InMed Pharmaceuticals

INM-901

Multifactorial Approach to Treating Alzheimer's Disease

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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 neuroinflammation is also a factor. Lifestyle and genetics are likely contributors to disease development.

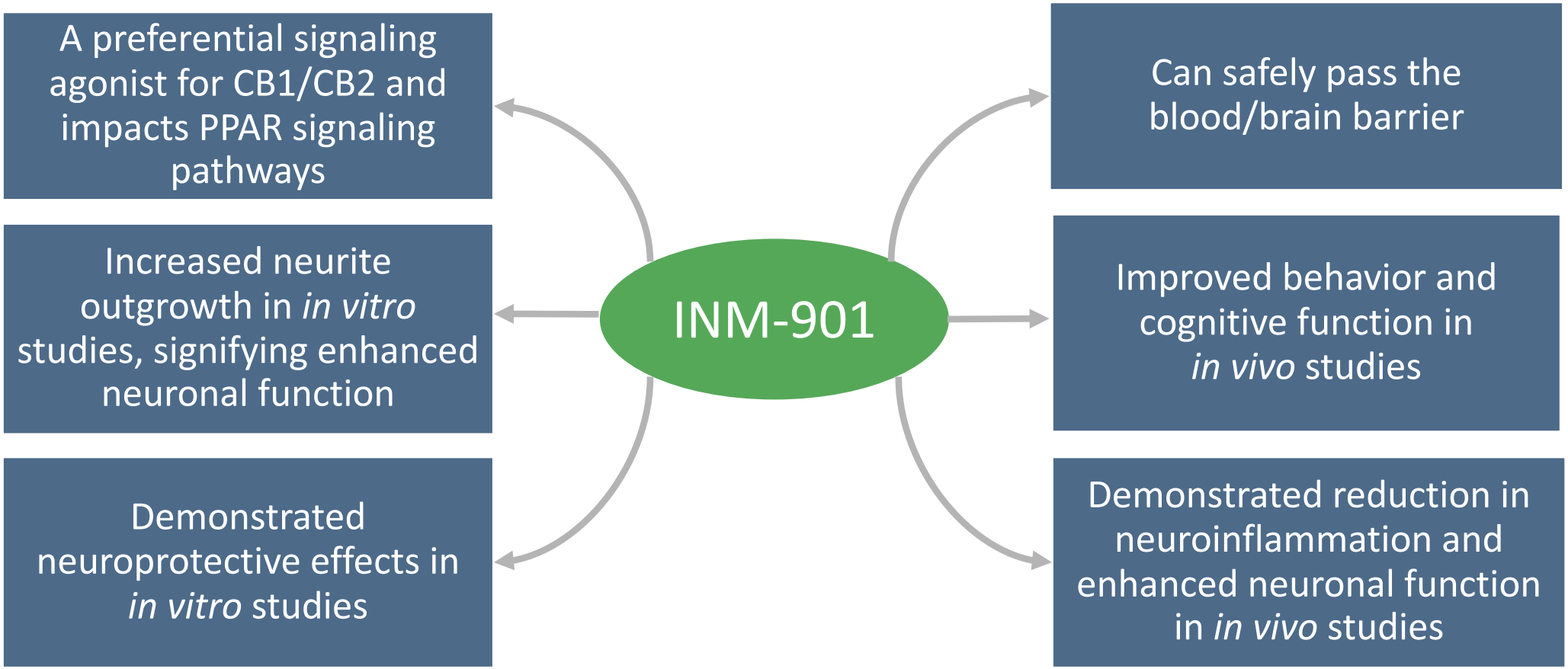
Impact

- Alzheimer's accounts for 60-80% of dementia cases
- 1 in 5 women, 1 in 10 men
- 6M+ Americans affected
- 5th leading cause of death for 65+
- U.S. annual financial impact $345B (Alzheimer's and other dementia)

