TauRx Pharmaceuticals Ltd

Therapies and Diagnostics for Neurodegenerative Disease

www.taurx.com
www.targetingtau.com

Brief History of TauRx – Key Scientific Discoveries

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Co-founder and Executive Chairman
TauRx Pharmaceuticals

Professor of Old Age Psychiatry,
University of Aberdeen

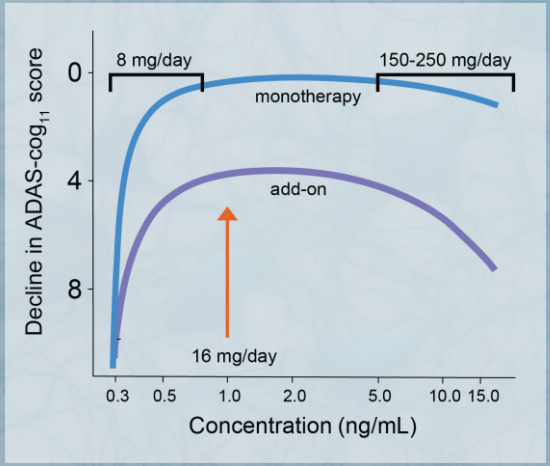
- TauRx is incorporated in Singapore with > 1000 shareholders, and has base of operations in Aberdeen, Scotland
- TauRx was founded in 2002 on the basis of two key discoveries:
  - Identification of the core tau unit of the Alzheimer tangle filament (PHF; Wischik et al., 1988)
  - Discovery of hydromethylthionine class of molecules able to dissolve PHFs and block tau aggregation through the core tau unit (Wischik et al., 1996)
- First Phase 2 trial of tau aggregation inhibitor in AD using oxidised precursor of hydromethylthionine (2004 – 2008; minimum effective dose 138 mg/day; Wischik et al., 2015)
- Development of hydromethylthionine (Harrington et al., 2015; Baddeley et al., 2015)
- First Phase 3 trials of hydromethylthionine in AD (2012 – 2016; Gauthier et al., 2016; Wilcock et al., 2018)
- First Phase 3 trial of hydromethylthionine in Frontotemporal Dementia (2012 – 2016; Shiells et al., 2020)
- Identification of 8 mg/day as minimum effective dose of hydromethylthionine and 16 mg/day as predicted optimal dose (Schelter et al., 2019)

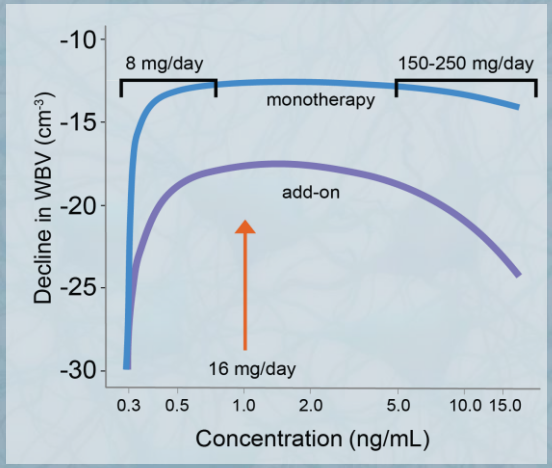
First Potential Tau-based Disease Modifying Treatment For Alzheimer's Disease

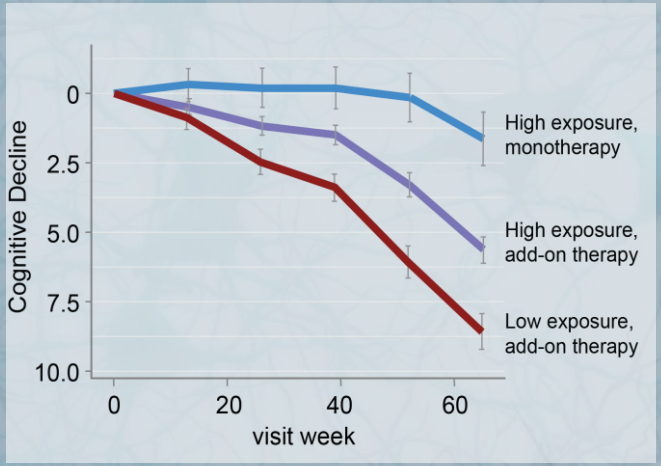
- Completed global trials in over 2000 patients have established exposure-dependent activity on clinical decline and brain atrophy in Alzheimer's disease and Frontotemporal dementia
- Hydromethylthionine program has now been substantially de-risked
- Confirmatory pivotal Phase 3 trial results due in 1Q 2022
- TauRx is currently raising funds to support expansion and commercialisation

