Science in the Service of Medicine

Unique Targets.
Novel Mechanisms.
New Medicines.

VX15 (pepinemab) Antibody Treatment for Huntington’s Disease

Forward Looking Statements

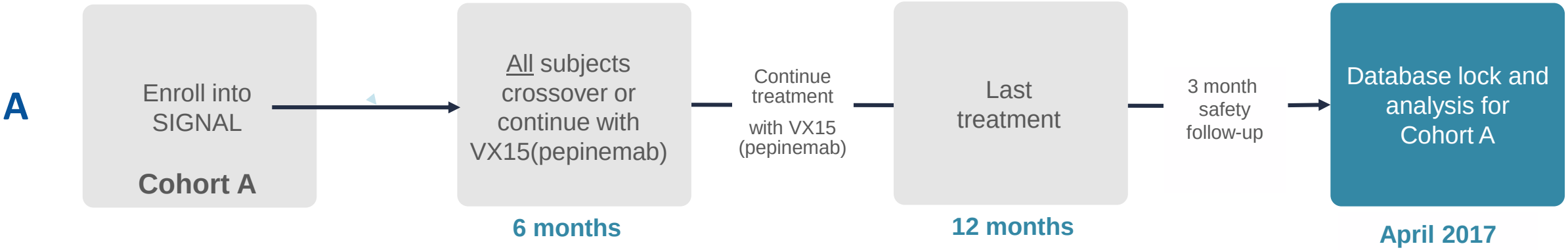
To the extent that statements contained in this presentation are not descriptions of historical facts regarding Vaccinex, Inc. (“Vaccinex,” “we,” “us,” or “our”), they are forward-looking statements reflecting management’s current beliefs and expectations. Words such as “may,” “will,” “expect,” “anticipate,” “estimate,” “intend” and similar expressions or their negatives (as well as other words and expressions referencing future events, conditions, or circumstances) are intended to identify forward-looking statements. Examples of forward-looking statements in this presentation include, among others, statements regarding: (i) the timing and success of the commencement, progress and receipt of data from preclinical and clinical trials; (ii) our expectations regarding the potential safety, efficacy or clinical utility of our product candidates; (iii) the expected results of any clinical trial and the impact on the likelihood or timing of any regulatory approval; (iv) financial and financing expectations and opportunities and (v) the performance of third parties.

Forward-looking statements in this presentation involve substantial risks and uncertainties that could cause our research and pre-clinical development programs, clinical development programs, future results, performance, or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, uncertainties inherent in the execution, cost and completion of preclinical and clinical trials, risks related to our dependence on third parties, uncertainties related to regulatory approval, risks related to our dependence on our lead product candidate VX15 (pepinemab), risks related to competition, other matters that could affect our development plans or the commercial potential of our product candidates, expectations regarding the use of proceeds from our initial public offering, changes in costs and operations, and other risks regarding our capital requirements and results of operations. Except as required by law, we assume no obligation to update these forward-looking statements, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future. For a further discussion of these and other factors that could cause future results to differ materially from any forward-looking statement, see the section titled “Risk Factors” in our quarterly report on Form 10-Q filed with the Securities and Exchange Commission (“SEC”) and the other risks and uncertainties described in our prospectus for our initial public offering dated August 9, 2018, filed with the SEC pursuant to Rule 424(b) under the Securities Act of 1933, as amended,.

No representations or warranties are offered in connection with the data or information provided herein. This presentation is intended for informational purposes only and may not be relied on in connection with the purchase or sale of any security. Any offering of our securities will be made, if at all, only upon the registration of such securities under applicable securities laws or pursuant to an exemption from such requirements.

Huntington's Disease Clinical Trial Design: Cohort A

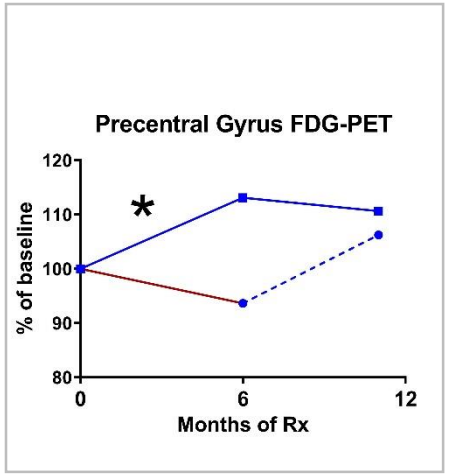
36 subjects
randomized 1:1 Drug:Placebo

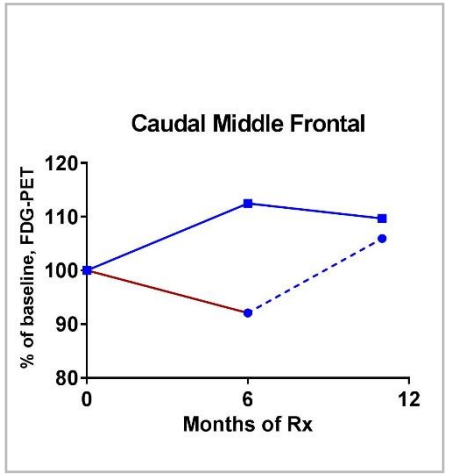


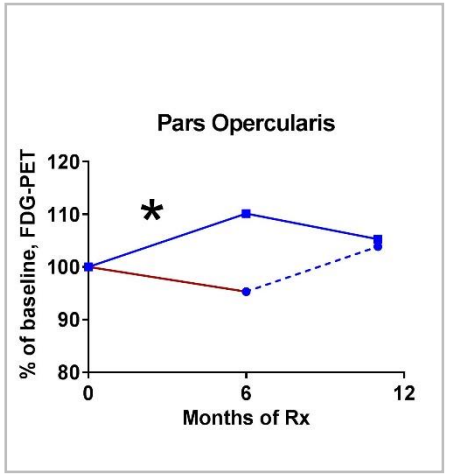
Adapt Cohort B design: sample size and treatment duration based on Cohort A data

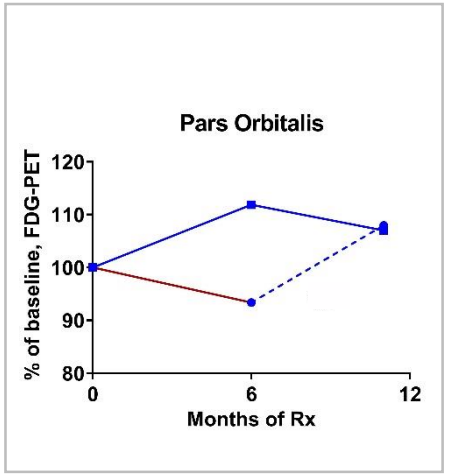
Disclaimer: VX15 (pepinemab) is under clinical investigation for the treatment of Huntington's disease and has not been demonstrated to be safe and effective for this indication. There is no guarantee that VX15 (pepinemab) will be approved for the treatment of Huntington's disease by the U.S. Food and Drug Administration or by any other health authority worldwide.

