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Title:

A 2-year study in monkeys to evaluate expression, bioactivity, and safety/tolerability of CERE-110, an AAV2-based vector encoding NGF for the potential treatment of Alzheimer's disease

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Neurotrophic factor-mediated support of degenerating cholinergic neurons in the nucleus basalis of Meynert (NBM) may provide therapeutic benefit in Alzheimer's disease (AD). CERE-110 is an AAV2-derived viral vector encoding nerve growth factor (NGF) that is currently in development as a potential therapeutic for AD. CERE-110 has previously been shown to be effective in the fimbria-fornix lesion model of cholinergic degeneration, to produce significant trophic effects on NBM cholinergic cells of aged rats, young intact rats, as well as monkeys, and to be safe and well tolerated in rats for up to 1 year and in monkeys for up to 3 months. CERE-110 is currently being assessed in a small Phase 1 clinical study in subjects with AD. To further characterize the potential long-term safety/tolerability and NGF expression of CERE-110 delivery to the NBM, we have conducted a 2-year GLP study in monkeys. Young adult cynomolgus monkeys (n=18) were bilaterally injected with CERE-110 or control formulation buffer and were sacrificed at either 1 or 2 years following administration. Three different dose levels of CERE-110 were tested, the highest dose being over 50 times higher (by brain weight) than the highest dose tested in the ongoing Phase 1 clinical study of CERE-110 in AD subjects. Over the 2-year in-life portion of this monkey study, no adverse effects of CERE-110 were observed on any in-life endpoint examined including daily observations, neurological and physical exams, body weight and food consumption, and clinical chemistry and hematology analyses. Immunohistochemical analysis confirmed persistent and localized dose-related expression of NGF in the NBM. No CERE-110 related histopathological abnormalities were observed on an extensive panel of organs and tissues including the cerebrum, cerebellum, medulla, and upper spinal cord. Analyses of the expression of NGF (intensity and volume), as well as long-term NGF bioactivity (ChAT cell analyses), and additional safety measures at 1 and 2 years are currently being examined and will be presented.

Disclosures:

K.M. Bishop, Ceregene Inc., A. Employment (full or part-time); Ceregene Inc., E. Ownership Interest (stock, stock options, patent or other intellectual property); **C.D. Herzog**, Ceregene Inc., A. Employment (full or part-time); Ceregene Inc., E. Ownership Interest (stock, stock options, patent or other intellectual property); **J.R. Zeller**, NBR, A. Employment (full or part-time); **M.A. Printz**, Ceregene Inc., A. Employment (full or part-time); Ceregene Inc., E. Ownership Interest (stock, stock options, patent or other intellectual property); **M. Gasmi**, Ceregene Inc., A. Employment (full or part-time); Ceregene Inc., E. Ownership Interest (stock, stock options, patent or other intellectual property); **E.P. Brandon**, Ceregene Inc., A. Employment (full or

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