

# Prevention and Treatment of Alzheimer's Disease by Anti-Bin1 Antibody

Technology Readiness Level 5: Validated in Relevant Environment

# **Lead Investigators**

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# **Unmet Need**

Late-Onset Alzheimer's Disease (LOAD), the most common sporadic form of Alzheimer's Disease, (AD) is skyrocketing in developed countries with aging populations. In the U.S. alone, about 5.8 million individuals have AD and it is the 6<sup>th</sup> leading cause of death, according to the Alzheimer's Association. Given the aging demographics of developed countries, there is an unprecedented need for strategies to prevent and treat dementia, most especially LOAD.

# **Opportunity**

Multiple human genetics studies have identified Bin1 as one of the top two risk factors for LOAD. Neurology studies indicate that Bin1 binds and influences turnover of the protein tau as a likely mechanism for how Bin1 promotes LOAD risk. LIMR scientists have developed a cell-penetrating anti-Bin1 antibody that promotes tau turnover to inhibit its expression and deposition in the brain. This therapeutic technology based on a novel MOA offers a route to prevent or attenuate AD driven by tau deposition. The global market for effective therapeutics for AD is estimated to grow from \$3.64B in 2017 to \$5.66B in 2024, according to Zion Market Research.<sup>1</sup>

#### **Unique Attributes**

Bin1 has been genetically validated in different human populations as a leading driver of LOAD. This scaffold and signaling molecule modifies the stress and inflammatory responses of cells that experience oxidative stress. The cell-permeable anti-Bin1 antibody developed by LIMR scientists offers the first biologic strategy to target the pathogenic function of Bin1, as demonstrated in inflammatory bowel disease. Moreover, anti-Bin1 has been found to block tau function and deposition in cell culture and animal models in multiple laboratories. Notably, emerging evidence suggests that gut-brain interactions drive the development of AD and other neurodegenerative diseases. Given the evidence that elevated Bin1 expression is a major risk factor for LOAD, the anti-Bin1 strategy created by LIMR scientists offer a new MOA to attack LOAD. Survival benefits have been observed from initial tests of anti-Bin1 administration in a tauopathy-based mouse model of AD. Accordingly, anti-Bin1 may be useful to prevent or treat LOAD in patients.

<sup>&</sup>lt;sup>1</sup> Zion Market Research, New York, NY. July 26, 2018.

# **Clinical Applications**

The LIMR mAb offers potential uses to treat LOAD and other tauopathy-based pathologies.

#### **Stage of Development**

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Current work is at a preclinical stage of development including ongoing mechanism studies.

# **Intellectual Property**

US Patent No. 11,345,747 issued May 2022 ("Methods and Compositions for the Treatment of Diseases and Disorders").

# **Collaboration Opportunity**

Optimization and humanization of murine anti-BIN1 mAb 99D exhibiting anti-tau properties.

#### **Published References**

- Thomas S, Hoxha K, Alexander W, Gilligan J, Dilbarova R, Whittaker K, Kossenkov A, Prendergast GC and Mullin JM. (2019). Intestinal barrier tightening by a cell penetrating antibody to Bin1, a candidate target for immunotherapy of ulcerative colitis. J Cell Biochem 120: 4225-4237.
- Thomas S, Hoxha K, Tran A and Prendergast, GC. (2019). Bin1 antibody lowers the expression of phosphorylated Tau in Alzheimer's disease. J Cell Biochem 120: 18320-18331.
- Thomas, S, Mercogliano G and Prendergast GC (2020). Bin1 targeted immunotherapy alters the status of enteric neurons and the gut microbiome during ulcerative colitis treatment. Preprints 2020: doi:10.20944/preprints202008.0643.v1.

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