Key results from completed trials

Phase 3 studies TRx-237-015 and TRx-237-005 established concentration-dependent activity on cognitive decline and brain atrophy - these identified 16 mg/day as optimal dose







Treatment effects of LMTM on cognitive decline depend on its level in the blood

The optimal dose identified as 16mg/day

Effect profile identical for reduction in progression of brain atrophy

Treatment effect greatest as monotherapy but also active as add-on

Patients taking with therapeutic blood levels on 8mg a day as monotherapy had minimal cognitive decline over 65 weeks

The benefit as add-on to symptomatic treatments was halved

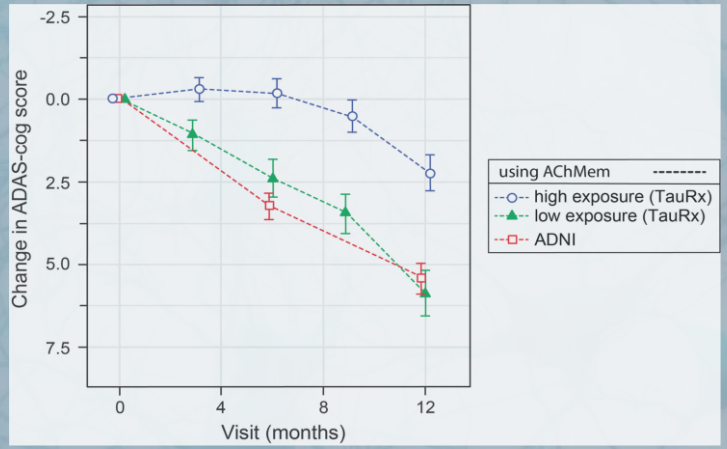
Schelter et al., 2019, J Alz Dis 72:931-946

Comparison of treatment effects with expected decline from ADNI[1]

LMTM subjects with therapeutic exposure at 8 mg/day as add-on had much less decline than ADNI patients receiving standard acetylcholinesterase inhibitor / memantine (AChMem) treatments

	AChMem Usage	
	Not Using	Using
ADNI	50	126
LMTM 8mg		
low exposure	30	112
high exposure	52	215

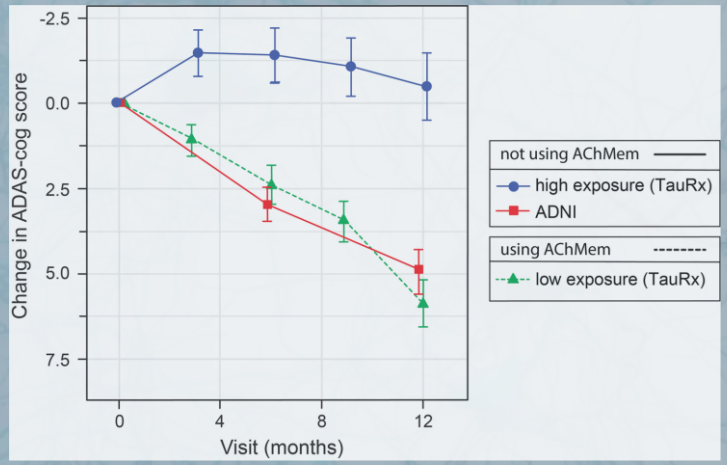
Difference over 12 months = 2.57 ± 0.74, p = 0.0006



LMTM subjects with therapeutic exposure at 8 mg/day as monotherapy had much less decline than untreated ADNI patients

	AChMem Usage	
	Not Using	Using
ADNI	50	126
LMTM 8mg		
low exposure	30	112
high exposure	52	215

