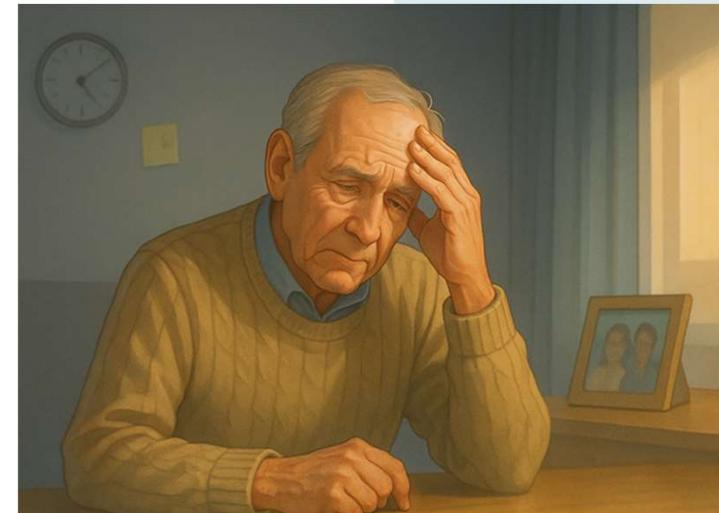


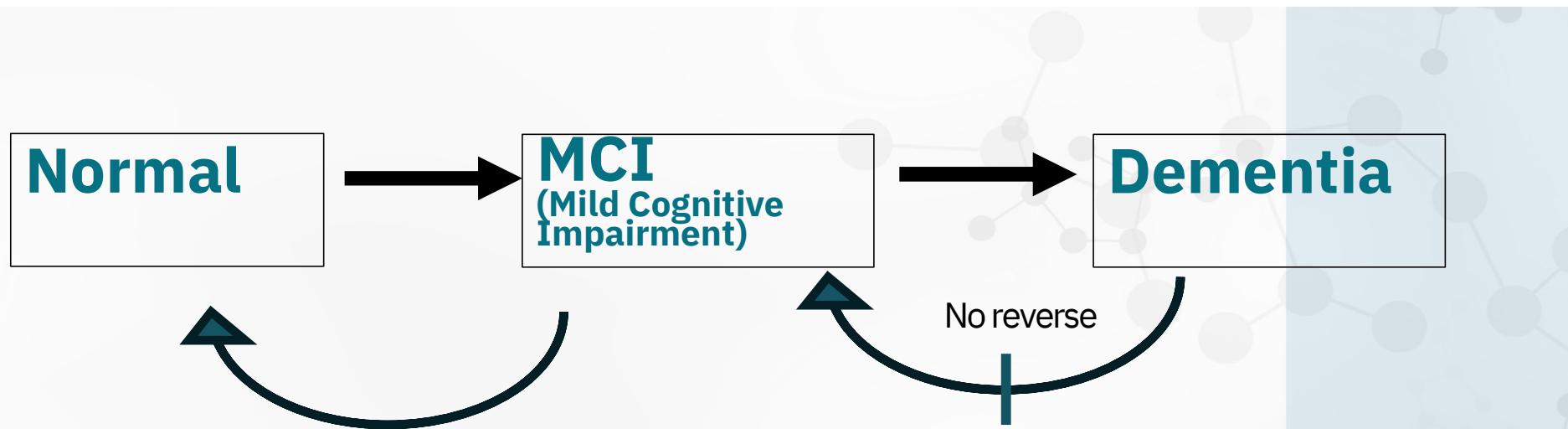
DEMENTIA

A big global headache with no effective treatment



NES Pharma developing

NeuroSurvive- A preventive treatment to improve quality of life in dementia and aging



Reversible MCI linked with:

- High fever (Infection or immune disorder)
- Metabolic or endocrine conditions
- Dehydration
- Medicine side effects-
- Drug usage
- Brain tumors
- Mild brain injury or stroke

