InMed Pharmaceuticals

INM-901

Multifactorial Approach to Treating Alzheimer's Disease

Nasdaq :INM

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Alzheimer's Disease – A Major Medical & Societal Burden

CURRENT TREATMENT OPTIONS DO NOT REVERSE EFFECTS

What is Alzheimer's Disease?

Alzheimer's is a subset of dementia that impacts the part of the brain that controls thought, memory and language and leads to increased morbidity and mortality.

The two most recognized hallmarks of Alzheimer's disease are the build-up of amyloid-beta plaques and neurofibrillary tangles caused by tau proteins. Emerging research indicates that the associated neuroinflammation is also a factor. Lifestyle and genetics are likely contributors to disease development.

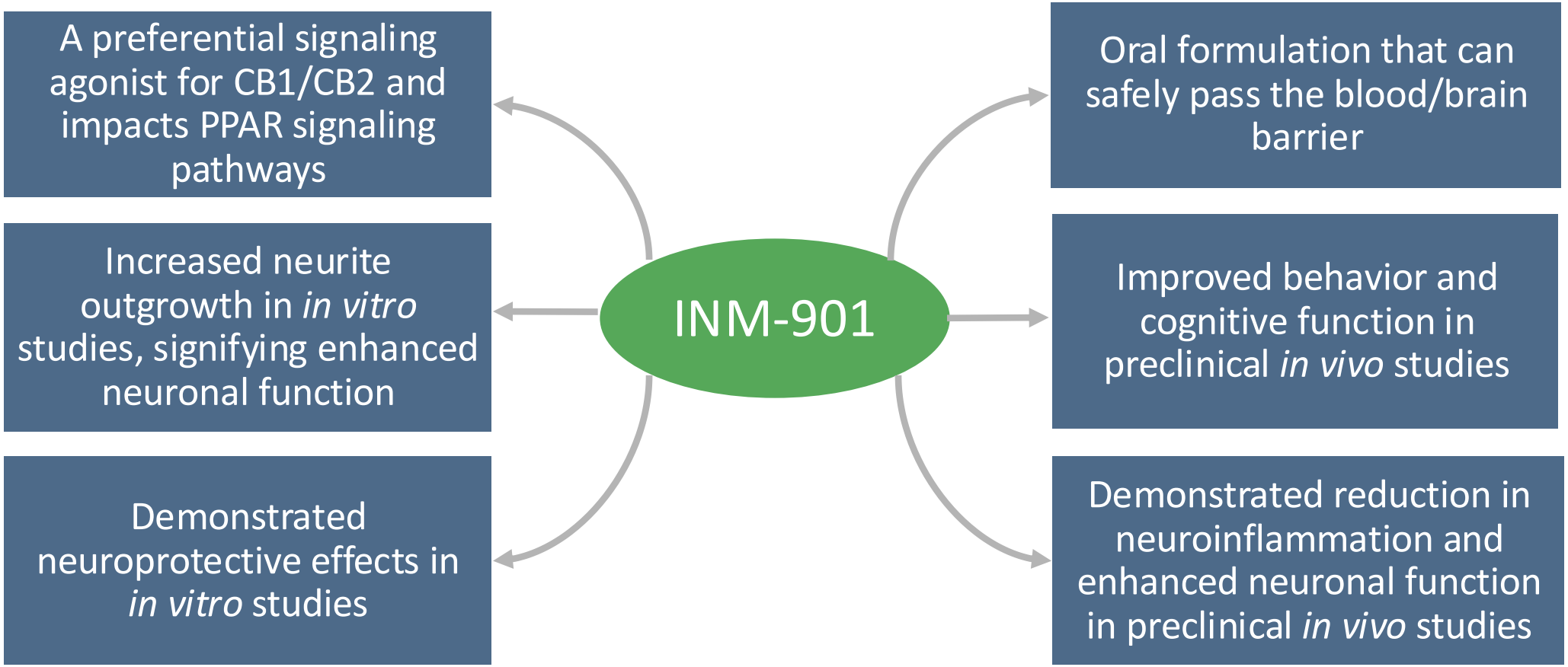
Impact

- Alzheimer's accounts for 60-80% of dementia cases
- 1 in 9 people age 65+ (10.7%)
- 1 in 5 women, 1 in 10 men
- 6.9M Americans affected
- 5th leading cause of death for 65+
- U.S. annual financial impact $360B
  (Alzheimer's and other dementia)

Source: Alzheimer's Association (U.S.)