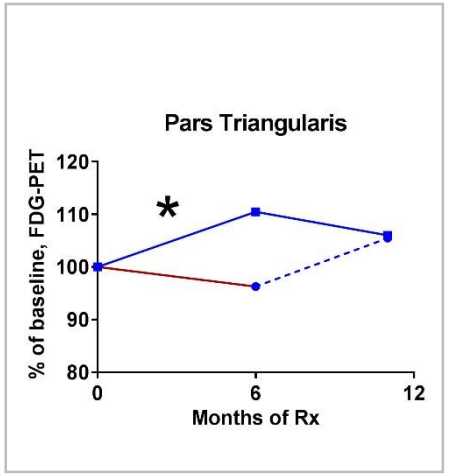
Clinical Evidence of Improved Brain Metabolic Activity in Frontal Lobe and Adjacent Parietal Regions: FDG-PET

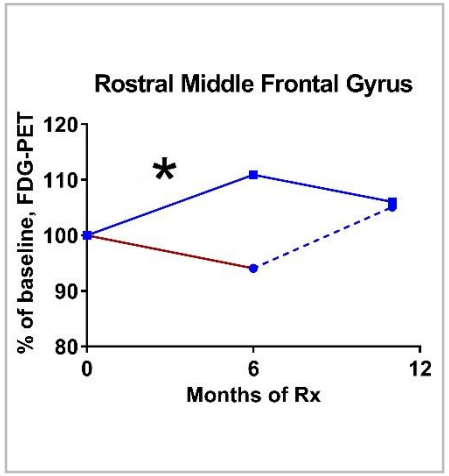


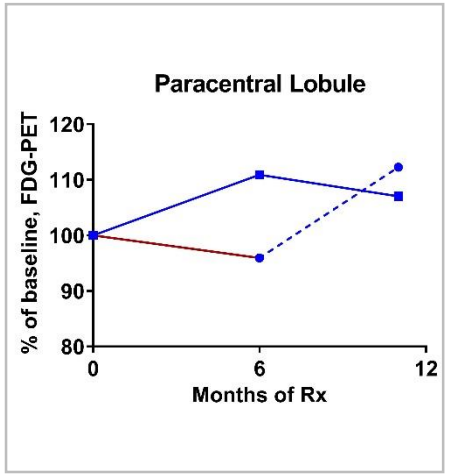


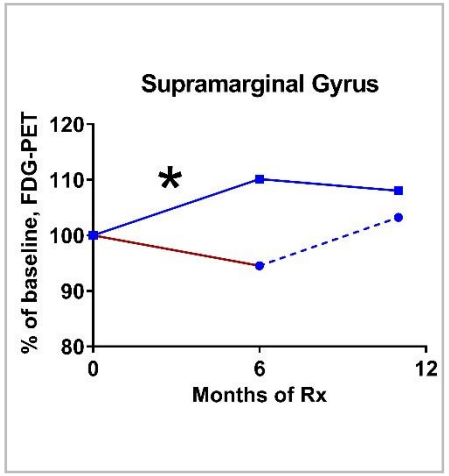


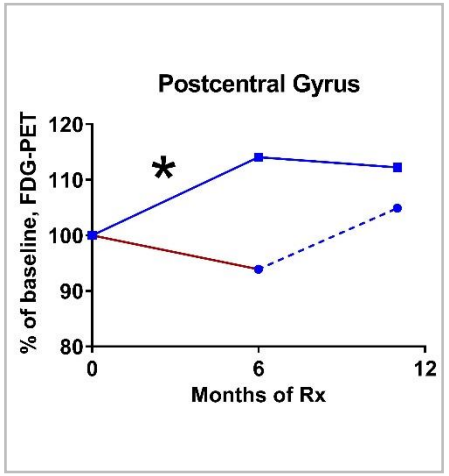


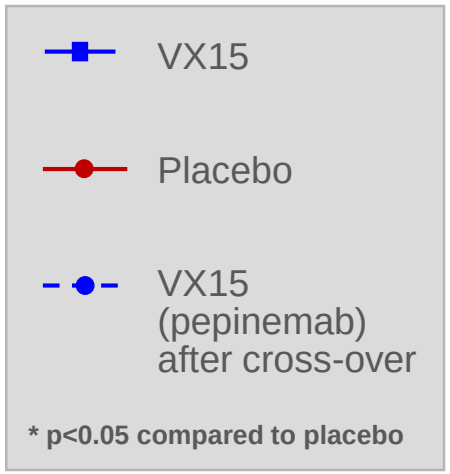












SIGNAL Cohort A Data Highlights

The Cohort A data includes both brain imaging results (FDG-PET and volumetric MRI) as well as quantitative motor and cognitive assessments of treatment effects

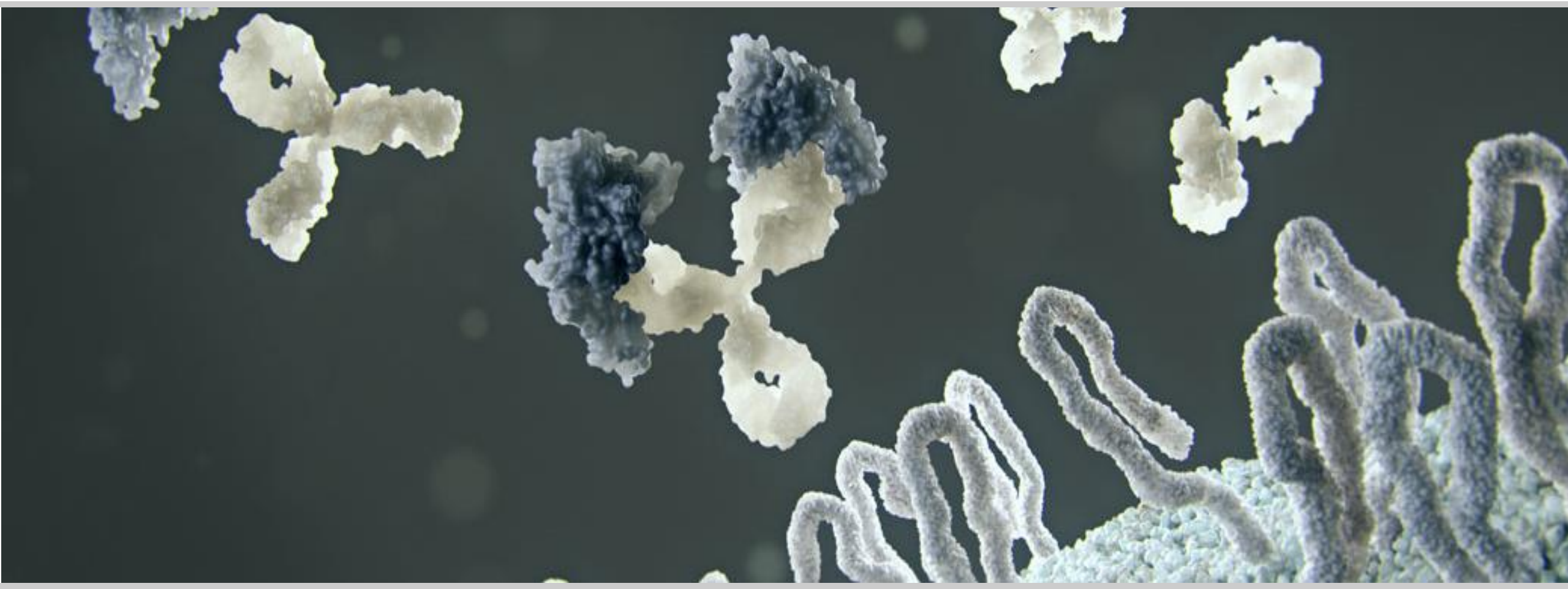
VX15 (pepinemab) treatment significantly increases metabolic activity as detected by FDG-PET:

- Previous studies in Alzheimer's Disease concluded that glucose metabolism is a sensitive measure of change in cognition and functional ability and has value in predicting future cognitive decline or as an outcome measurement for monitoring clinically-relevant change over time*.

Consistent and encouraging treatment effects on preservation of brain matter (reduced atrophy) and improvement in multiple motor and cognitive assessments were also seen in Cohort A

No concerning safety signals were identified

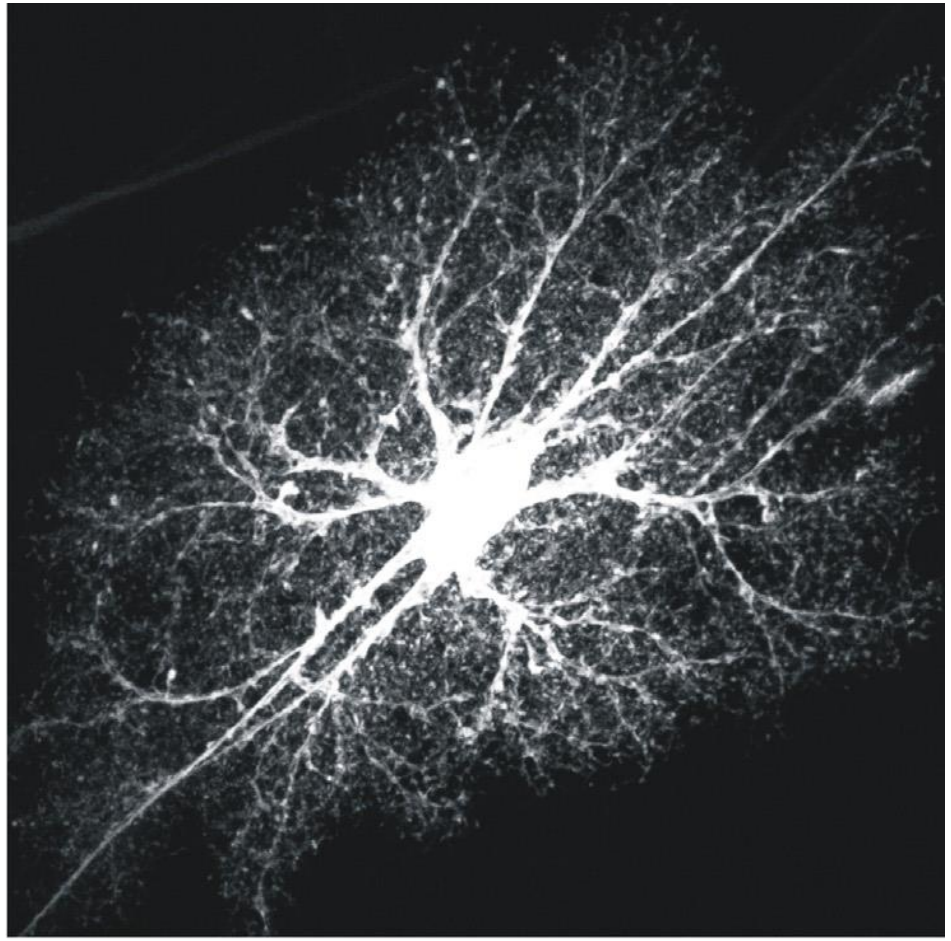
* Landau et. al., *Neurobiol Aging*. 2011; 32(7): 1207–1218



VX15 (pepinemab)/Anti-Semaphorin 4D for HD

HOW DOES IT WORK?