Progressive non reversible :

- Alzheimer's disease- AD** (link to protein deposits)
- Vascular** (link to damage to blood supply)
- Lewy body** (protein clumps)
- Frontotemporal** (breakdown of nerve cells)
- Mixed dementia-** combined AD, Vascular, Lewy
- Huntington's disease (HD)-** (genetic)
- Traumatic brain injury (TBI)-**
- Creutzfeldt-Jakob disease-** caused by prions
- Parkinson's disease**

Available treatments to slow progression

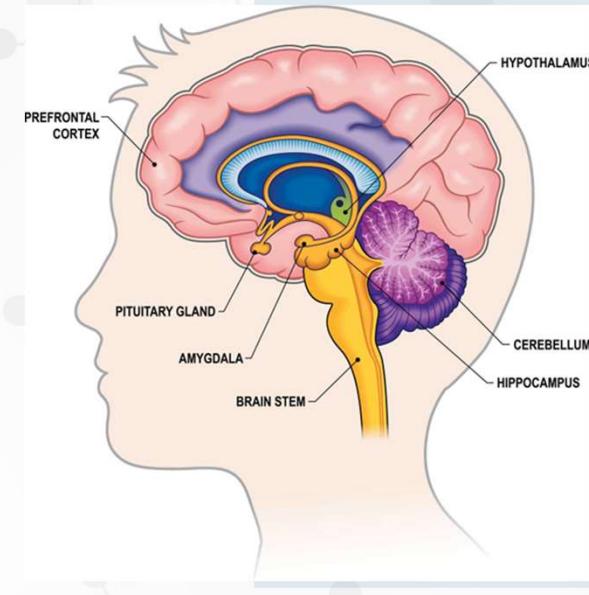
- **Medications:**
 - Cholinesterase inhibitors
 - Memantine (NMDA receptor antagonist)
 - lecanemab-irmb (Leqembi) and donanemab-azbt (Kisunla)
- **Therapies**
 - Occupational therapy to prevent accidents, such as falls
 - Changes to the environment- reduce noise and clutter
 - Simpler tasks- easier steps and focusing on success, reduce confusion

No current treatment can reverse or prevent progression from MCI to dementia

Cause

Ageing drives dysregulation of the glutamatergic system, mitochondrial failure and oxidative stress, all of which accelerate cognitive decline.

Growing evidence implicates chronic **glutamate dysregulation and excitotoxicity** as a shared mechanism across multiple neurodegenerative diseases, such as Alzheimer's, Parkinson's, ALS, and vascular cognitive impairment.



www.hopkinsmedicine.org

Elevated brain Glutamate levels, due to Glutamate dysregulation is a potential cause

Brain ECF (extracellular Fluid)

Glutamate levels

Healthy	1–5 μ M
MCI/Early AD	3–10 μ M
Established AD	5–20 μ M
Severe AD	20–30 μ M
TBI/Ischemia	50–100+ μ M
Blood (Plasma)	100-150 μ M

Excitotoxicity is the process which kills

neuron cells due to elevation in glutamate concentrations in brain.

The excessive amounts of the neurotransmitter act as a toxin to neurons.

Dementia and related glutamate dysregulation

Vascular dementia:

- Traumatic Brain Injury (TBI)
- Ischemia

Non-Vascular dementia:

- Glutamate Transporters
- Blood-Brain-Barrier (BBB)
- A process of chronic glutamate neurotoxicity

NES-Pharma

NES Pharma is leading the development of a new approach to neurodegeneration based on restoring glutamate homeostasis and reversing ageing-associated excitotoxic damage.

Early data supports:

- A novel mechanism reversing glutamate-induced neuronal injury.
- A companion biomarker signature reflecting pathway activity.
- Candidate molecules with promising neuroprotective effects.