INM-901: A Multi-factorial Approach

POTENTIALLY DISEASE-MODIFYING SMALL MOCECULE DRUG CANDIDATE



Snapshot: Alzheimer's Disease Treatments in Development

ANTI-AMYLOID BETA AND ANTI-TAU TARGETS DOMINATE ALZHEIMER'S TREATMENTS IN LATE DEVELOPMENT

Therapeutic Targets

- 28 neurotransmitter receptors (22%)
- 25 neuroinflammation (20%)
- 23 amyloid beta (18%)
- 15 synaptic plasticity/neuroprotection (12%)
- 11 tau-related processes (9%)
- 8 metabolism and bioenergetics (6%)
- 5 ApoE, lipids, and lipoprotein receptors (4%)
- 4 proteostasis/proteinopathy (3%)
- 4 growth factors/hormones (3%)
- 3 oxidative stress (2%)
- 3 neurogenesis (2%)
- 3 circadian rhythm (2%)
- 2 vasculature factors (2%)
- 1 gut-brain axis (1%)
- 1 epigenetic regulators (1%)

Alzheimer's Therapeutic Development

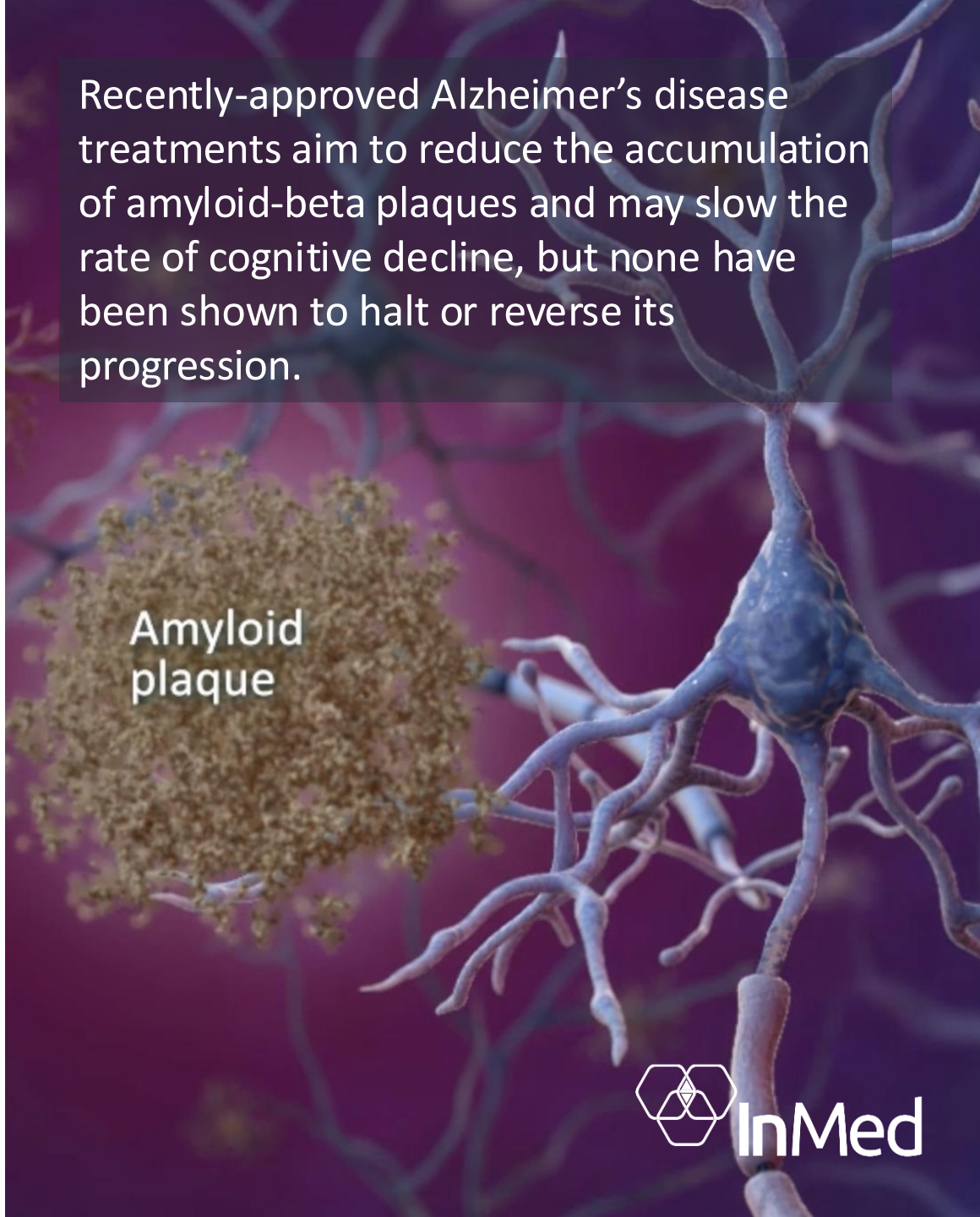
- 2 approved disease-modifying products (large molecule, anti-amyloid betas)
- 127 drugs in clinical trials (32 in Phase 3; 81 in Phase 2; 25 in Phase 1)
- 57 small molecules, 39 biologics