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

INM-901: A Multi-factorial Approach

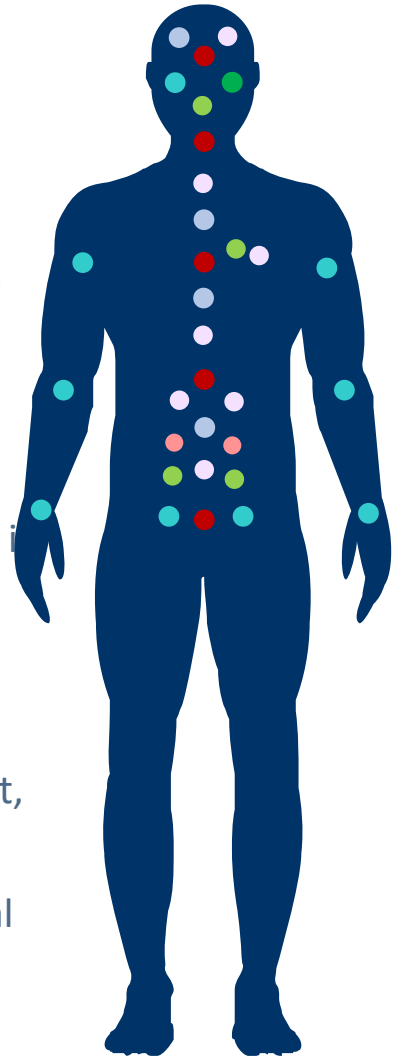
POTENTIALLY DISEASE-MODIFYING SMALL MOCECULE DRUG CANDIDATE



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 mostly in peripheral organs, especially cells associated with the immune system
- **PPAR** Receptors expressed in tissues in the brain, heart, kidney and skin
- **GPR6** Receptors mainly expressed in the brain, particularly i 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 impacts the PPAR signaling pathway.

