

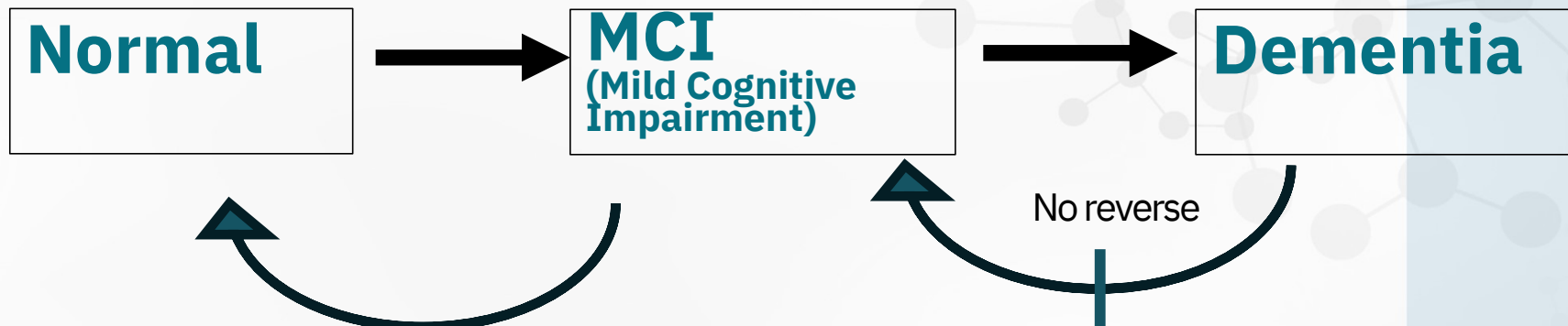
# **DEMENTIA**

**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

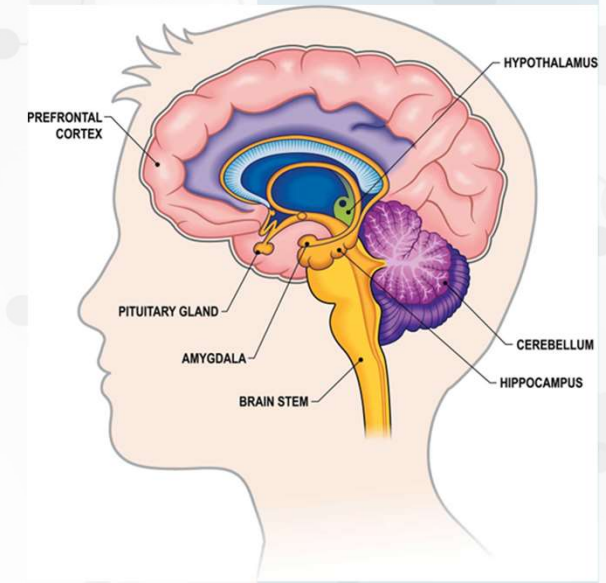
- **Medications:**
  - Cholinesterase inhibitors
  - Memantine (NMDA receptor antagonist)
  - lecanemab-irmb (Leqembi) and donanemab-azbt (Kisunla)
- **Therapies**
  - Occupational therapy to prevent accidents, such as falls
  - Changes to the environment- reduce noise and clutter
  - Simpler tasks- 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](http://www.hopkinsmedicine.org)

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

## Brain ECF (extracellular Fluid) Glutamate levels

Healthy	1–5 $\mu\text{M}$
MCI/Early AD	3–10 $\mu\text{M}$
Established AD	5–20 $\mu\text{M}$
Severe AD	20–30 $\mu\text{M}$
TBI/Ischemia	50–100+ $\mu\text{M}$
Blood (Plasma)	100-150 $\mu\text{M}$

**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

**Clinical  
Target**

- 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

## NES Pharma

### 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

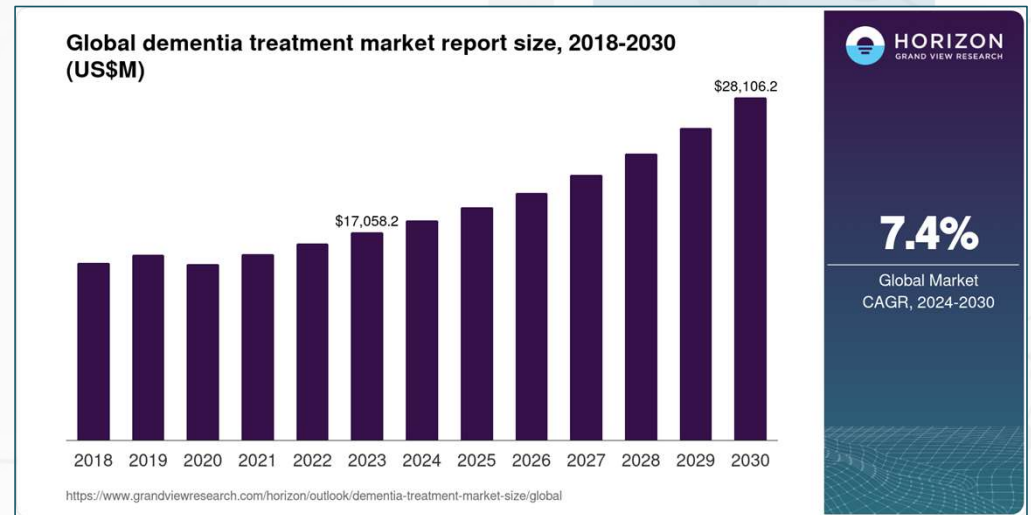


\*Illustration



# 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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