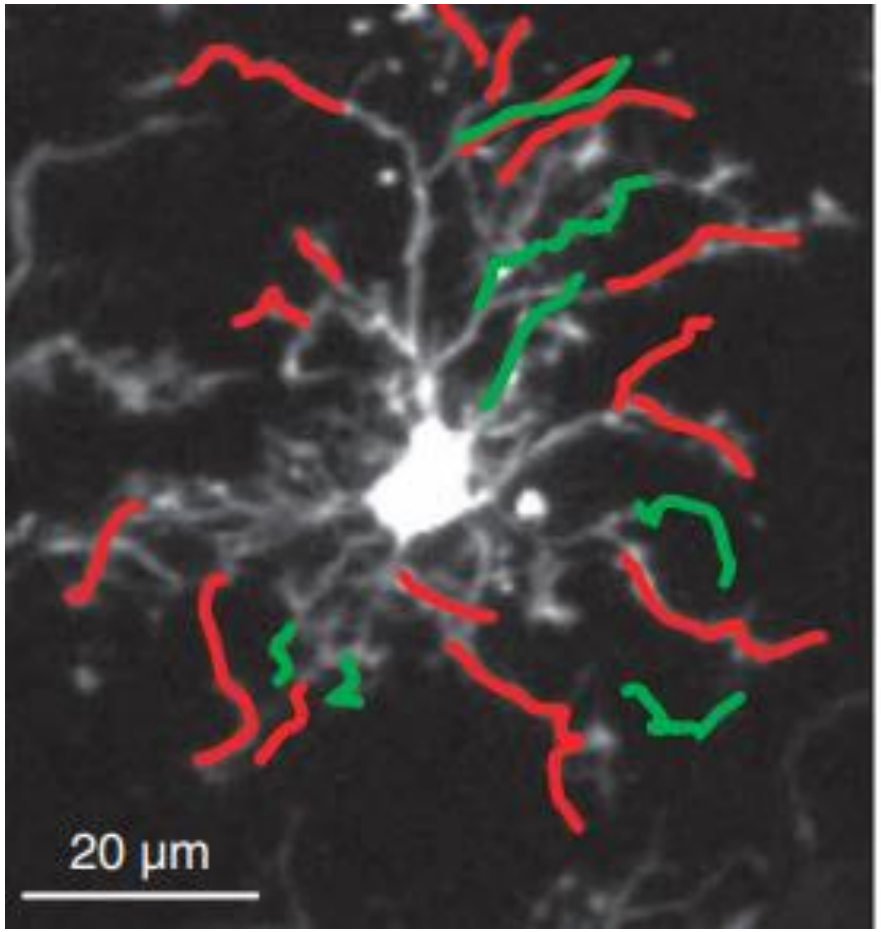
Astrocytes and Microglia



A single astrocyte can make >100,000 contacts with capillaries and neurons.

Human glia can both induce and rescue aspects of disease phenotype in HD.

Nature Communications 7:11758 (2016)



Extensions (green) and retractions (red) of microglial processes over the time course of 20 min. Average velocity is 1.5 µm/minute.

Science 308:1314 (2005)

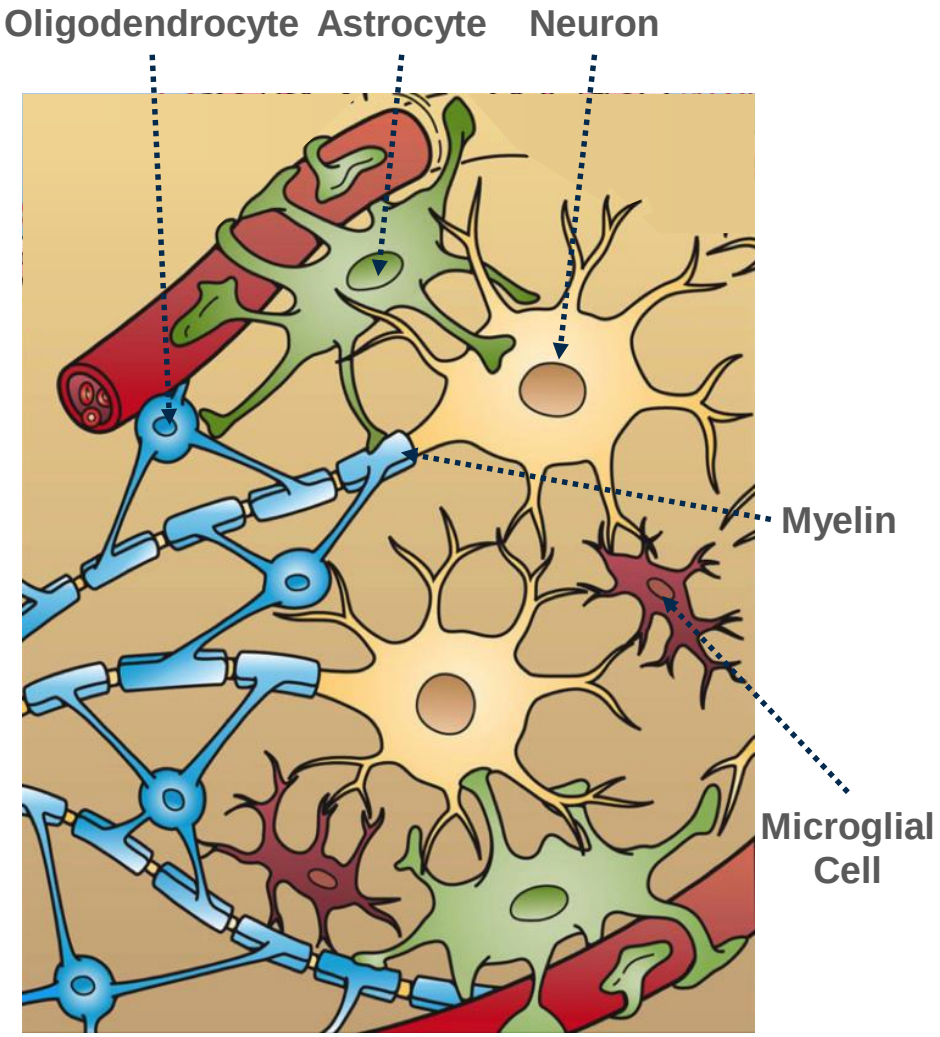
Glial Cells Undergo Inflammatory Transformation that Aggravates Brain Damage in HD

Glial cells are the most abundant cells in the brain

1. **They provide essential functional support to neurons.** Glial cells participate in glucose transport and regulate synaptic activity

2. **CNS damage triggers dramatic change in glial cell morphology and function** (a) Beneficial in the context of acute focal injury, but (b) maladaptive in broad chronic injury such as HD

3. **How do glial cells recognize and respond to damage?** SEMA4D is upregulated at site of injury and signals through plexin receptors to trigger glial transformation from normal to inflammatory state