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

INM-901: Potential Multiple Mechanisms of Action

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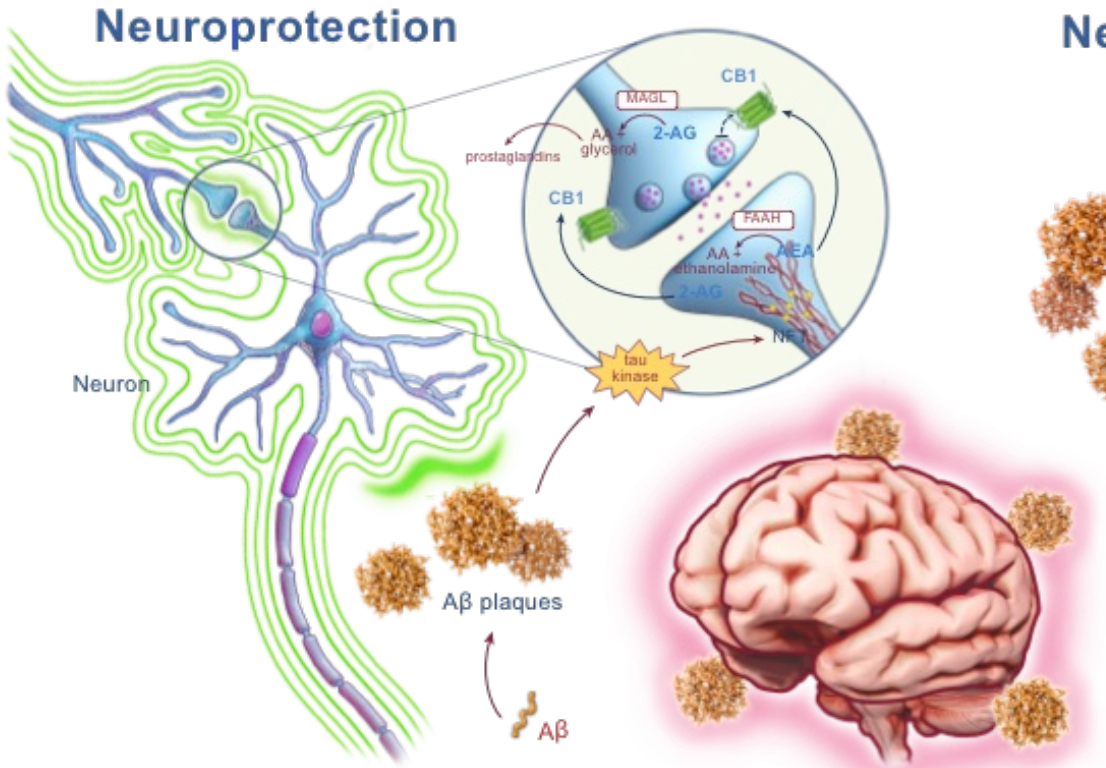
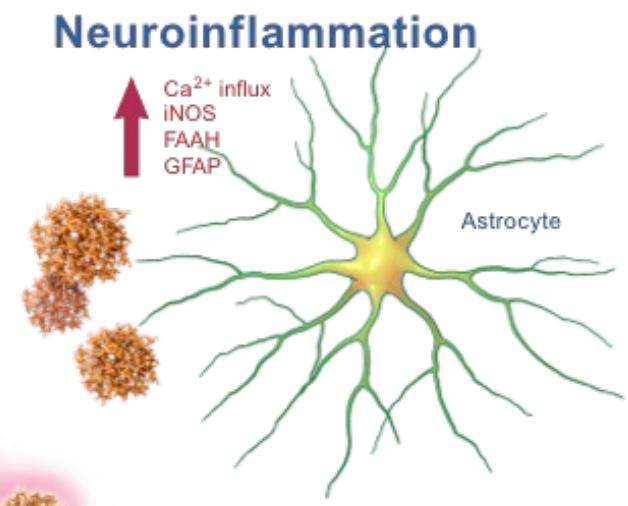
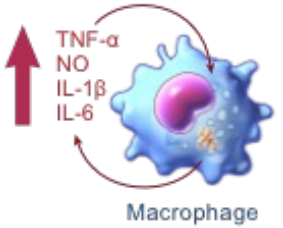
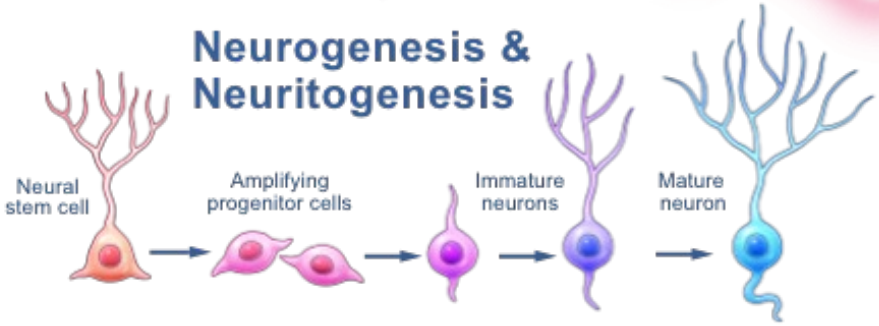
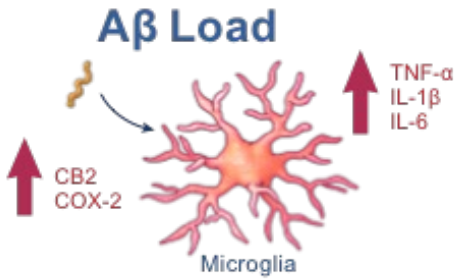
- ↓ Cytotoxicity
- ↓ Neuroinflammation
- ↑ Neuroprotection
- ↑ Neurite outgrowth
- ↑ Neuronal function
- ↑ Locomotion
- ↑ Memory
- ↑ Cognition





