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PRESS RELEASE

Samumed Announces Publication of Preclinical Data Demonstrating That SM07883 is a Potential Treatment for Alzheimer's Disease

SAN DIEGO – July 18, 2019 - Samumed, LLC, announced today the publication of preclinical data demonstrating that SM07883 inhibits tau pathology and associated neuroinflammation, both of which are implicated in Alzheimer's disease. The article titled "Tau pathology reduction with SM07883, a novel, potent, and selective oral DYRK1A inhibitor: A potential therapeutic for Alzheimer's disease" has been published in *Aging Cell*. SM07883 is a novel, small-molecule dual-specificity tyrosine phosphorylation-regulated kinase 1A (DYRK1A) inhibitor currently being evaluated in a Phase 1 clinical trial (ACTRN12619000327189).

"Patients urgently need a treatment for Alzheimer's disease. DYRK1A represents an important target to potentially change the course of this devastating disease," said Yusuf Yazici, M.D., Chief Medical Officer of Samumed. "These published data show that treatment with our potentially first-in-class DYRK1A inhibitor significantly reduces effects of pathological tau and neuroinflammation while improving performance on a motor task compared to vehicle in animal models."

Data highlights include:

- SM07883 demonstrated good oral bioavailability and brain distribution across multiple species.
- SM07883 was shown to be a potent and specific inhibitor of DYRK1A ($IC_{50} = 1.6nM$) and GSK-3β ($IC_{50} = 10.8nM$), two kinases thought to contribute to tau pathology and β-amyloid production.
- Both *in vivo* and *in vitro* treatment with SM07883 reduced tau phosphorylation of multiple tau epitopes.
- Long-term (3-month) effects of SM07883 treatment, assessed in tau transgenic mice, showed significant reductions in tau hyperphosphorylation, oligomeric and aggregated tau, and tau-positive inclusions compared to vehicle in brain samples.
- SM07883-treated tau transgenic mice had a significant reduction in disease-associated neuroinflammation compared to vehicle.
- SM07883 was well tolerated and treatment led to significantly improved general health, weight gain, and functional improvement during a motor task compared to vehicle-treated mice.

About Alzheimer's Disease

Alzheimer's disease (AD), the most common cause of dementia, is a chronic neurodegenerative disease affecting an estimated 5.8 million people in the U.S. and over 46 million people worldwide. The disease is characterized by progressive memory loss and slow progression to

severe difficulty in accessing basic brain functions, prompting mental disorders. With the world's aging population, AD is quickly becoming "The Disease of the Century," a global epidemic, and a socioeconomic burden impacting families, social service, and healthcare delivery systems. Currently available therapies treat symptoms, not the disease itself, which is ultimately fatal.

About Samumed and SM07883

SM07883 is an oral, small-molecule dual-specificity tyrosine phosphorylation-regulated kinase 1A (DYRK1A) inhibitor in development as a potential therapy for the treatment of Alzheimer's disease. Preclinical data suggest that SM07883 reduces tau and amyloid pathology as well as neuroinflammation while also improving behavior compared to controls. Additional information on Samumed's SM07883 Alzheimer's disease program can be found here: https://www.samumed.com/pipeline/detail.aspx?id=18.

Learn more about Samumed's potential regenerative drug candidates and broad clinical pipeline at https://www.samumed.com/pipeline/default.aspx.

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