



SELECTED OPPORTUNITIES IN NEUROSCIENCES

Gene therapy coding for anti-Tau Nanobody to treat rare tauopathies (BIO18023)

Product factsheet

▶ **Product** : Gene therapy coding for anti-Tau Nanobody that prevents Tau aggregation

▶ **Rational / PoC:**

- ◆ Tau proteins aggregate into filaments in brain cells in different disorders referred to as tauopathies
- ◆ A VHH targeting the microtubule-binding domain, composing the core of Tau fibrils has been selected
- ◆ This lead VHH was optimized to improve its biochemical properties, intracellular expression, and to fully inhibit *in vitro* Tau aggregation in in vitro assays
- ◆ In vivo validation is ongoing using lentiviral CNS expression of the VHH

These specific constructs would be of particular interest for the therapy of rare Tauopathy disorders such as progressive supranuclear palsy (PSP), Down syndrome; Fronto-temporal dementia (FTDP); Pick disease; myotonic dystrophies; ...

▶ **Patent** : Priority 18 306 684.4 filed 13/12/2018

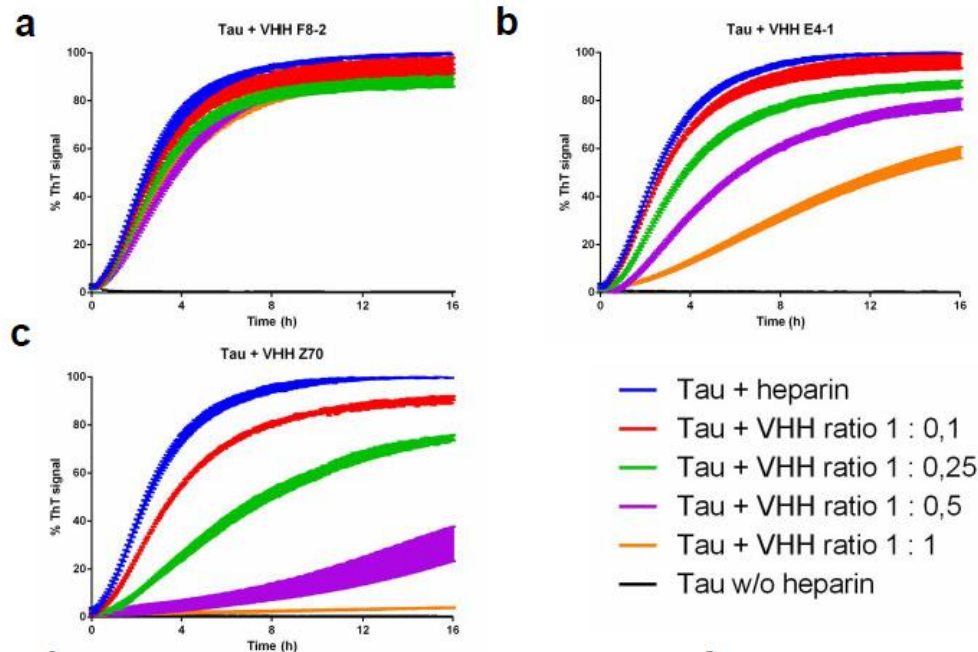
▶ **Publication:**

- ◆ under review

GENE THERAPY CODING FOR ANTI-TAU NANOBODY TO TREAT TAUOPATHIES

In vitro Proof of concept

VHH preventing Inhibition of Tau aggregation in biochemical assay



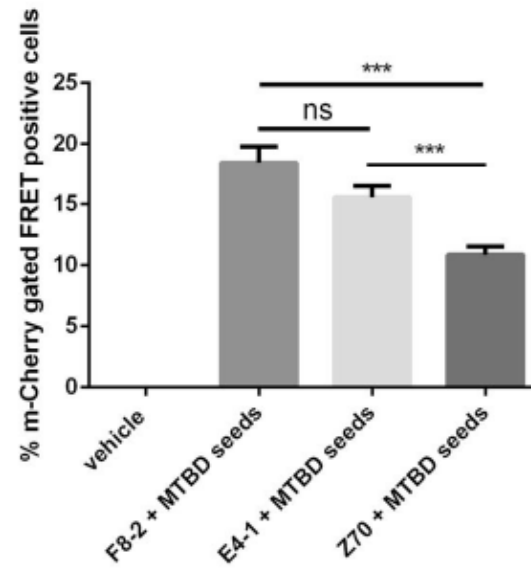
Tau recombinant protein in the presence of heparin : thioflavin T is a dye whose fluorescence is increased in presence of aggregates

lead VHH E4-1 and its optimized variant VHH Z70 had both the capacity to inhibit the aggregation of Tau in vitro and their relative activity is related to their affinity for Tau.