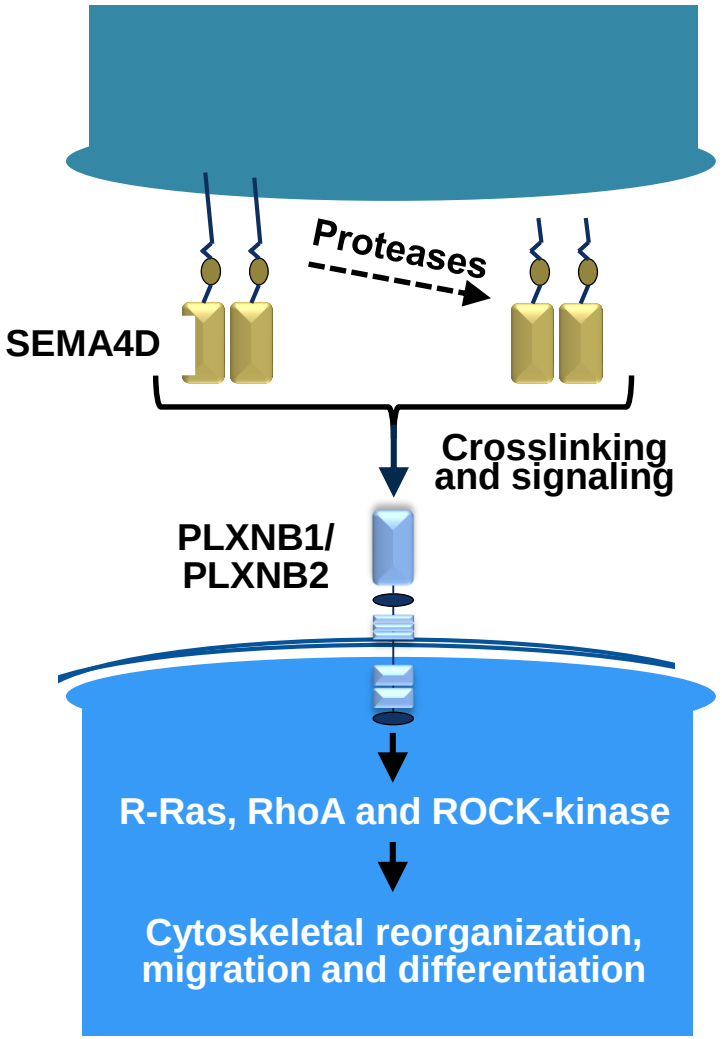


Semaphorin 4D (SEMA4D)

- SEMA4D is an extracellular signaling molecule that regulates the activity of inflammatory cells at sites of injury
- SEMA4D signals through PLXNB1 and PLXNB2 receptors to regulate (1) cell cytoskeleton (2) cytokine synthesis and secretion

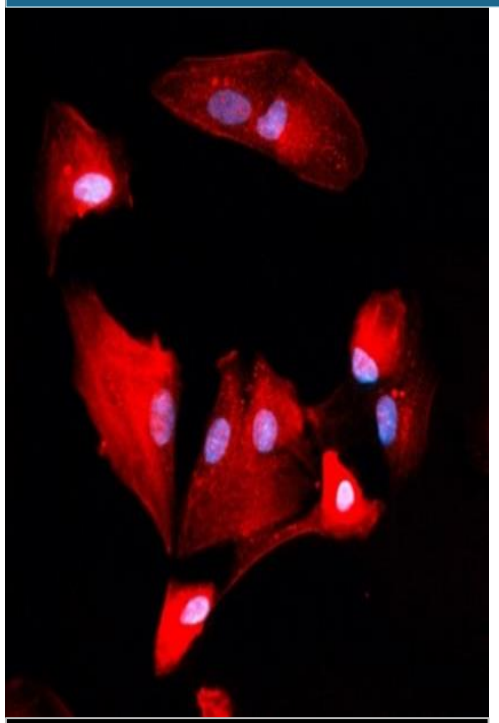
SEMA4D and Plexin receptors on glial cells:

- SEMA4D and PLXN B1/B2 are upregulated at site of injury
- SEMA4D triggers depolymerization of F-actin in astrocytes which inhibits process extension and migration and alters cytokine secretion
- Glial progenitor cells also express PLXN receptors and are inhibited by SEMA4D from migrating to site of injury to replace or replenish damaged glial cells

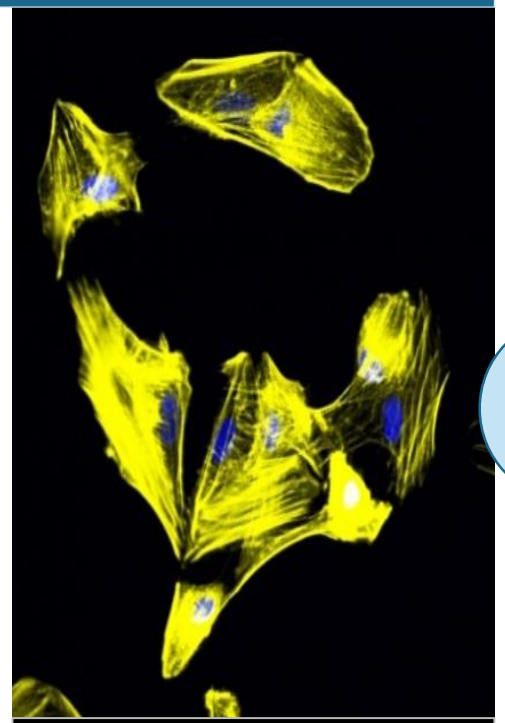


SEMA4D Inhibits Cell Migration and Process Extension

Normal Control

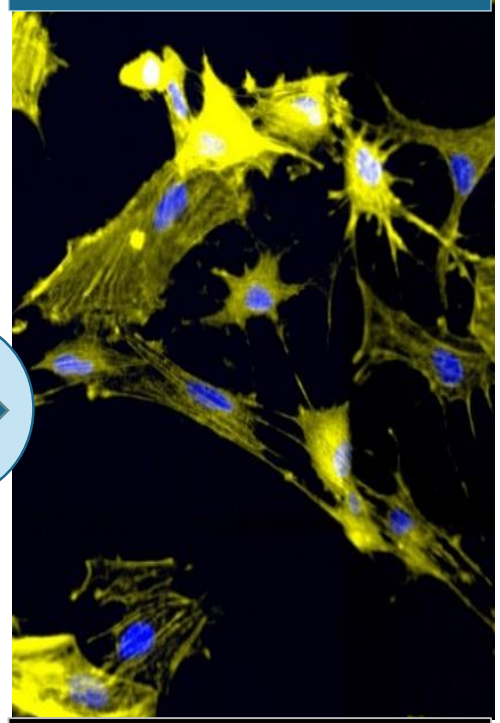


PlexinB1 DAPI



PHALLOIDIN DAPI

rSEMA4D



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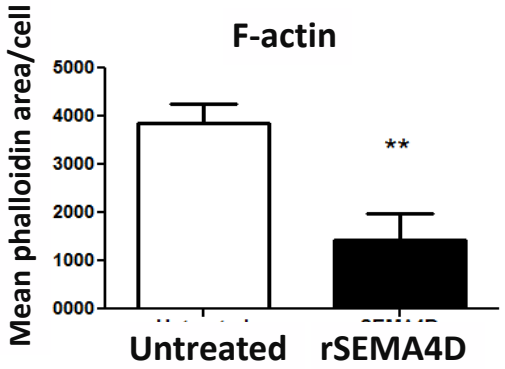
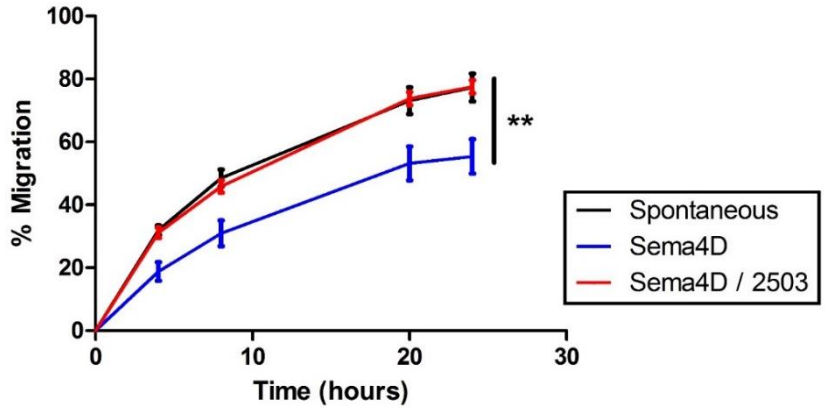
SEMA4D inhibits F-actin polymerization in astrocytes

