term  
Survivals with  
complete tumor  
eradication

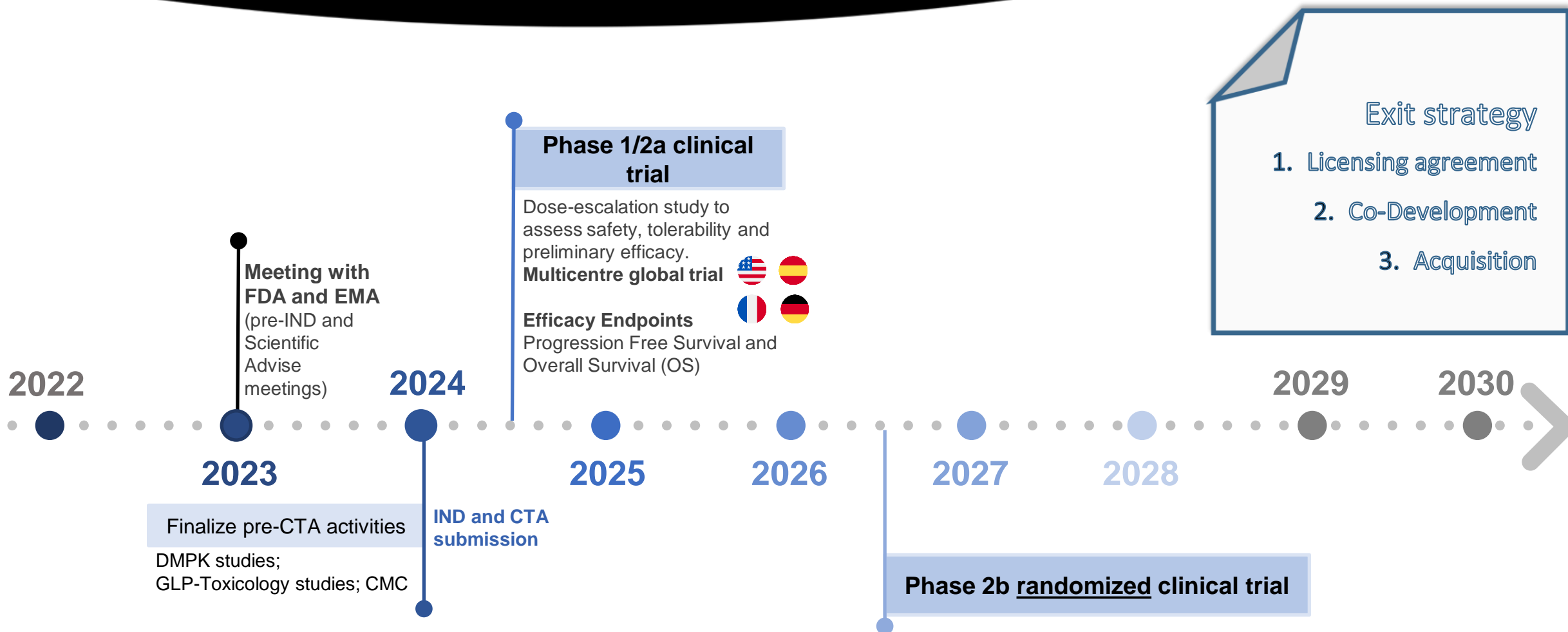
Next Steps: increase  
drug load and  
improve % survival  
and long term  
survival further



# Looking to the future

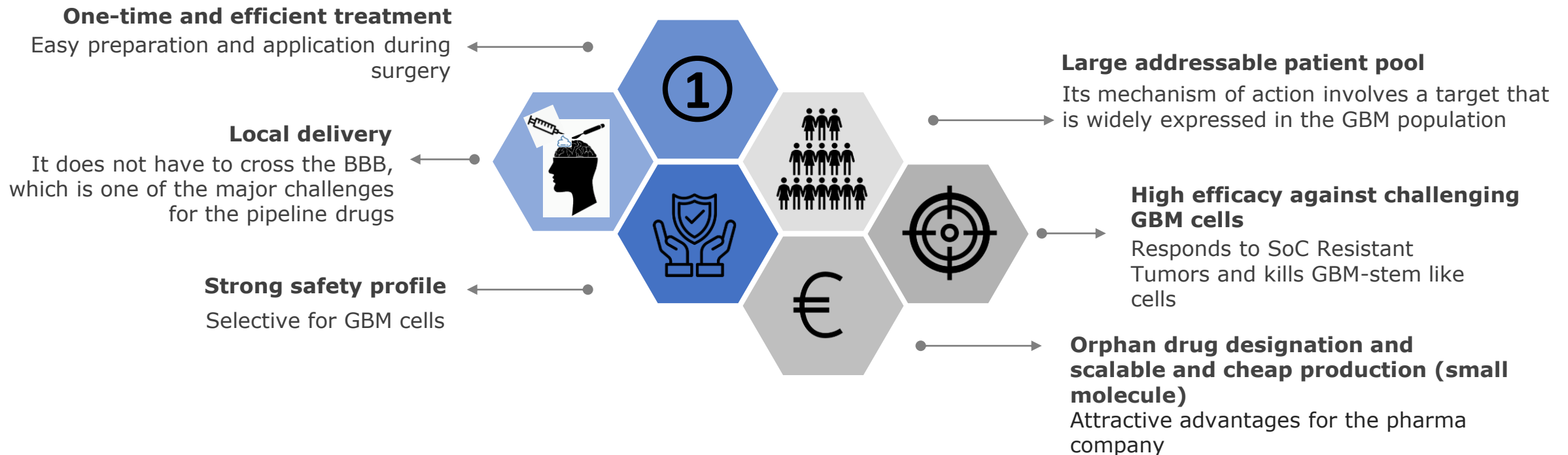


# Roadmap





# Product Differentiation for GBM





small is  
powerful®

# Summary

# TargTex and Nanoform Partnership Enabled....

- **Tumor eradication** in rodents (rat) with only 44% of maximum drug loading dose
- **Deep brain penetration** demonstrated by MSI (Mass Spectrometry Imaging)
- PK data shows **no systemic exposure**
- **Non-toxic** at maximum loading concentration
- **GMP-scalable** formulation; manufacturing agreement signed with Nanoform
- Together we will explore the ***power of small*** for other localized oncology treatments!

***FURTHER ENQUIRIES***

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