GENE THERAPY CODING FOR ANTI-TAU NANOBODY TO TREAT TAUOPATHIES

In vitro Proof of concept

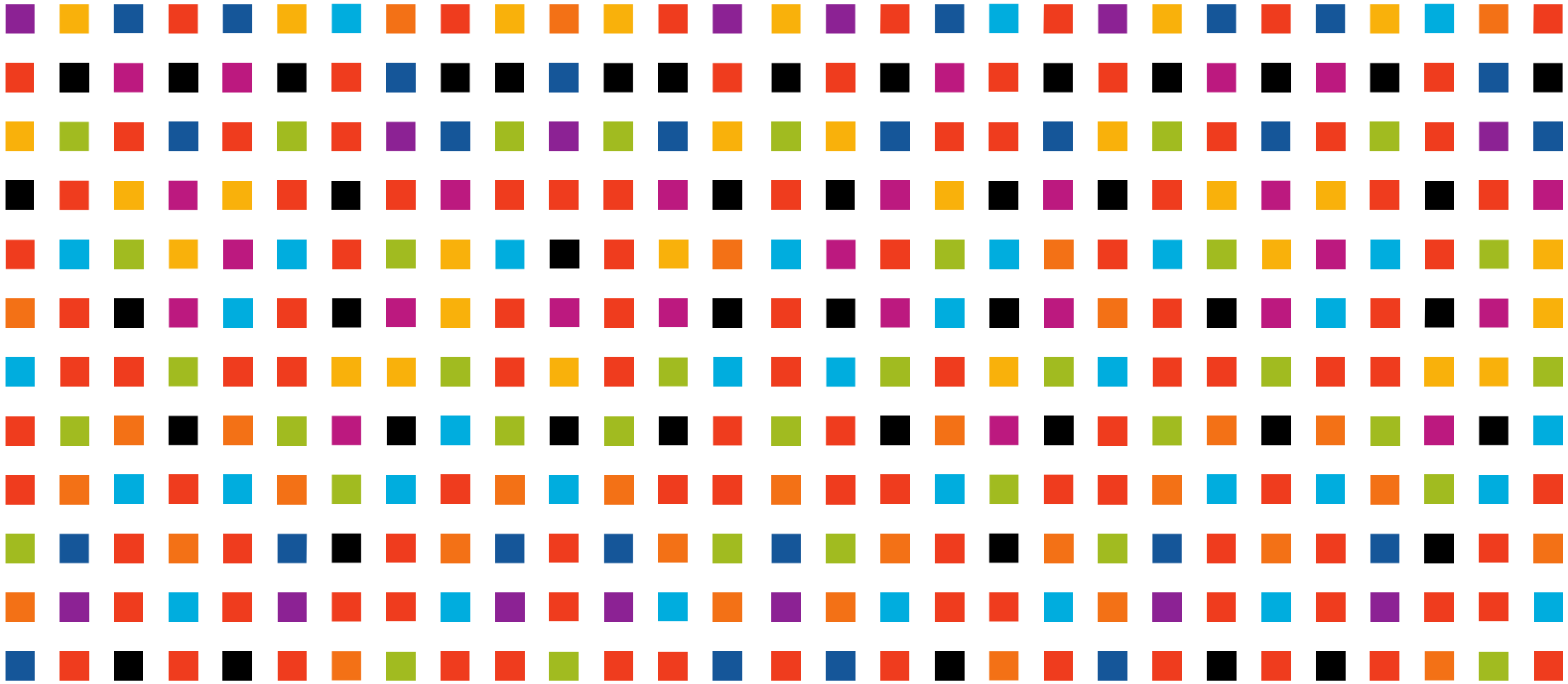
VHH preventing Inhibition of Tau aggregation in vitro



FRET reporter cell line RDP301S is used to measure signal induced upon MTBD-Tau aggregation

Plasmids expressing tagged-VHH were transfected one day prior to addition of the Tau seeds

lead VHH is able to block Tau seeding in this cellular model



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