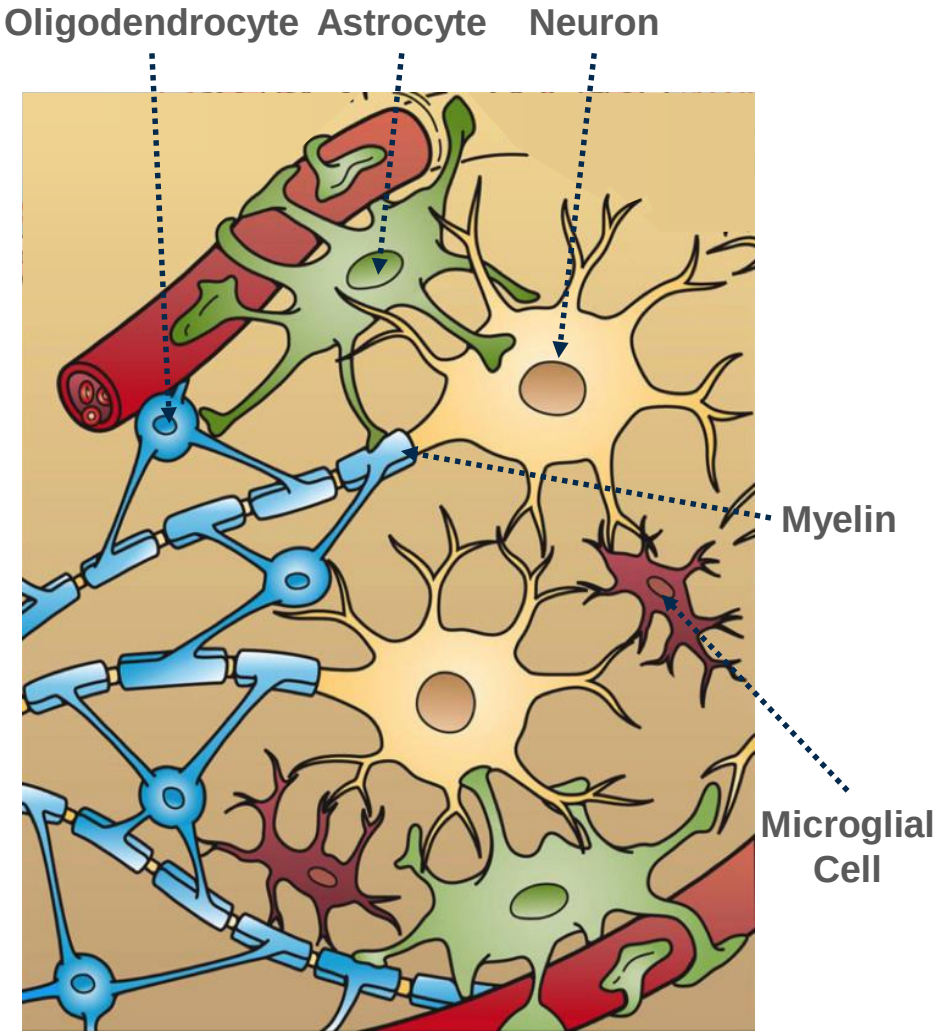


SEMA4D inhibits astrocyte process extension/migration

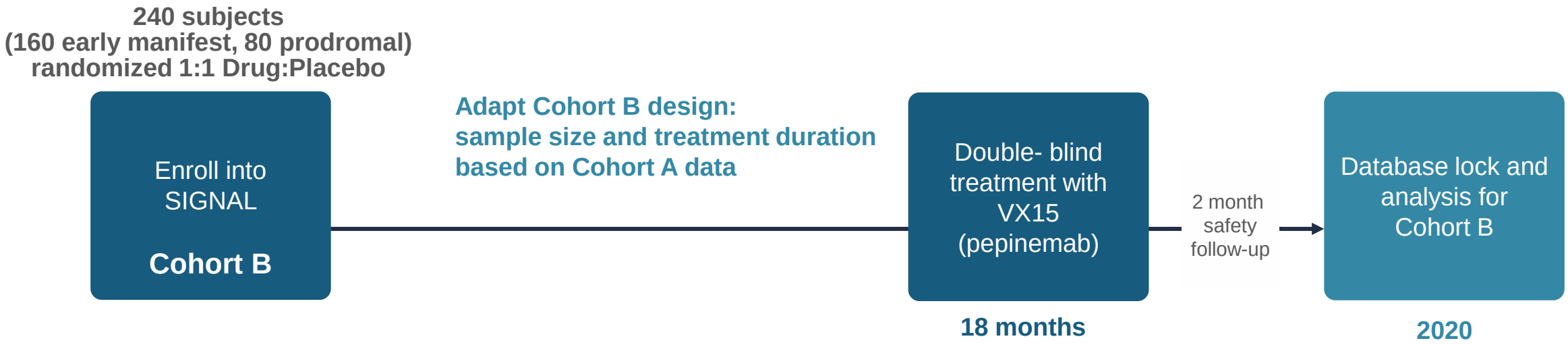


Differentiating Features of SEMA4D Blockade by VX15 (pepinemab)

1. **HD pathology is an extended process aggravated by inflammation over a long period of time**
   - It is triggered by mutant HTT, but inflammation may continue at reduced concentrations or even in the absence of mHTT
2. **SEMA4D blockade targets pathogenic inflammatory effects of mHTT and is not expected to interfere with normal HTT function**
3. **Drug distribution is determined by route of administration**
   - VX15 (pepinemab) is administered intravenously (not by intrathecal injection) and its effect is mediated through the numerous blood vessels that feed the brain.
4. **SEMA4D blockade may be applicable to other neurological diseases aggravated by inflammation, e.g. Alzheimer's disease, multiple sclerosis, ALS**



Huntington's Disease Clinical Trial Design: Cohort B



Enrollment in Cohort B is expected to be completed by December 31, 2018
Last patient last visit is anticipated in July, 2020
after which the data will be unblinded for analysis and submitted to FDA for review