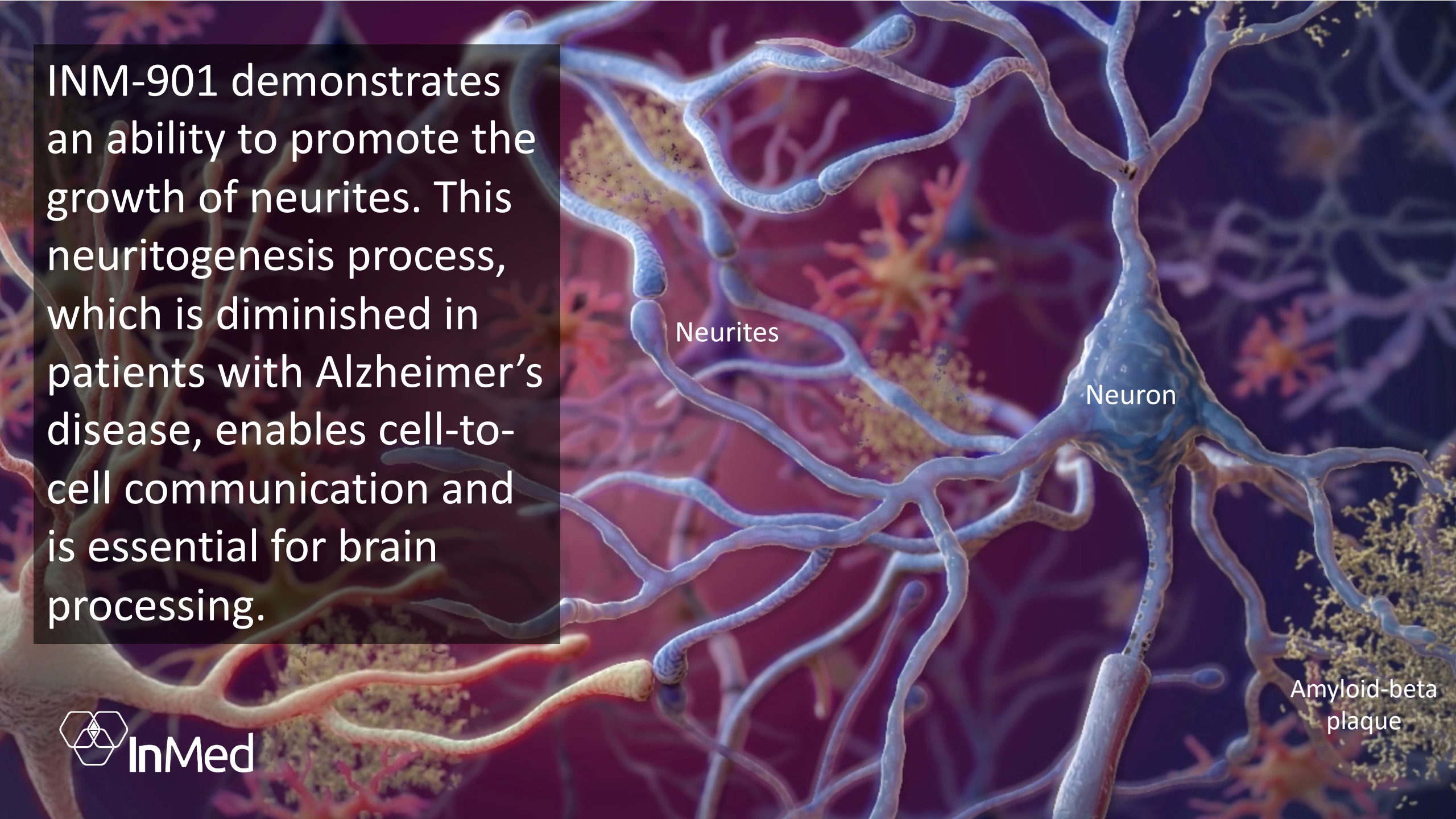






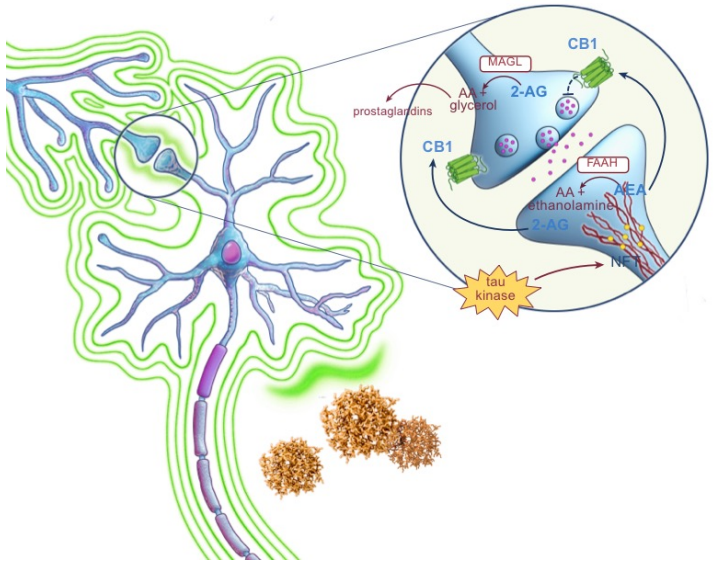
INM-901

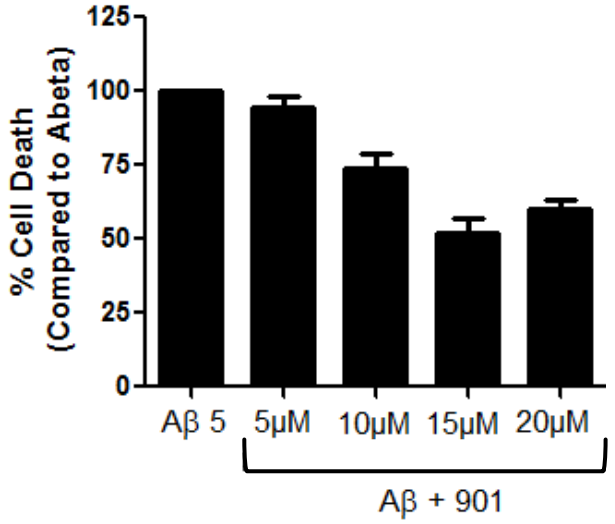
- Proprietary small molecule compound can cross BBB
- May be formulated orally
- NOT expected to have intoxicating effects
- Preferential signaling agonist for CB1/CB2
- Impacts PPAR signaling pathways


