HSG 2019: VX15 (pepinemab) Antibody Treatment for HD
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The pepinemab Story
Neurons, Astrocytes, and SEMA4D

- **Neurons**: Neuronal degeneration and atrophy is observed in HD.
- **Astrocytes**: Most common glial cell in the brain, performs many functions (structural and metabolic support, BBB, vasomodulation among others).
- **SEMA4D**: Triggers collapse of the astrocyte cytoskeleton which results in loss of normal astrocyte functions and gain of inflammatory activity.
The pepinemab Story

• Why is SEMA4D important in HD?
  • SEMA4D is upregulated on neurons, binds to astrocytes
  • SEMA4D triggers collapse of the astrocyte cytoskeleton aggravating damage to the brain in HD.

• Enter pepinemab! How does Vaccinex’s drug work?
  • Pepinemab antibody blocks SEMA4D, a molecule that triggers collapse of a cell’s cytoskeleton
Treatment Rationale: Anti-SEMA4D Antibody can Prevent Inflammatory Transformation of Astrocytes that Aggravate Brain Damage in HD

- Glucose transport in brain is one of several important normal astrocyte functions that are known to be compromised in HD

- In a previous clinical study, Vaccinex has shown that treatment with pepinemab has a dramatic effect in preventing loss of glucose transport in the brain
Huntington’s Disease Clinical Trial Design: Cohort B

**Cohort B Group 1**
- 179 early manifest subjects randomized 1:1 Drug:Placebo
- Double-blind treatment with VX15 (pepinemab)
- 18 months
- 2020

**Cohort B Group 2**
- 86 late prodromal subjects randomized 1:1 Drug:Placebo
- Double-blind treatment with VX15 (pepinemab)
- 18 or 36 months
- 2020

1 month safety follow-up

Database lock and analysis for Cohort B

- November 2019
Our Current Chapter

• Enrollment completed December 2018

• Surpassed any previous enrollment rates in an HD treatment trial due to the extraordinary efforts of the entire SIGNAL team

• Deep in preparations for database lock and subsequent data analysis

• Preparing for BLA submission and commercialization

What’s the Next Chapter in Our Story?

• We don’t know, but we’re going to find out together
Sincerest Gratitude

Amazing science doesn’t mean much without the VISION of organization like the HSG, the COMMITMENT of organizations like the CTCC, the SUPPORT of our vendor collaborators the DEDICATION of investigators and their staff, or the SACRAFICE of participants living with HD and their families.