Difference over 12 months = 4.92 ± 1.18, p < 0.0001



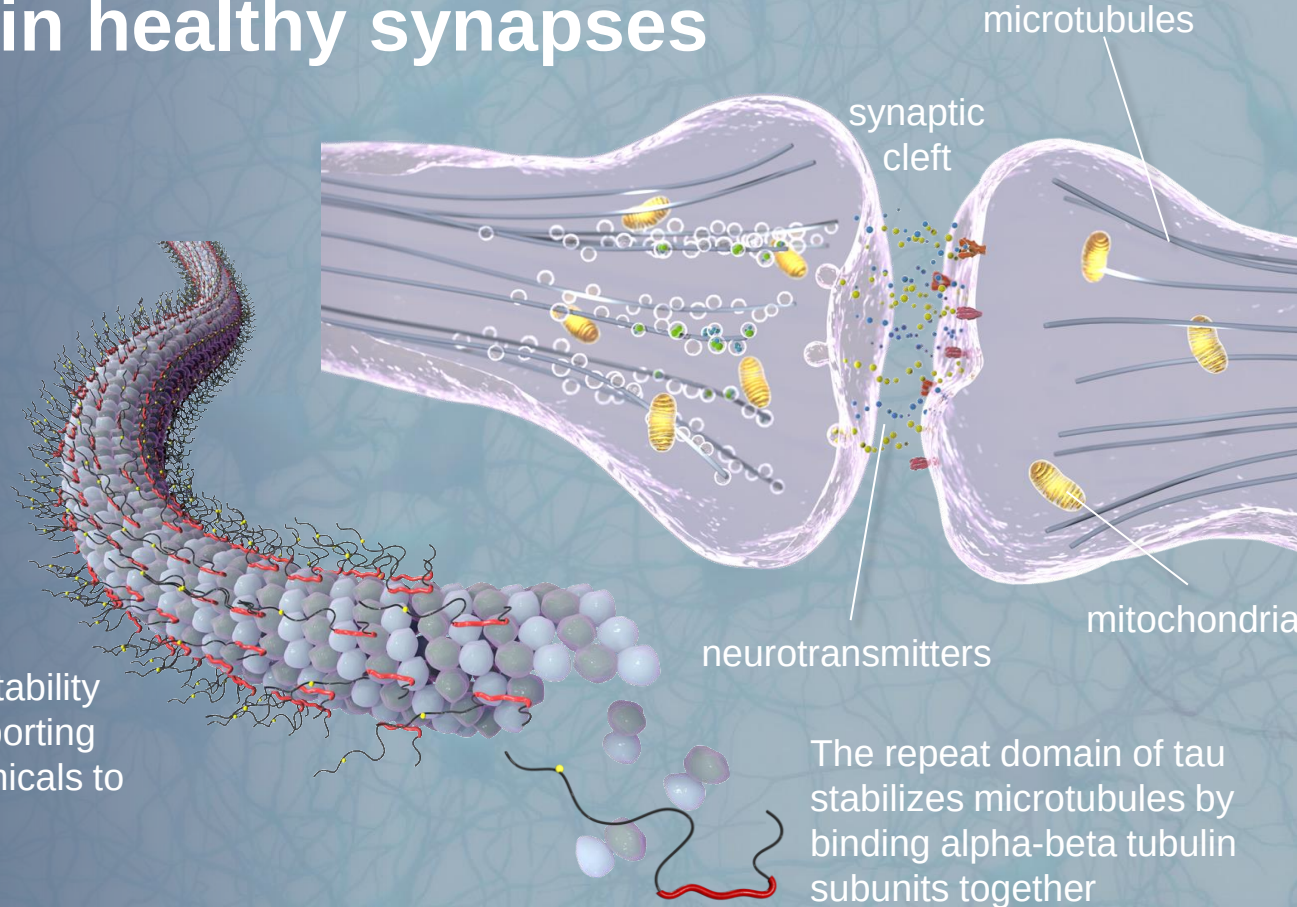
Alzheimer's Disease Neuroimaging Initiative (ADNI) is a consortium of all US AD centres

The role of tau in healthy synapses

Neurotransmitters are exchanged between healthy neurons at junctions called synapses

Synapses host a high concentration of mitochondria to power energy-intensive chemical signaling processes

