

# Lead Lankenau Institute for Medical Research Investigators

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## **Unmet Need**

The incidence of late-onset Alzheimer's disease (LOAD) in developed countries with aging populations is skyrocketing. In the U.S. alone, about 5.8 million have Alzheimer's disease (AD), and it is the sixth leading cause of death, according to the Alzheimer's Association. Medical advances paralleling aging demographics in developed countries have created an unprecedented need for strategies to prevent and treat dementia, most especially LOAD.

## Opportunity

Human genetics studies have identified Bin1 as second only to ApoE as a risk factor for LOAD. Neurology studies indicate that Bin1 binds and influences the turnover of tau as a likely mechanism in promoting LOAD risk. LIMR scientists developed a cell-penetrating Bin1 antibody that appears to promote tau turnover to inhibit its expression and cellular deposition. This therapeutic technology based on novel MOA may offer a route to 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**

The scaffold and signaling molecule Bin1 modifies stress and inflammatory responses of cells under stress. A cell-permeable anti-Bin1 antibody — developed by LIMR scientists as a strategy to blunt its pathogenic function in inflammatory bowel disease — was found to exert anti-tau effects in cell culture and animals when examined. With the emergence of elevated Bin1 expression as a risk factor in LOAD development, this experimental therapeutic may be effective. Indeed, given emerging evidence of gut-brain interactions in the development of neurodegenerative diseases, including LOAD, this therapeutic intersection may be relevant.

A survival benefit has been observed in early tests of anti-Bin1 administration in a tauopathybased mouse model of AD. Accordingly, anti-Bin1 may offer a novel tractable target to limit the development or progression of AD pathophysiology in patients.

### **Clinical Applications**

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

### **Stage of Development**

Current work is at a preclinical stage of development, including ongoing mechanism studies and antibody humanization.

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

# **Intellectual Property**

U.S. 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 exhibiting anti-tau properties.

## **Published References**

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- 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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