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

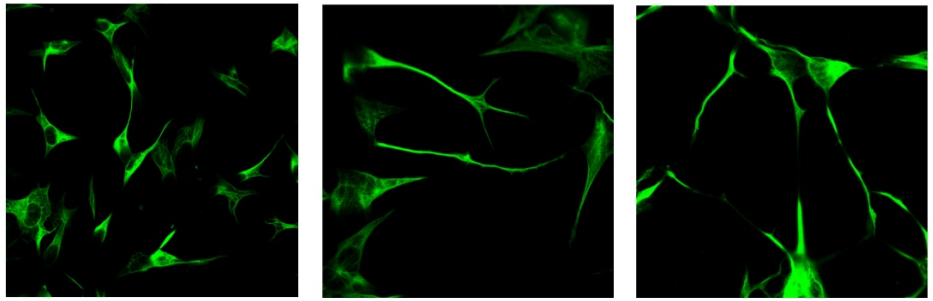
- Amyloid-β-induced toxicity model
- Blocking of cytotoxicity and apoptosis
- Neuroinflammation decreased

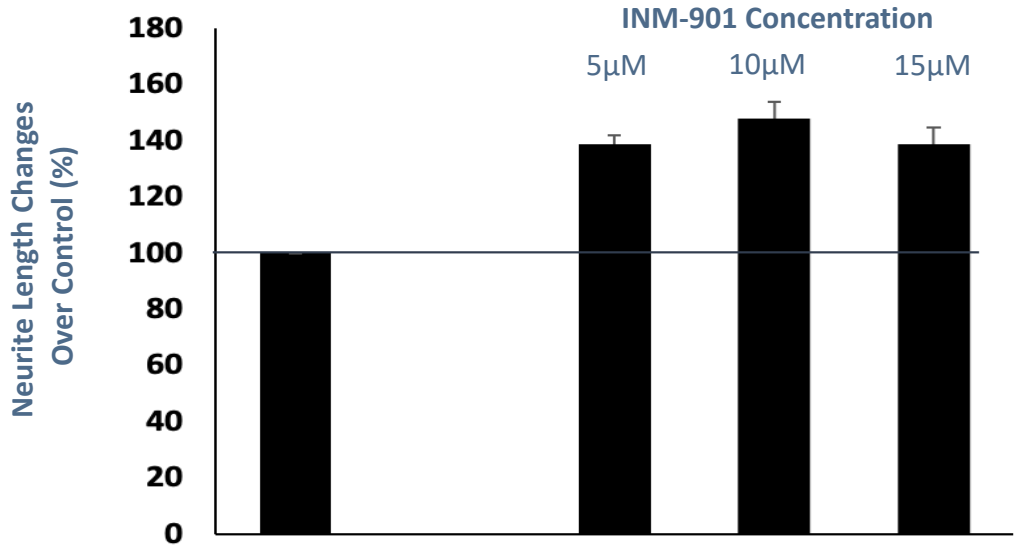
Result

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.





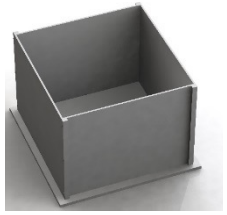
Neuritogenesis Studies

- Measured neurite length compared to control and THC
- 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 DISEASE PROOF-OF-CONCEPT MODELS



Open Field-Single Enclosure (basal and locomotor activity)

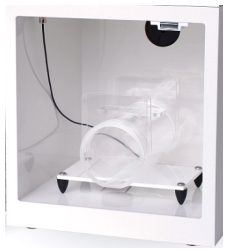
- Treated groups have similar behavior as normal

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

- 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 mRNA 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.

Summary: Demonstrates Multiple Pharmacological Effects

POTENTIAL TO TARGET SEVERAL BIOLOGICAL PATHWAYS ASSOCIATED WITH ALZHEIMER'S DISEASE

Neuroprotection Studies

- Amyloid-β-induced model
- Cytotoxicity and apoptosis
- Neuroinflammation decreased

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Neuritogenesis Studies

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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 6-month in 5xFAD with increasing sample size (on-going)
- Planning study in PS19 Tau 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

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Thank you!

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