Science in the Service of Medicine

Unique Targets.
Novel Mechanisms.
New Medicines.

Pepinemab (VX15) Antibody Treatment for Huntington's Disease and Cancer

Forward Looking Statement

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. Such statements include, but are not limited to, statements about our plans, expectations and objectives with respect to clinical trials, and other statements identified by words such as “may,” “will,” “appears,” “expect,” “anticipate,” “estimate,” “intend,” “hypothesis,” “potential,” “advance,” and similar expressions or their negatives (as well as other words and expressions referencing future events, conditions, or circumstances). Forward-looking statements 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, uncertainties related to regulatory approval, risks related to our dependence on our lead product candidate pepinemab (VX15/2503), and other matters that could affect our development plans or the commercial potential of our product candidates. Except as required by law, we assume no obligation to update these forward-looking statements. 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 periodic reports filed with the Securities and Exchange Commission (“SEC”) and the other risks and uncertainties described in our Form 10-K dated March 13, 2019 and subsequent filings with the SEC.

INVESTMENT HIGHLIGHTS

Topline HD data expected October 2020

Potentially pivotal for registration in Huntington's Disease (HD)

Currently no approved disease modifying therapies in HD

- Pepinemab is most advanced product in development with lead of ≥ 2 years

FDA Orphan Drug and Fast Track Status

Market opportunity

Estimated patient population in US

- ~40,000 with manifest disease
- 150,000 pre-manifest with inherited mutation (prodromal) in the U.S.

Similar number in EU 5

Precommercial activities underway

Proprietary antibody
Unencumbered asset
Ongoing partnering discussions

De-risked pipeline expansion opportunities

Alzheimer's Disease

- Two awards for total of $3.75 million

Oncology

- Completed Ph2 study in Lung Cancer
  - combination with avelumab (Merck KGaA)
  - Promising data reported at ASCO 2020
- New study in Head and Neck Cancer
  - combination with pembrolizumab

Research/Preclinical	Phase 1	Phase 2	Phase 3

Pepinemab Antibody Platform

Neurology

POTENTIALLY PIVOTAL TOPLINE DATA, October 2020

Pepinemab in Huntington's Disease (Orphan Drug and Fast Track Designations) — SIGNAL

Pepinemab in Alzheimer's Disease — SIGNAL-AD

Oncology

FINAL DATA RELEASED

Pepinemab in Non-Small Cell Lung Cancer (Collaboration with Merck KGaA, Darmstadt, Germany) — **CLASSICAL – Lung**

Pepinemab in First-line Head and Neck Cancer — In combination with an anti-PD-1 checkpoint inhibitor

Pepinemab in Multiple "Window of Opportunity" Studies, HNSCC, Melanoma, PDAC — Multiple IST sponsored by Emory University, Winship Cancer Institute

ActivMAb® Antibody Platform

VX5 (Anti-CXCL13) for Autoimmune Diseases

Huntington's is a Genetically Inherited Disease

HD is caused by mutation in a single gene. Every child born to parent with HD has 50% chance of inheriting the mutation and disease.

- Neuronal degeneration, neuroinflammation, and severe atrophy is observed in multiple brain regions
- Symptoms usually appear between the ages of 30 to 50