NES Pharma development plan integrates mechanistic biology, novel biomarkers, therapeutics, and AI-enabled data modelling to build a translational pathway from discovery to the clinics

Glutamate excitation has been proved as clinical target in various neurodegenerative diseases

- Glutamate is the major neurotransmitter for memory and thinking
- Glutamate excitation has been proved as clinical target in various neuro diseases (i.e TBI)
- MoAs targeting glutamate:
 - Synapse glutamate receptor blocking
 - Blood glutamate scavenging/modulating
 - Blocking of co-receptors

Clinical Target

Target Product Profile

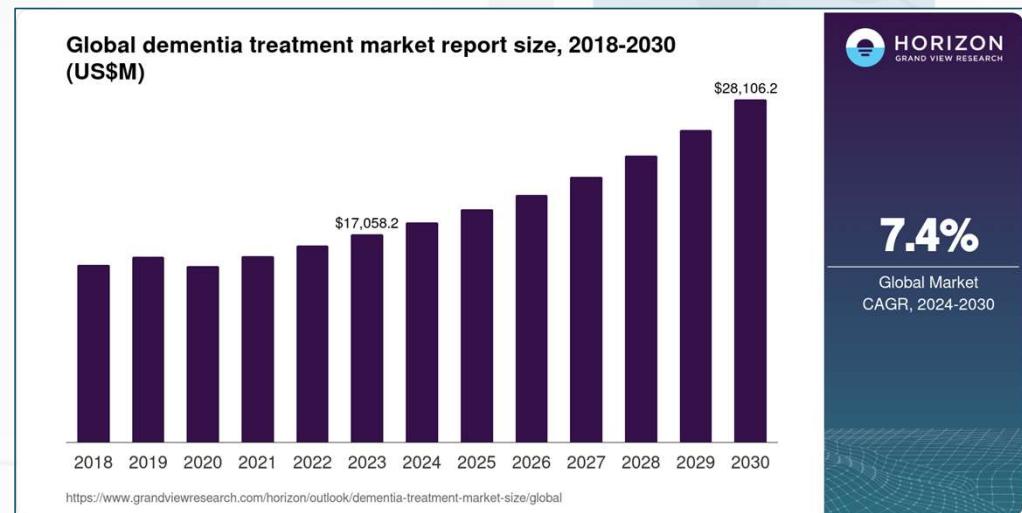
- Drug for oral administration
- Taken once weekly (or as prescribed)
- Prescription by physician
- Dosage according to clinical data
- Prescribed for people at MCI (mild Cognitive Impairment) or people at high risk to develop Dementia



*Illustration

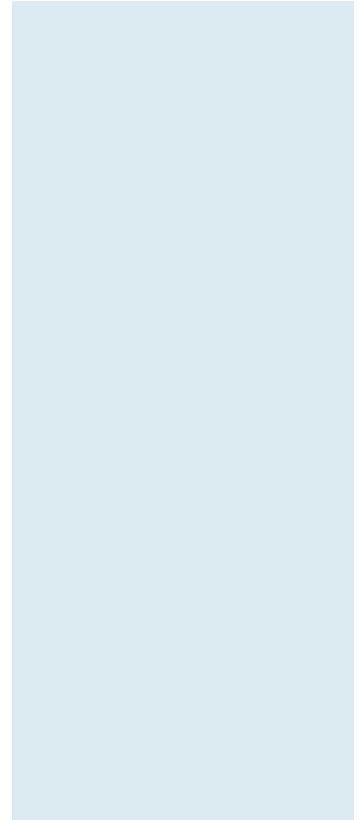
Dementia Market

- According to the WHO, in 2023, more than 55 million people suffer from dementia worldwide; predicted to reach 78 million and 139 million by 2030 and 2050, respectively
- The global dementia treatment market size was estimated at USD 17.06 billion in 2023 and is projected to grow at a CAGR of 7.4% from 2024 to 2030



NES-Pharma

**NeuroSurvive- A preventive treatment
to improve quality of life in dementia and
aging**



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