We thank the **Huntington Study Group** for its invaluable assistance
in coordinating the SIGNAL study at 31 clinical sites in the US and Canada

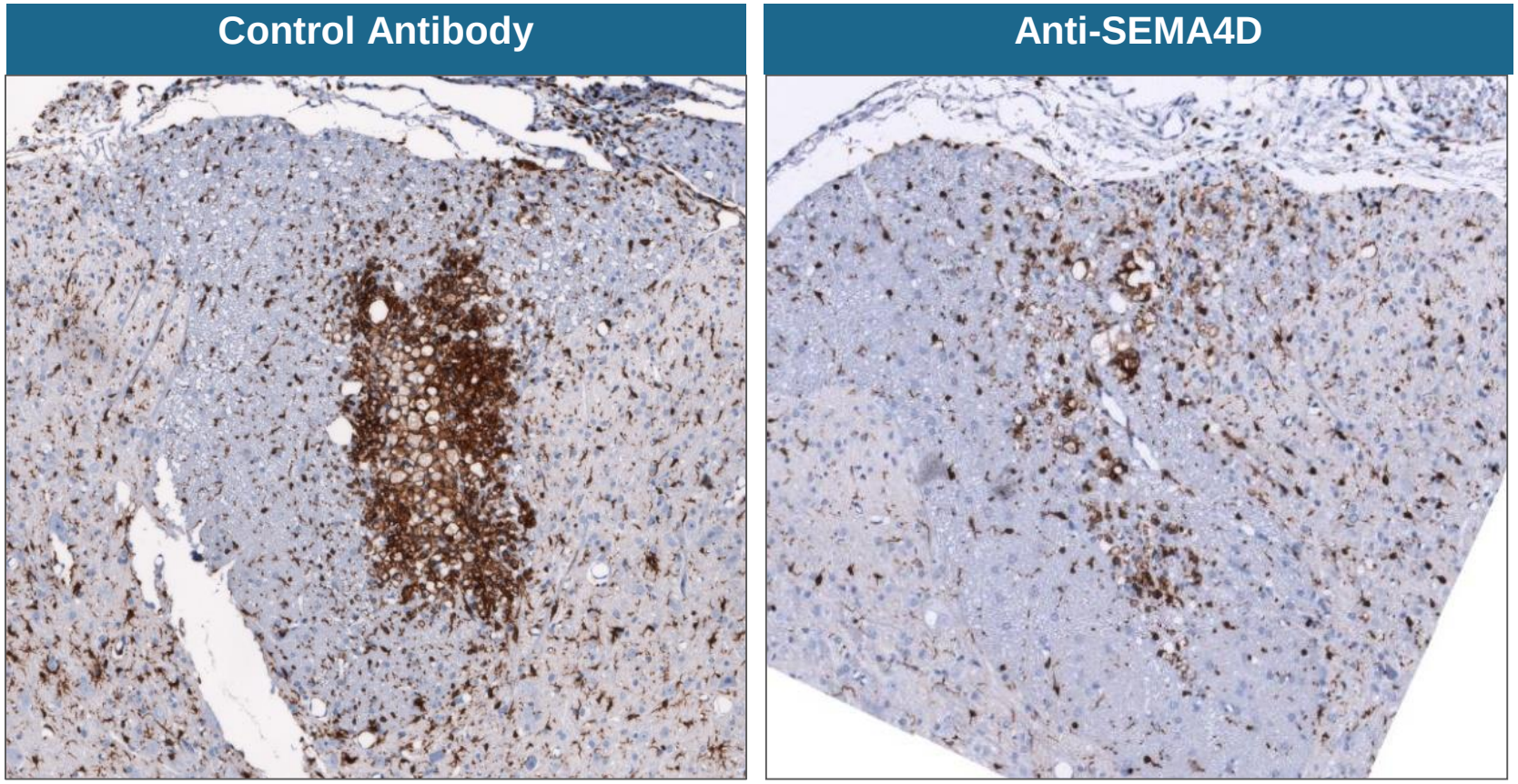
Meeting the HD Challenge with a Team of Patients and Clinicians

- Enrollment in SIGNAL Cohort B will soon be complete. In the future, depending on clinical results and FDA approval, we hope that our drug will become more broadly available.
- In the meantime, we encourage patients in search of investigational treatment to consider enrollment in other ongoing HD studies.
- We all need to keep in mind that at this time there is no basis for concluding which, if any, of the drugs currently in development, including VX15 (pepinemab), can successfully treat or delay progression of HD.
- It is you, the patients enrolled in these studies, who will ultimately provide the answer through your participation in clinical trials.
- That is why it is of great importance that, insofar as possible, you complete the study in which you have enrolled. Your initiative and vision in volunteering for these studies provides hope of benefit to all HD patients.

“Enroll and Complete” so that someday we may “Treat and Prevent”