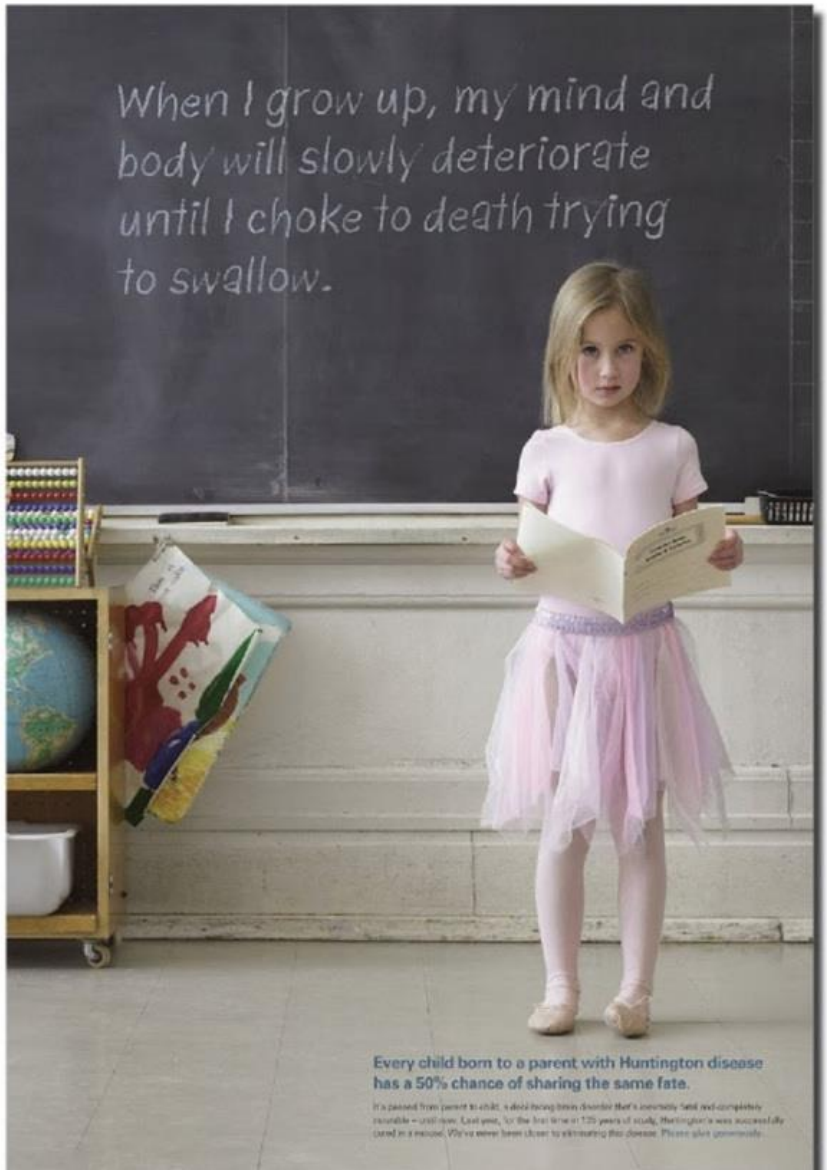


Photo credit: Huntington Society of Canada

There are Currently no Approved Treatments to Alter the Course of Huntington's Disease

Estimated patient population ~40,000 manifest disease and >150,000 pre-manifest with inherited mutation (prodromal) in the U.S.