Source: Alzheimer's disease drug development pipeline: 2024 (Cummings et al), April 2024

Limitations of Anti-Amyloid Beta Targeting Monoclonal Antibodies

RECENTLY-APPROVED DISEASE-MODIFYING DRUGS COME WITH MAJOR TREATMENT LIMITATIONS

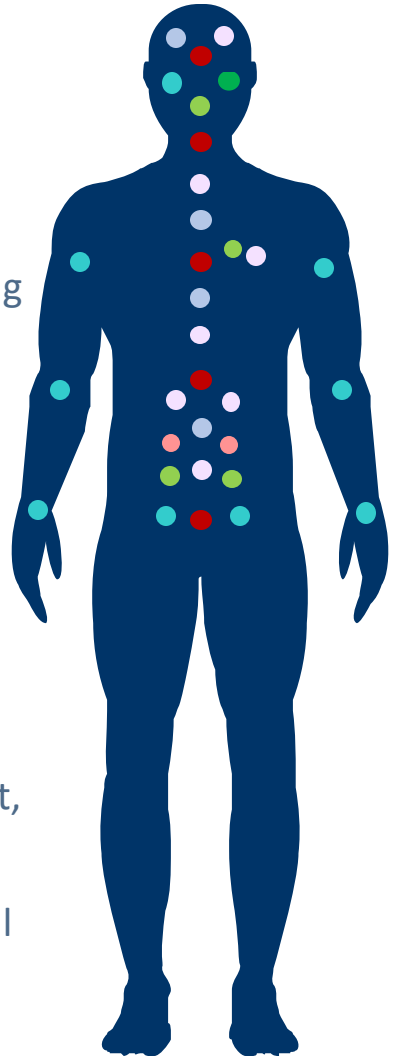
Limited Therapeutic Effects	Limited evidence of restoring lost cognitive function
Side Effects Risk/Benefit Profile	Amyloid-related Imaging Abnormalities (ARIA), brain swelling, brain bleeding
Ongoing Screening Requirement	Requires MRI brain scan 1-2X/yr
Drug Delivery Challenges	Intravenous 45-60min infusion every 2-4 weeks with trained medical staff
Accessibility	Typically available only at specific infusion sites, limiting accessibility to those living nearby



