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**Neurogenetic Pharmaceuticals announces studies showing
its proprietary compound reduces brain plaques
associated with Alzheimer's disease**

*Data published in Neuron demonstrates proof of concept in long term prevention
of disease pathology in a mouse model, without GI side effects*

SAN DIEGO -- In the Sept 9, 2010 issue of *Neuron*, Neurogenetic Pharmaceuticals, Inc. (NGP) reports proof of concept studies that show its proprietary compound, NGP 555, is effective in preventing the amyloid pathology of Alzheimer's disease (AD) in a transgenic mouse model. The study further demonstrates that following chronic treatment with the gamma secretase modulator (GSM) compound from NGP, the mice were devoid of gastrointestinal side effects, an adverse finding commonly associated with gamma secretase inhibitors (GSIs).

A major pathological hallmark of Alzheimer's disease is an abundance of neuritic plaques in key areas of the brain involved in memory and cognition. Decades of studies have confirmed that $A\beta_{42}$ forms the "seed" of these amyloid plaques, which gradually accumulate in the brain and induce neuronal cell death in the underlying brain tissue. This "toxic" molecule is generated by a stepwise process involving a pivotal enzyme, gamma secretase. Modification of gamma secretase activity to decrease production of $A\beta_{42}$, thereby reducing the deposits of $A\beta_{42}$ -seeded plaques, would be beneficial for the prevention of Alzheimer's disease-related pathology.

"We are pleased to make public these data on our gamma secretase modulator, NGP 555," said Dr. William T. Comer, President and CEO of Neurogenetic Pharmaceuticals. "Deposition of amyloid plaques can precede dementia by many years, and the progression of plaques to dementia reflects neuronal loss which is irreversible. We believe that halting this gradual progression of AD from pathology to dementia represents a major unmet need, especially given the growth of an aging population and the enormous cost to society for care and hospitalization. Recent advances in the use of $A\beta$ biomarkers in the cerebrospinal fluid and brain scans should permit early diagnosis of AD pathology and allow us to show that NGP 555 prevents the amyloid pathology."

The work published in *Neuron* is the first to describe these mechanistically and biochemically distinct GSM compounds and how they provide a more selective mechanism than GSIs. The key advantages of these small molecules include reduction of the "toxic" form of beta amyloid ($A\beta_{42}$), direct binding to components of the gamma secretase complex, and excellent brain

exposure. The paper demonstrated that Neurogenetic Pharmaceuticals' approach of gamma secretase modulation allows for selective reduction of A β ₄₂ and amyloid pathology. Oral administration of NGP 555 (identified as compound 4 in *Neuron*) in transgenic AD mice resulted in a dose-related lowering of both plasma and brain A β ₄₂. Chronic daily administration for 7 months led to significant reduction in both diffuse and neuritic plaques, without the GI-related side effects found with GSI compounds, according to the paper in *Neuron*. The work, conducted by researchers at TorreyPines Therapeutics (TPTX) in collaboration with academic institutions, concludes that these types of GSM compounds warrant further investigation as a potentially safe and effective approach for prevention of AD.

"This study links A β biomarker and pathology findings with a mechanistic understanding of how our compounds selectively target a key enzyme involved in the pathology of Alzheimer's disease," said Maria Z. Kounnas, Ph.D., lead author on the study and vice president of Alzheimer's Research at NGP. "Combining early disease identification with a treatment capable of preventing AD-related pathology, such as NGP 555, would represent an important advance in our ability to prevent AD or hinder its progression to dementia. Clearly, the earlier AD is detected and treated, the better the likelihood of a good outcome."

For further information, email the Media Contact listed below (tom@gablepr.com) for a copy of the full paper or read after Sept. 9 in *Neuron* at: <http://www.cell.com/neuron/current>

About Alzheimer's disease

The Alzheimer's Association (www.alz.org) describes Alzheimer's as a progressive and fatal brain disease, with as many as 5.3 million Americans and up to 30 million worldwide currently living with the disease. The National Institute of Health reports that unless the disease can be effectively treated or prevented, the number of people with AD will increase significantly. The number of people age 65 and older in the U.S. is expected to grow from 39 million in 2008 to 72 million in 2030, with the number of people with AD doubling every 5-year interval beyond age 65, according to the NIH. For further information:

<http://www.nia.nih.gov/Alzheimers/AlzheimersInformation/GeneralInfo/>

About Neurogenetic Pharmaceuticals, Inc.

Neurogenetic Pharmaceuticals, Inc. (NGP) is a biopharmaceutical discovery and development company founded in 2009 which is focused on developing innovative drug therapies for use in the treatment of neurodegenerative disorders such as Alzheimer's disease. Based in San Diego, Calif., the company's next objective is to obtain an Investigational New Drug approval for its

clinical candidate, NGP 555. This compound is expected to prevent the deposition of amyloid plaques in the brain, thereby precluding neuronal cell death and the dementia associated with AD. Future clinical trials will utilize specific A β biomarkers and/or brain scanning as an early diagnostic and to monitor drug efficacy in clinical trials. NGP licensed the GSM intellectual property from TPTX and expanded its portfolio to include issued patents in the US, Europe, China, India, Japan, Australia, and other countries. For further information, see www.neurogeneticpharmaceuticals.com

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