Similar number in EU 5

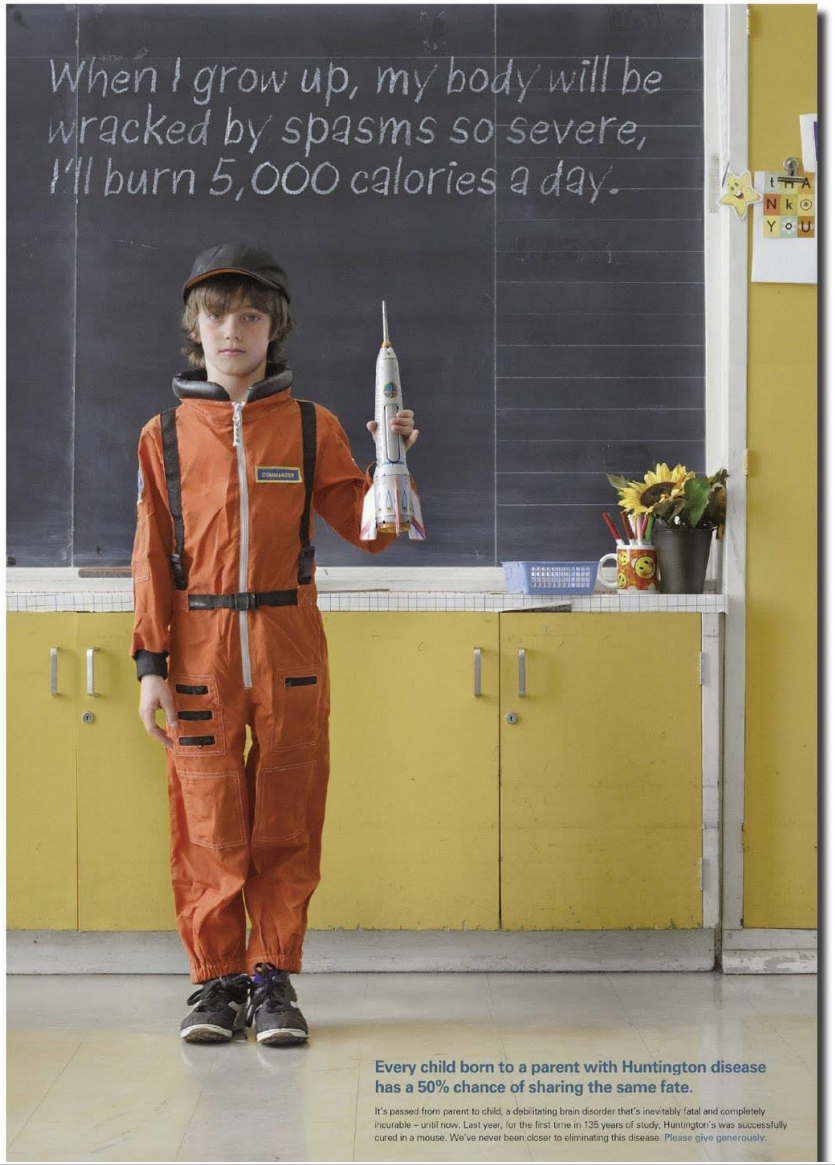
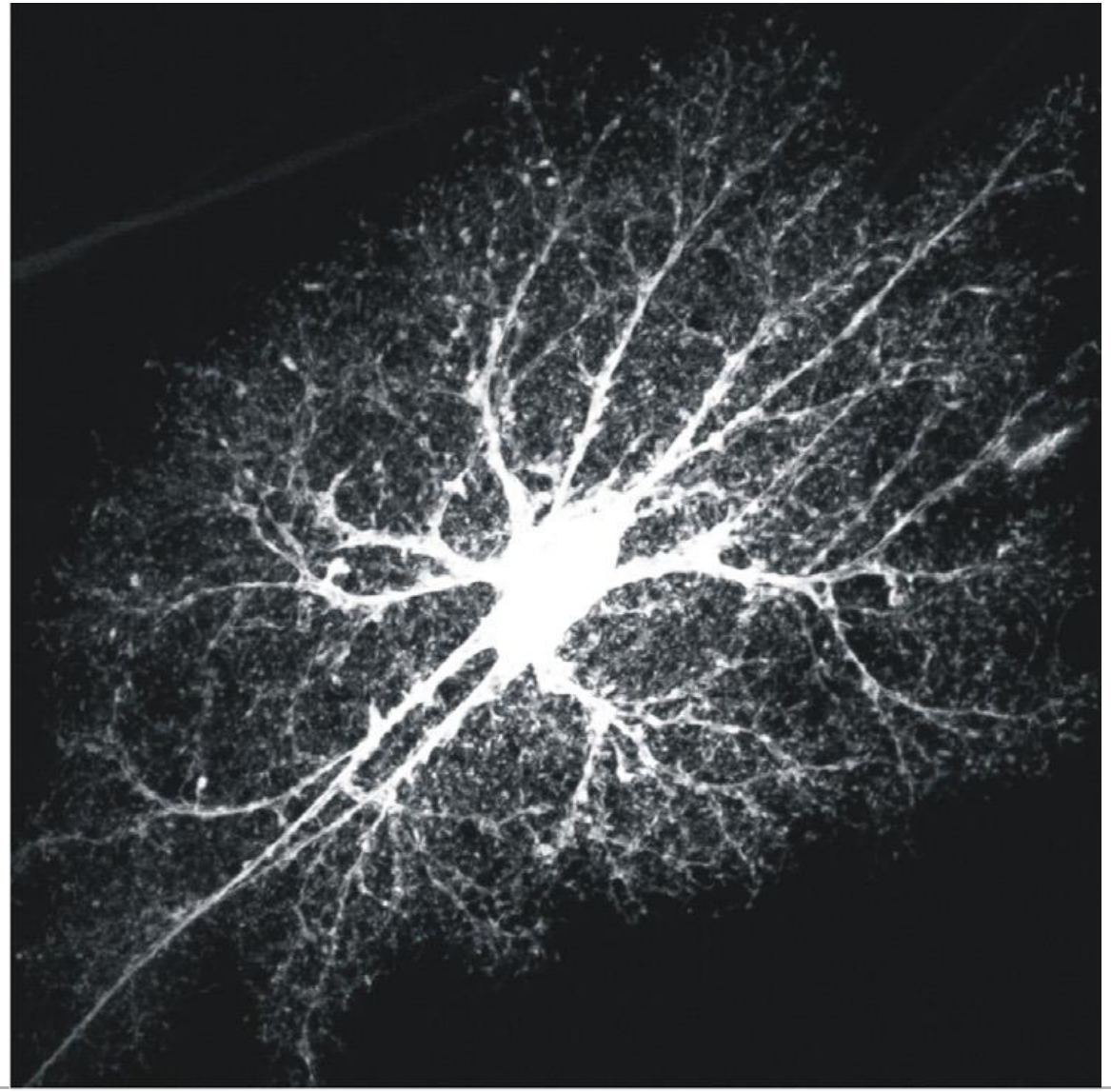