Appendix

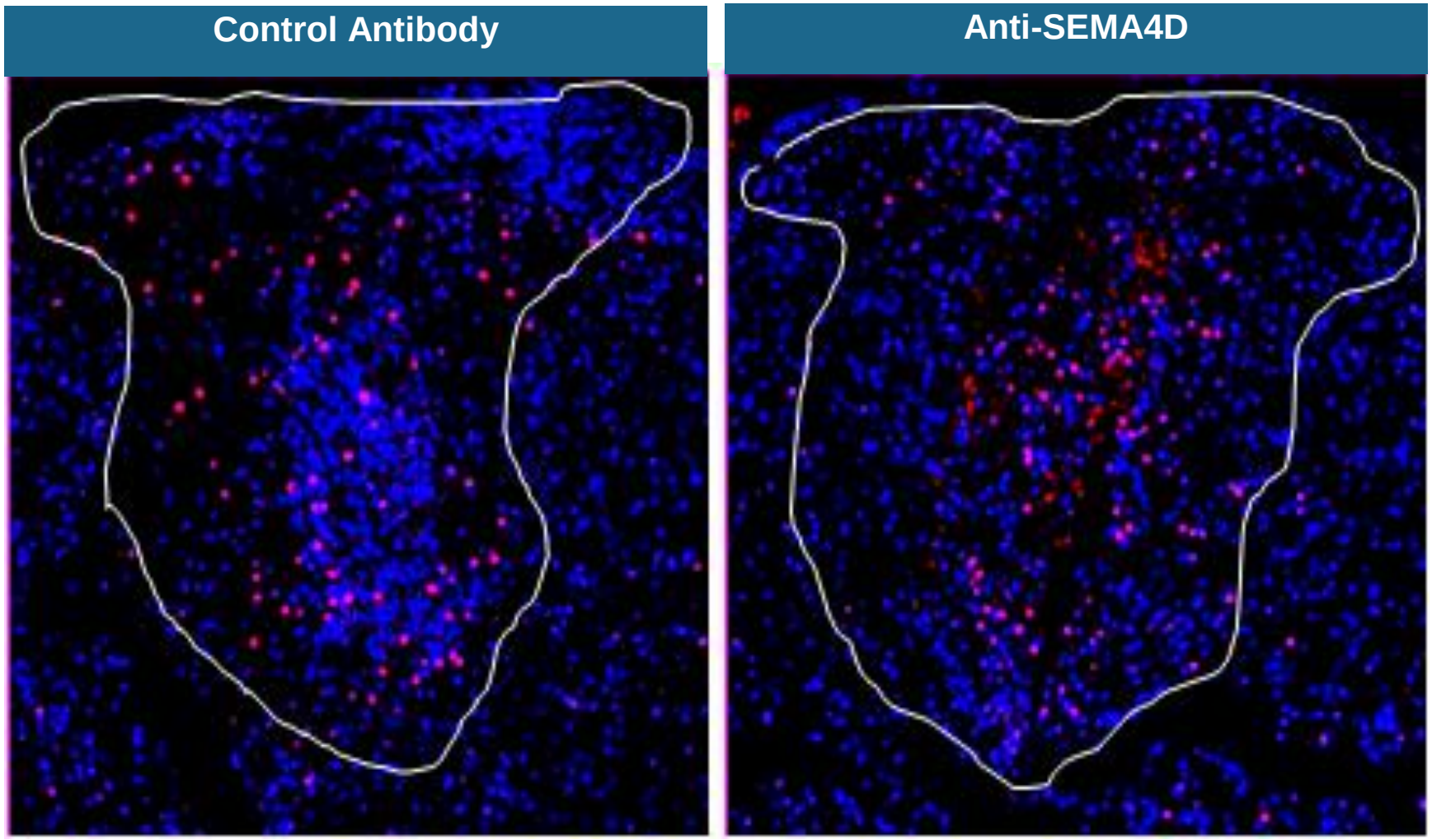
Anti-SEMA4D Antibody Inhibits Activation of Microglia at Site of Lesion



staining for Iba1 marker of microglial activation

Smith et al. Neurobiology of Disease, 73:254-268, 2015

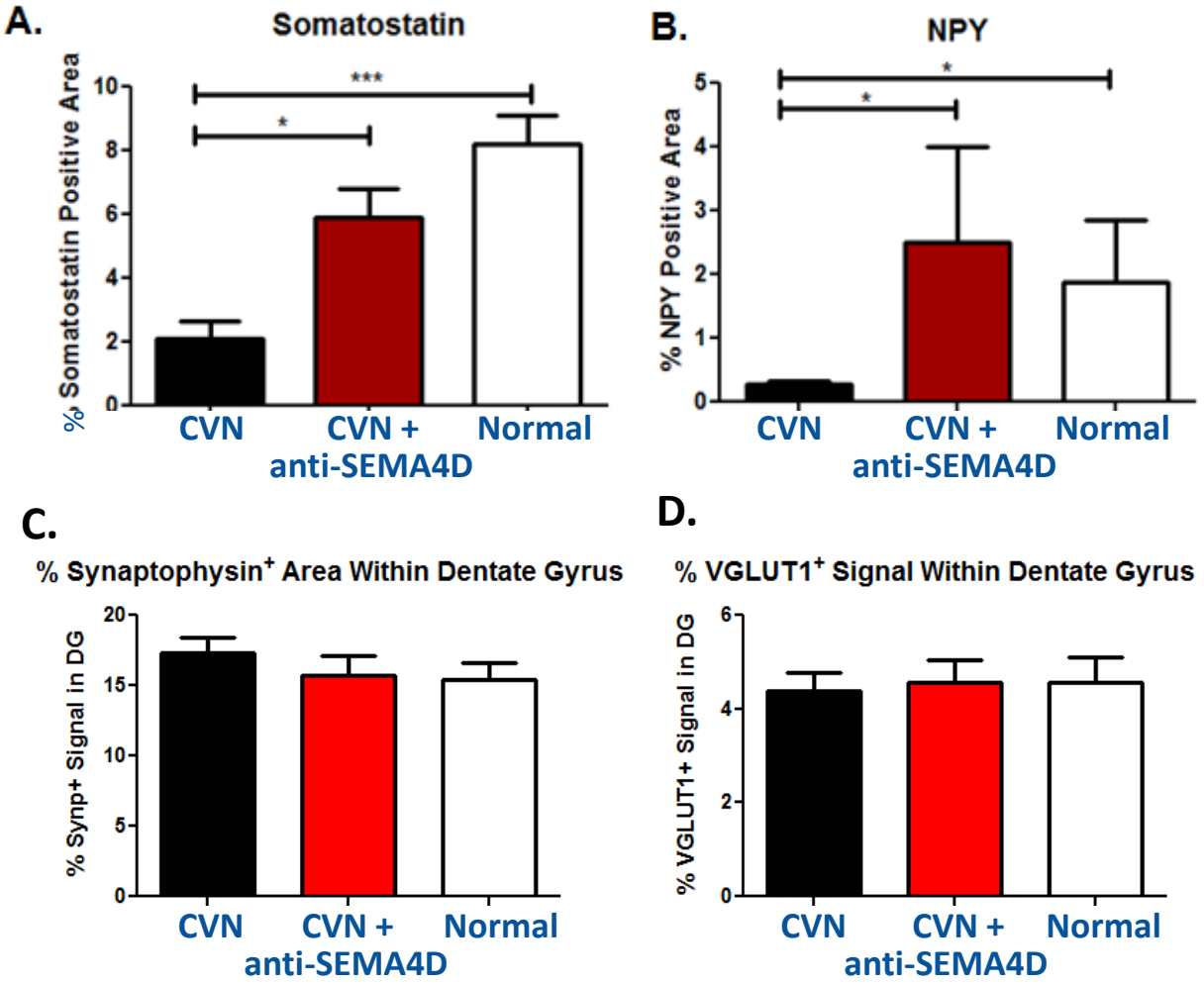
Anti-SEMA4D Antibody Promotes Migration of Glial Progenitor Cells to Site of Lesion



Antibody blockade increases concentration of NKX2.2+ Glial Progenitor Cells in area of lesions

Smith et al. Neurobiology of Disease, 73:254-268, 2015

Blocking SEMA4D protects against loss of inhibitory Neurons in CVN Murine Model of Alzheimer's Disease



Blocking SEMA4D protects against loss of inhibitory neurons in the CVN murine model of AD. Restoration of synaptic activity and, potentially, neural networks could also contribute to significantly increased FDG-PET signal.