Introduction

- Intrathalamic delivery of AVB-101 (FTD-GEN9) shows a promising therapeutic effect in FTD patients.
- AVB-101 is an adeno-associated virus serotype 9-based gene therapy that encodes human PGRN and is in development to treat patients with FTD.

Varieties of Vector Biodistribution

- Vector biodistribution is crucial for understanding the safety and efficacy of the therapy.

Study Design

- Table 1: Study Details for the Distribution and Toxicology Studies Conducted in Cynomolgus Monkeys

Results

- Preclinical Safety of AVB-101 up to 6 Months
  - No neurologic adverse events
  - No noxious effects on haematology, coagulation, urinalysis, or cerebrospinal fluid (CSF) clinical pathology
  - No changes in functional observation battery, electrocardiography, or ophthalmology
  - No significant increase in baseline in urine, vaccine, or urine rate at any time point

- Histopathology Summary
  - No test article-related organ weight changes, macroscopic observations, or microscopic findings in non-nervous tissues at 3- and 6-month timepoints

- Table 2: Incidence and Grade (G)*/Observed for Major Test-Article-Related Findings in the Brain at 3- and 6-Months Post-Intrathalamic Administration (n=48)

Conclusions

- AVB-101 has been engineered for specific, effective, and targeted CNS expression of PGRN in patients with FTD.
- AVB-101 is designed to normalize central PGRN levels in patients with FTD due to G4N mutations while restricting PGRN expression to neurons and enhancing secretory efficiency to minimize the required dose of vector.

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References: A list of references is provided to support the information presented in the study.

AVB-101 delivered by intrathalamic injection results in novel and promising approaches to address various medical needs in FTD. ASPT’s FTD is an ongoing Phase I/II clinical trial to evaluate the safety and preliminary efficacy of AVB-101 in FTD.

Table 1: Study Details for the Distribution and Toxicology Studies Conducted in Cynomolgus Monkeys

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>Toxicology</th>
<th>Biodistribution</th>
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<tbody>
<tr>
<td>3 months</td>
<td>Dose (VG/day)</td>
<td>0, 2.5×10^11 VG/hemisphere</td>
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<tr>
<td>6 months</td>
<td></td>
<td>2.5×10^11 VG/hemisphere</td>
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Table 2: Incidence and Grade (G)*/Observed for Major Test-Article-Related Findings in the Brain at 3- and 6-Months Post-Intrathalamic Administration (n=48)

<table>
<thead>
<tr>
<th>Finding</th>
<th>3-month cohort</th>
<th>6-month cohort</th>
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<tbody>
<tr>
<td>Neuropil changes</td>
<td></td>
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<tr>
<td>Glial proliferation</td>
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<tr>
<td>Reactive gliosis</td>
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<tr>
<td>Microgliosis*</td>
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Figure 3: VG Presence in Various Monochromes Upon Intrathalamic Delivery of AVB-101

Figure 4: VG Biodistribution in Various Tissues Following Intrathalamic Delivery of AVB-101

Figure 5: PGRN Expression in Brain Tissue Following Intrathalamic Delivery of AVB-101

Figure 6: PGRN Levels in CSF (A) and Serum (B) Following Intrathalamic Delivery of AVB-101

Figure 7: Neurotransmitterimbalance (A), Neuroinflammation (B), and Neurodegeneration (C) following intrathalamic delivery of AVB-101

Figure 8: Neurotransmitterimbalance (A), Neuroinflammation (B), and Neurodegeneration (C) following intrathalamic delivery of AVB-101

Figure 9: Neurotransmitterimbalance (A), Neuroinflammation (B), and Neurodegeneration (C) following intrathalamic delivery of AVB-101