Photo credit: Huntington Society of Canada

Astrocytes Reach out to Touch and Interact with other Brain Cells



Astrocyte “arms” provide essential functional support to neurons.

- Fully cover capillaries and facilitate glucose uptake from circulation
- Cradle synapses and recycle glutamate
- Positioned to couple energy metabolism with neuronal activity

Astrocytes Undergo Inflammatory Transformation that Aggravates Brain Damage in Neurodegenerative Diseases

- **CNS damage triggers a dramatic change in astrocyte morphology and function**
  - this is beneficial in the context of acute focal injury such as stroke
  - but becomes maladaptive in broad chronic injury such as that caused by mHTT aggregates in HD or Aβ amyloid/Tau fibrils in AD

How do astrocytes recognize and respond to damage?

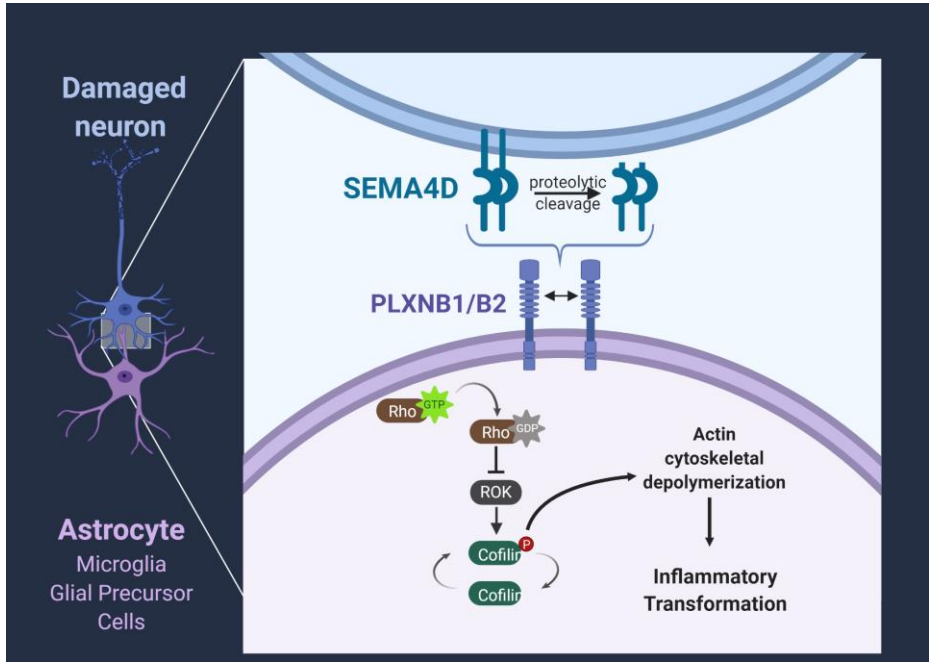
- SEMA4D is upregulated on neurons during underlying Huntington's disease progression
- Astrocytes, in close proximity to neurons, express high levels of receptors for SEMA4D
- SEMA4D triggers change in astrocyte morphology and altered gene expression which results in loss of normal astrocyte functions and gain of inflammatory activity