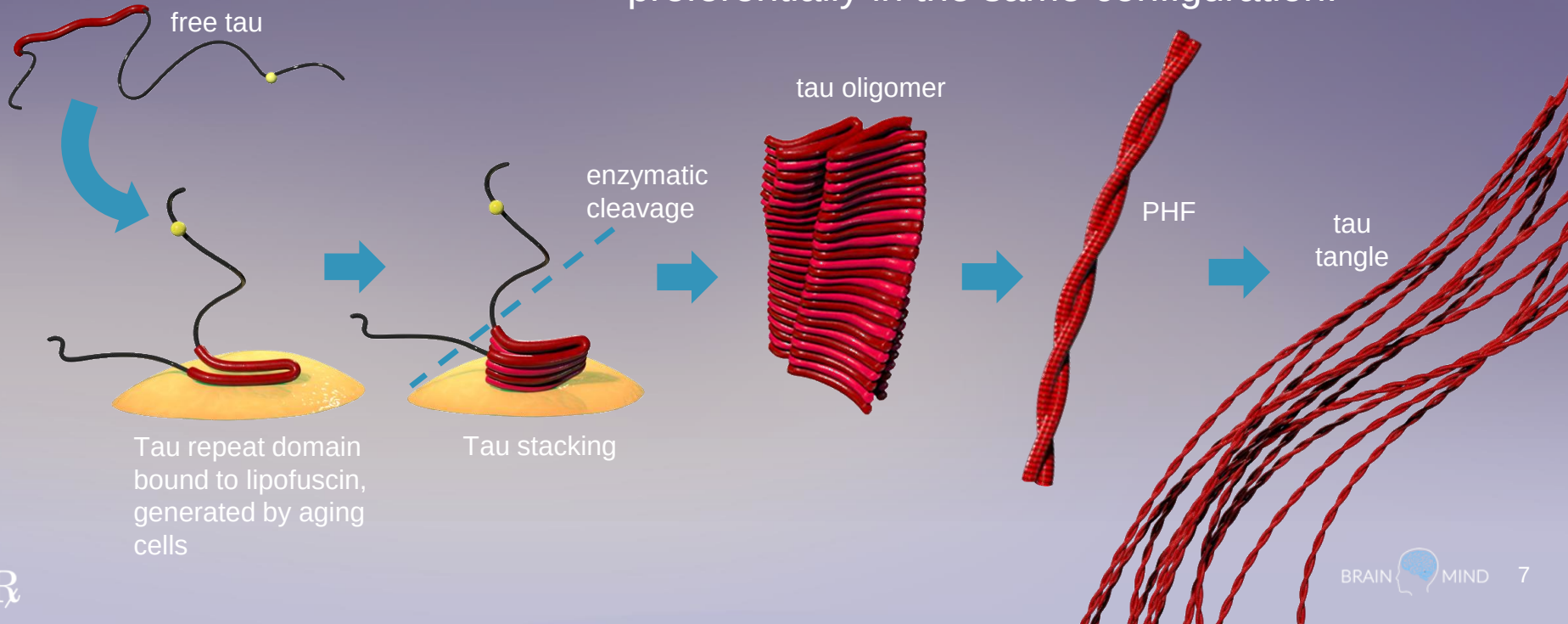
Microtubules provide structural stability and a physical scaffold for transporting vesicles, mitochondria, and chemicals to the synaptic junction



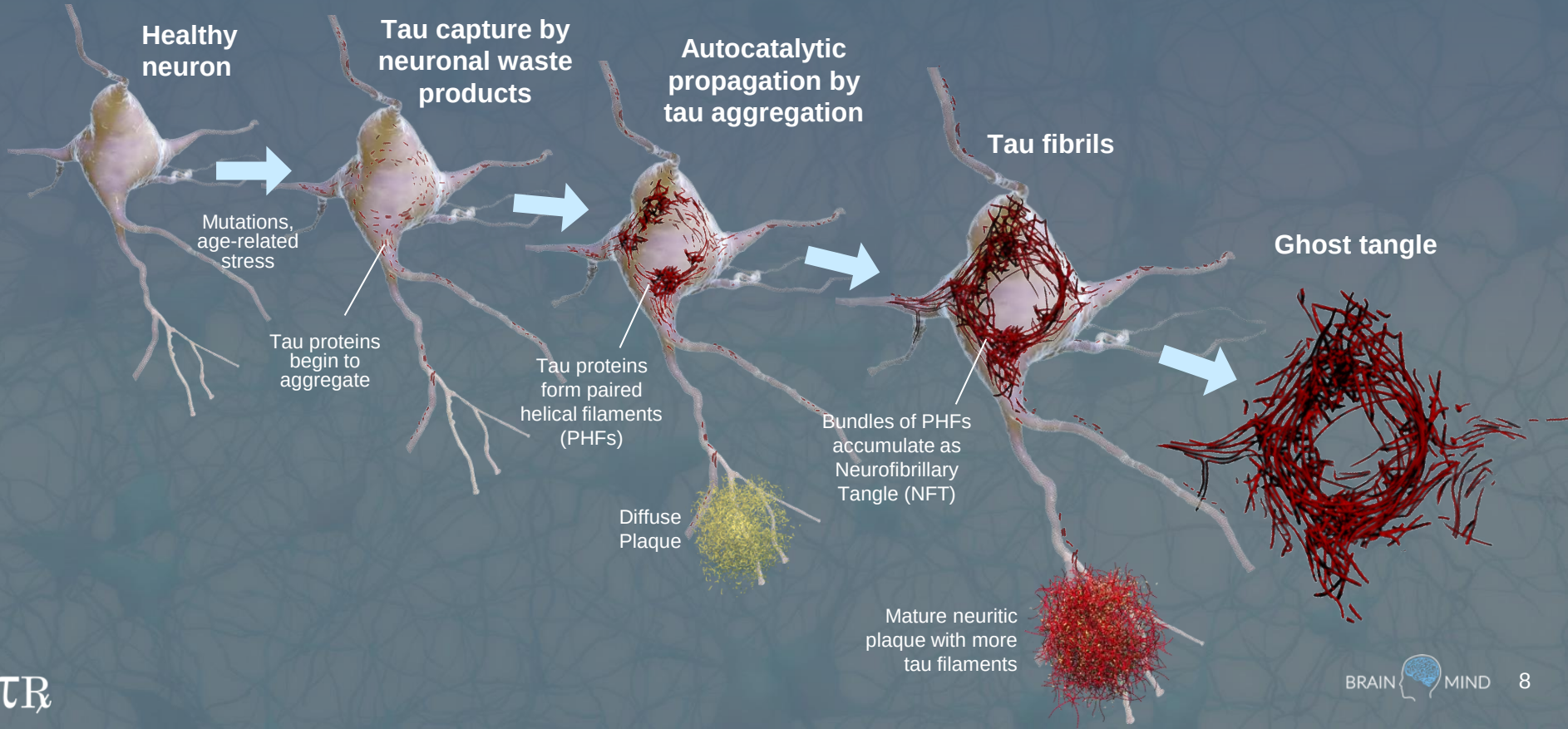
The repeat domain of tau stabilizes microtubules by binding alpha-beta tubulin subunits together