INM-901 Interacts with Specific Receptors in the Brain

Examples of receptors expressed in the body

- **CB1** Receptors concentrated in the brain and central nervous system but are also present in some nerves and organs
- **CB2** Receptors are associated with immune cells, including in the brain, and also found in peripheral organs
- **PPAR** Receptors expressed in tissues in the brain, heart, kidney and skin
- **GPR6** Receptors mainly expressed in the brain, particularly in the striatum.
- **GPR55** Receptors found in the bones, the brain (particularly the cerebellum), and the jejunum and ileum
- **TRPV4** Receptors mainly expressed in the kidney, lung, heart, brain, skin, spine
- **TRPM8** Receptors found primarily in the spine and trigeminal ganglion



INM-901:

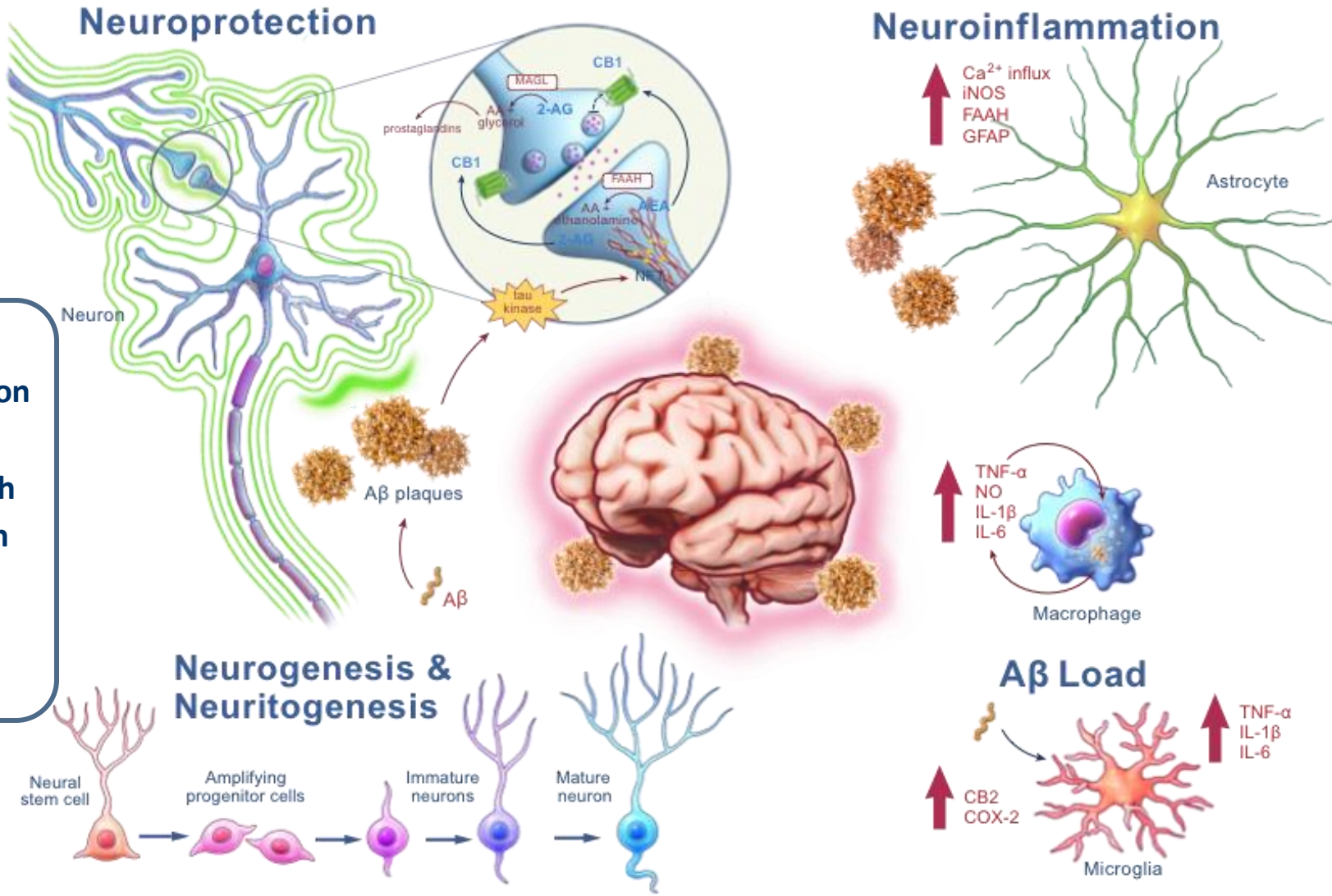
Preferential signaling agonist of CB1 and CB2 receptors and impacts the PPAR signaling pathway.

