



Presentation Abstract

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Title: AAV2-neurturin (CERE-120) for advanced Parkinson's disease (PD):  
Efficacy and safety results from a controlled Phase 2 clinical trial

Location: South Hall A

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Abstract: 58 patients with advanced PD and motor fluctuations were randomized (2:1 ratio) to receive either intraputaminatal CERE-120 or sham surgery. All patients, investigators, and study personnel were blinded to treatment, except the immediate neurosurgical team. The primary efficacy endpoint was UPDRS motor score in the practically defined "off" state (i.e., assessed with PD medications held for 12 hours) at 12 months. Safety was evaluated by standard methods and reviewed by an independent data monitoring committee.

At 12 months, no difference was seen between CERE-120 and sham surgery in the primary efficacy measure (7.2 point improvement versus 6.9 point

improvement, respectively;  $p=0.9$ ), though several secondary endpoints did suggest a modest difference favoring CERE-120. Protocol-prescribed analyses of data from a subset of 30 subjects under double-blind conditions up to 18 months suggest increasing effects of CERE-120 over time, with clinically modest but a statistically significant treatment effect in the primary efficacy measure at 18 months ( $p=0.025$ ), as well as in several secondary measures ( $p<0.05$ ). No measurement favored the sham surgery group. Adverse events were consistent with the nature of the surgical delivery procedure and none were deemed definitively related to CERE-120, which was considered safe and well-tolerated. An analysis of the brains of two CERE-120 patients who died of unrelated causes revealed clear evidence of neurturin expression in the targeted putamen, but no evidence for protein in the substantia nigra (SN) and minimal tyrosine hydroxylase increase (*see related CERE-120 abstract by Kordower et al; this meeting*). These findings suggest that a deficit in axonal transport in degenerating nigrostriatal neurons impaired transport of CERE-120 and/or neurturin from the terminals in the putamen to the cell bodies in the nigra, thereby reducing its bioactivity. Administration of CERE-120 directly into the SN, as well as the putamen, will be considered in future trials of advanced PD as a means to ensure neurturin is also expressed in the SN.

Disclosures:

**J. Siffert**, Ceregene Inc., A. Employment (full or part-time); **W.J. Marks**, Ceregene inc., B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); **P.A. Starr**, Ceregene inc., B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); **M.A. Stacey**, Ceregene inc., B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); **N.M. Boulis**, Ceregene inc., B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); **J.L. Vitek**, Ceregene inc., B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); **L. Verhagen**, Ceregene inc., B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); **R.L. Watts**, Ceregene inc., B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); **J. Jancovic**, Ceregene inc., B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); **M. Tagliati**, Ceregene inc., B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); **M.B. Stern**, Ceregene inc., B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); **J.G. Nutt**, Ceregene inc., B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); **J.H. Kordower**, Ceregene Inc., F. Consultant/Advisory Board; **C.W. Olanow**, Ceregene Inc., F. Consultant/Advisory Board; **R.T.**

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