Pathologic Tau Oligomerization

Tau binds to cellular debris generated by aging neuronal cells and forms a stable hairpin structure. Additional tau proteins then stack preferentially in the same configuration.

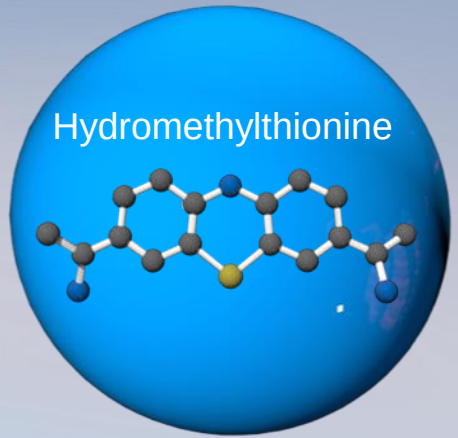


Tau Aggregation Impairs and Destroys Neurons

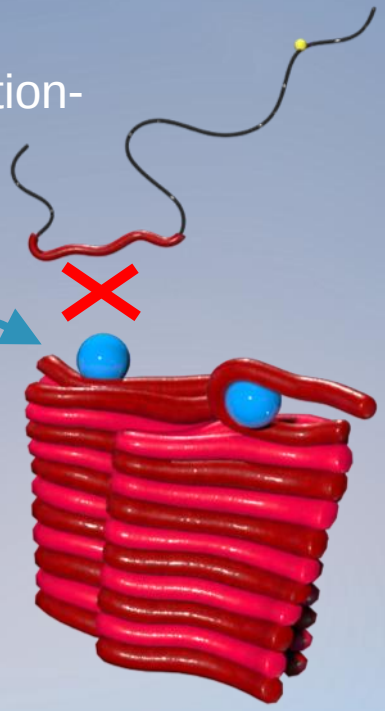


Blocking Tau Aggregation

Hydromethylthionine blocks tau oligomerization by inducing an aggregation-incompetent conformational change

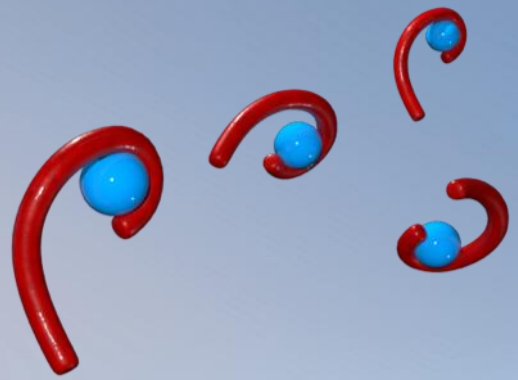


Tau oligomers cannot recruit more tau once they are bound to hydromethylthionine



Tau units are stripped off the stack

The new drug-bound conformation renders them unable to form oligomers



Hydromethylthionine provides potential for the transformation of dementia care globally

The ongoing LUCIDITY Study aims to confirm the efficacy of hydromethylthionine in MCI/mild/moderate AD – if successful, market launch could be by the end of 2023.

Hydromethylthionine is a convenient and well-tolerated oral treatment which has shown a benign safety profile.

Current expensive diagnostic work up with limited symptomatic treatments need to be replaced by early economical diagnostics and early disease modifying treatment.

Hydromethylthionine could open the door to the future of dementia treatment.