Activation of CB1 & CB2 has been shown to have neuroprotective effects.

INM-901: Potential Multiple Mechanisms of Action

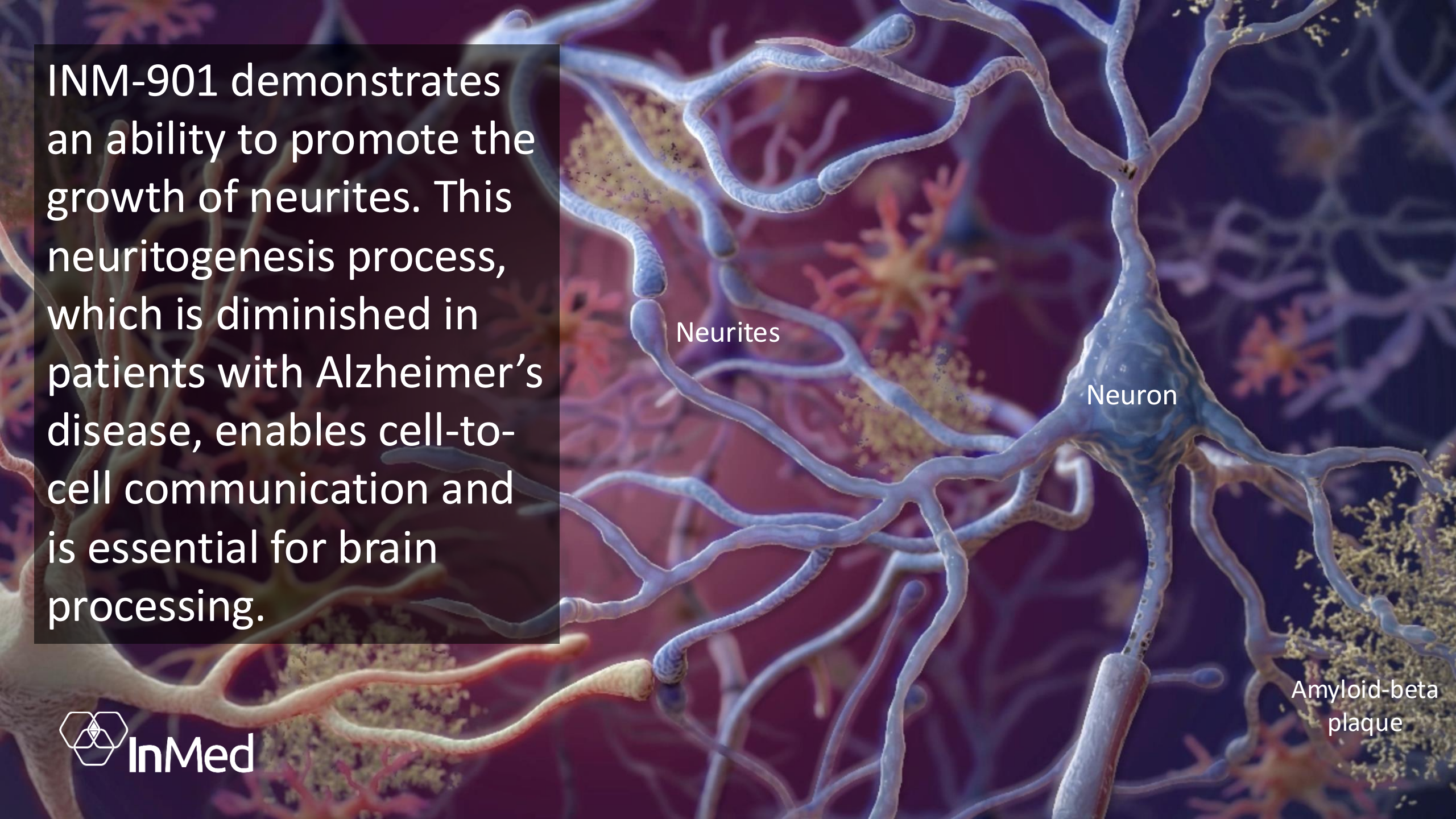
INM-901

- ▼ Cytotoxicity
- ▼ Neuroinflammation
- ▲ Neuroprotection
- ▲ Neurite outgrowth
- ▲ Neuronal function
- ▲ Locomotion
