NEUROPHAGE’S NPT001 REDUCES AMYLOID PLAQUE LOAD, INCREASES SYNAPTOPHYasin
AND IMPROVES FUNCTIONAL ENDPOINTS IN A MOUSE MODEL OF ALZHEIMER’S DISEASE

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Introduction: NeuroPhage Pharmaceuticals is developing a novel therapy for the treatment of
neurodegenerative diseases, including Alzheimer’s disease. Our leading drug candidate, NPT001, is a
filamentous M13 bacteriophage that binds to Abeta with high affinity. NPT001 has been shown to
disaggregate Abeta plaque in a concentration-dependent manner in vitro.

Aims: The current study was conducted to assess the in vivo effect of NPT001 on neuropathology and
behavior in aged B6;SJL-Tg(APPswe)2576Kha mice.

Methods: Nineteen-month-old female Tg2576 mice received bilateral intrahippocampal injections of
NPT001 or vehicle. Following recovery from surgery, locomotor activity was monitored in a 60-min test
and spontaneous alternation was assessed in a Y-maze. Animals were sacrificed 24-hrs following
behavioral measures and Abeta and synaptophysin levels were assessed via immunohistochemistry in
both the hippocampus and cortex.

Results: Tg2576 mice (vehicle-treated) exhibited significantly increased plaque load, decreased
synaptophysin staining, pronounced hyperactivity and reduced spontaneous alternation compared to
nontransgenic controls receiving vehicle. Tg2576 mice that received NPT001 treatment had significantly
reduced amyloid plaque and significantly increased synaptophysin staining in the hippocampus and
cortex compared to vehicle-treated Tg2576 mice. In addition, Tg2576 mice receiving NPT001 had
reduced hyperactivity and increased spontaneous alternation compared to vehicle-treated Tg2576 mice.

Conclusions: Bilateral intrahippocampal injections of NPT001 in aged Tg2576 mice produced significant
reductions in amyloid plaque along with increased synaptophysin levels in both hippocampal and cortical
areas of the brain. In addition, improvement was noted in a spatial working memory task and hyperactivity
was reduced. NPT001 was well-tolerated and produced no observable adverse effects.