Gene Therapy for Epilepsy

Unmet medical need with a strong rationale for gene transfer

- R. Jude Samulski PhD
  - CEO and Founder
  - ASKLEPIOS BioPharmaceutical Inc (Askbio)
ASKCNS109:
Mechanism of Action

Why Choose Galanin?

• Infusion of galanin into the CNS significantly attenuates seizure activity in a number of animal models.
• Galanin knockout mice exhibit a significantly greater seizure sensitivity while galanin overexpressing mice exhibit a reduced seizure sensitivity.
• Galanin exhibits neuroprotective actions

Why Choose AAV?

• Efficiently mediates stable long term gene delivery to the CNS
• Excellent safety profile (Pre-clinical & Clinical (PI-III))

LETTERS

Attenuation of seizures and neuronal death by adeno-associated virus vector galanin expression and secretion

Rebecca P Haberman¹, R Jude Samulski¹,³ & Thomas J McCown¹,²

Relevant Publications

Platform & Pipeline Technology

- Mature gene delivery IP platform based on Adeno-Associated Virus (AAV), with over 64 patents and applications.

- Based on 25 years experience & >$40M R&D

- IP licensed by GSK, Merck, Medtronic & others

- Multiple POC and clinical studies support as CNS gene delivery system

- Unique IP improves upon efficiency and safety and has been validated in the clinic

- Epilepsy program builds on IP for anti-epileptic neuropeptide gene expression.
Ongoing-Preclinical Studies

Rodent models - early risk mitigation:
- Preliminary behavioral and cognitive testing.
- Optimization of expression cassette
- Top level toxicity

Primate studies:
- Proof of principle in cortically robust species.
- Allows for assessment of both kindling and spread.
- Accurate test of surgical technique is well as proof of principle.
- Allows comparison of gene Tx and resection procedures.

Phase I clinical trial of dsAAV2.5-FIB-Galanin gene vector infusion in Intractable Mesial Temporal Lobe Epilepsy
- Demonstrate safety of ASKCNS109
- Establish Dosing of ASKCNS109
- Initial efficacy of ASKCNS109.
Milestones & Timelines

- Small animal POC Completed
- Epilepsy Pre-clinical Program Initiation 11/2007
- BNP-CNS Rodent Studies Underway
- BNP-CNS Primate Studies Underway
- Pre-IND Meeting ~ Q4/2008
- Phase I Trial initiation ~Q1/2010
Potential

- TLE is the most common form of treatment-resistant epilepsy.
- Studies indicate that approximately 50% of patients have either no or limited response to medical therapy even on multiple AED.
- Approximately 300-400 thousand individuals are affected

» Galanin Gene Therapy

- Potential seizure reduction without loss of cognitive function associated with resection
- Neuro-protective & Anti-convulsant benefits with single treatment
- Potential to treat refractory TLE patients who are not candidates for resection due to localization