- ▲ Memory
- ▲ Cognition



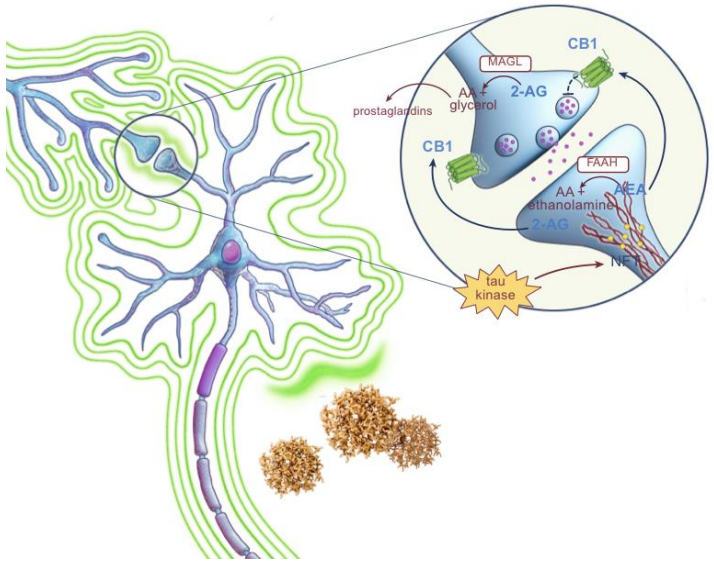
INM-901

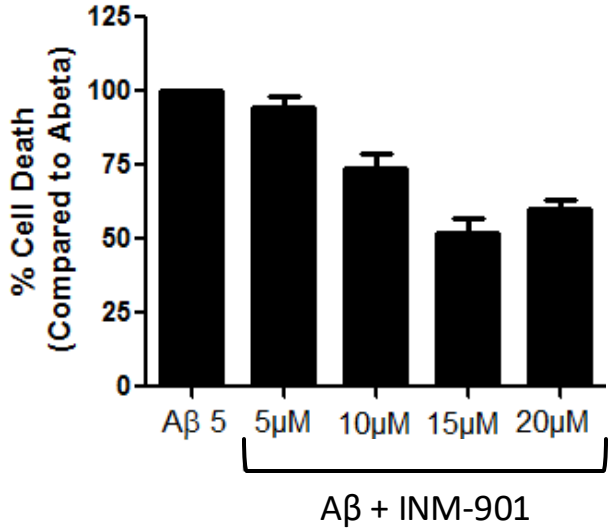
- Proprietary small molecule compound can cross BBB
- May be formulated orally
- Preferential signaling agonist for CB1/CB2
- Impacts PPAR signaling pathways


INM-901 demonstrates an ability to promote the growth of neurites. This neuritogenesis process, which is diminished in patients with Alzheimer's disease, enables cell-to-cell communication and is essential for brain processing.
Neurites
Neuron
Amyloid-beta plaque
InMed

INM-901 Demonstrates Neuroprotective Effects

INM-901 PROMOTES CELL SURVIVAL AND PROLIFERATION





Neuroprotection studies

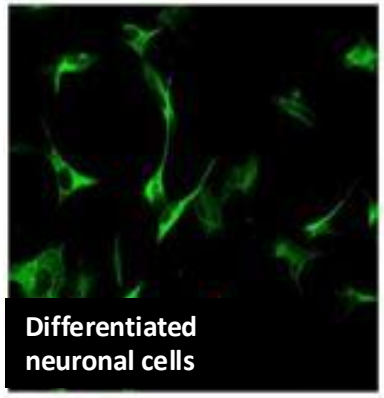
- Amyloid-β-induced toxicity model
- Blocking of cytotoxicity and apoptosis
- Neuroinflammation decreased

Result

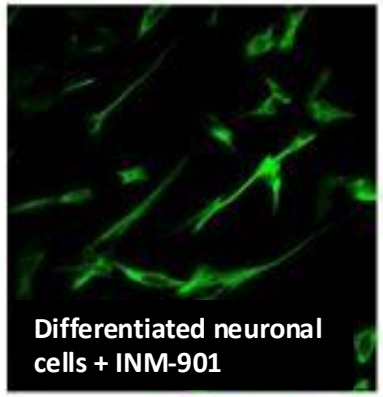
INM-901 treated groups demonstrated dose-dependent cell survival and proliferation

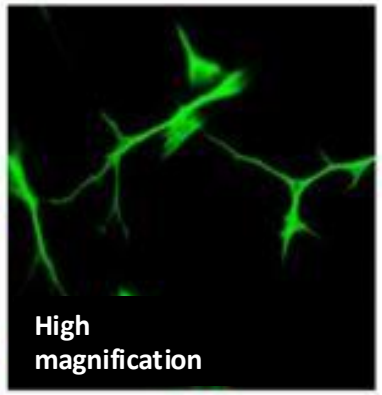
INM-901 Demonstrates Increased Neurite Formation

NEURITE OUTGROWTH INDICATES ENHANCED NEURONAL FUNCTION, WHICH IS DIMINISHED IN ALZHEIMER'S DISEASE.

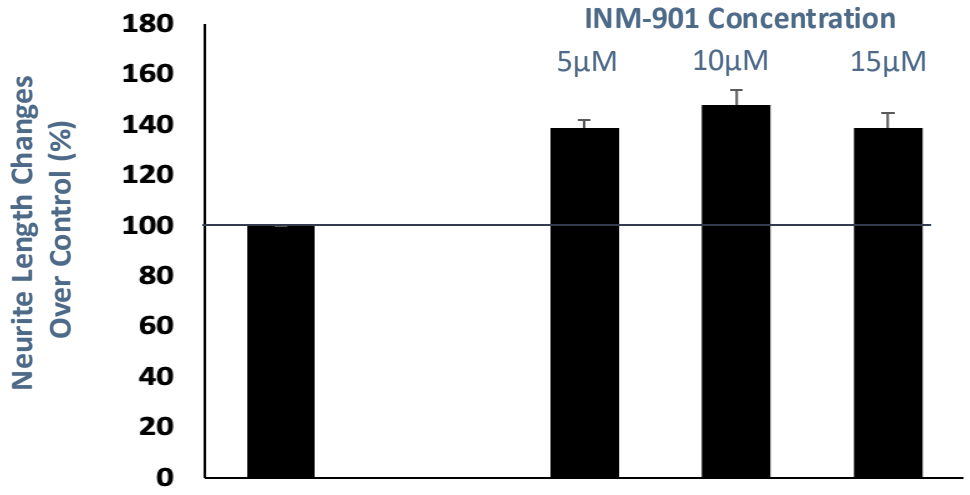


Neuronal cells are fragmented





When exposed to INM-901, neurites are extended, potentially restoring the function of these neurons



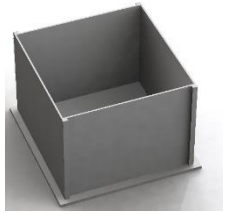
Neuritogenesis Studies

- Measured neurite length compared to control
- INM-901 promotes the regeneration of neurites in a dose-dependent manner

Result:
INM-901 treated groups displayed extended neurite length, signifying enhanced neuronal function

INM-901 Demonstrates a Trend in Improvement in Behavior

PRECLINICAL STUDIES IN VALIDATED ALZHEIMER'S PROOF-OF-CONCEPT MODELS



Open Field-Single Enclosure (basal and locomotor activity)

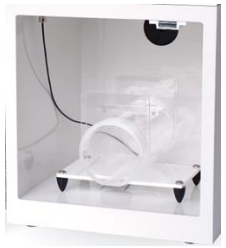
- Treated groups have similar behavior as normal

Elevated Plus Maze Test (anxiety-related behavior)

- Treated groups have similar behavior as normal

Novel Object Recognition (cognitive function and memory)

- Treated have similar behavior as normal



Acoustic startle (sound awareness)

- Treated groups have improvement in pre-pulse inhibition

ALZ Behavioral Studies (3-month study)

- Basal and locomotor activity
- Anxiety-related behavior
- Cognitive function and memory
- Sound awareness

Result:
INM-901 treatment led to improvement in behaviors and cognitive functions

INM-901 Molecular Data Supports Observations from Behavioral Studies

RNA sequencing of the brain mRNA indicates:

- Pro-inflammatory genes are elevated and neuronal function genes are reduced for the TG (AD-diseased) group when compared to the Control (Normal WT).
- INM-901 treated group: pro-inflammatory genes are reduced and neuronal function genes are elevated for the treatment group when compared to the TG group.

Protein analysis of the brain indicates:

- Some reduction in amyloid plaque levels
- Reduction in glial fibrillary acidic protein (GFAP), a pro-inflammatory marker

INM-901 Long-term Preclinical Studies Confirm Earlier Study Data

Study Design

- 7-month of dosing, *in vivo*
- 5xFAD amyloidosis model
- Extended dosing duration and increased sample size compared to earlier three month study
- Increased severity of Alzheimer‘s disease
- Assessed
  - basal and locomotor activity
  - anxiety-related behavior
  - cognitive function and memory
  - sound awareness

INM-901 Results

- **Confirmed improvements in cognitive function, memory and locomotor activity**
- **Achieved statistical significance in certain behavioral assessments**
- **Most assessment showing a clear dose response**
- **Results supported and, in several instances, improved upon prior short-term study outcomes**

INM-901 Summary

- **Small molecule, systemic delivery across the BBB**
  - Possibly deliverable via oral ingestion
- ***In vitro:*** **Demonstrates 2 distinct features**
  - Neuroprotection and neuritogenesis
- ***In vivo:*** **5xFAD model**
  - **Behavioral improvements:**
    locomotion, cognition, memory
  - Reduced neuroinflammation
  - Increased neuronal function

Next steps

Research & Development

- Long-term molecular analysis studies on-going
- Planning study in neuroinflammation model
- On-going activities on CMC for drug substance and oral drug product
- On-going studies of receptor interactions (MoA) and DMPK
- GLP studies to follow

Business Development

- Identify co-development partners
- Identify strategic investors

InMed Pharmaceuticals

Thank you!

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