Semaphorin 4D (SEMA4D) Mechanism of Action

SEMA4D signals through PLXNB1 and PLXNB2 receptors to trigger dissociation of polymerized F-actin and collapse of cell's cytoskeleton

The cell cytoskeleton regulates process extensions which enable direct cell to cell interactions

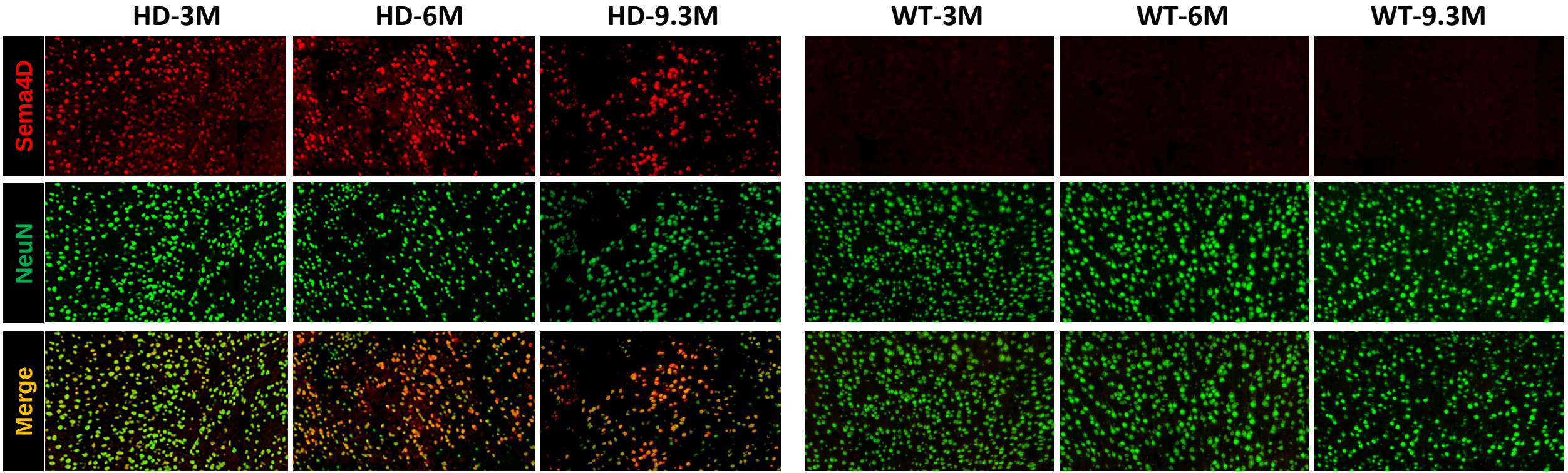
Because of their complex morphology with numerous cytoplasmic projections, astrocytes are dependent on intact cytoskeleton for normal functions



Pepinemab (VX15 antibody) binds to SEMA4D and blocks its signaling activity. This preserves normal astrocyte morphology and function and averts inflammatory transformation

SEMA4D is progressively upregulated in NeuN+ neurons of HD mice

Q175 transgenic mouse model of HD

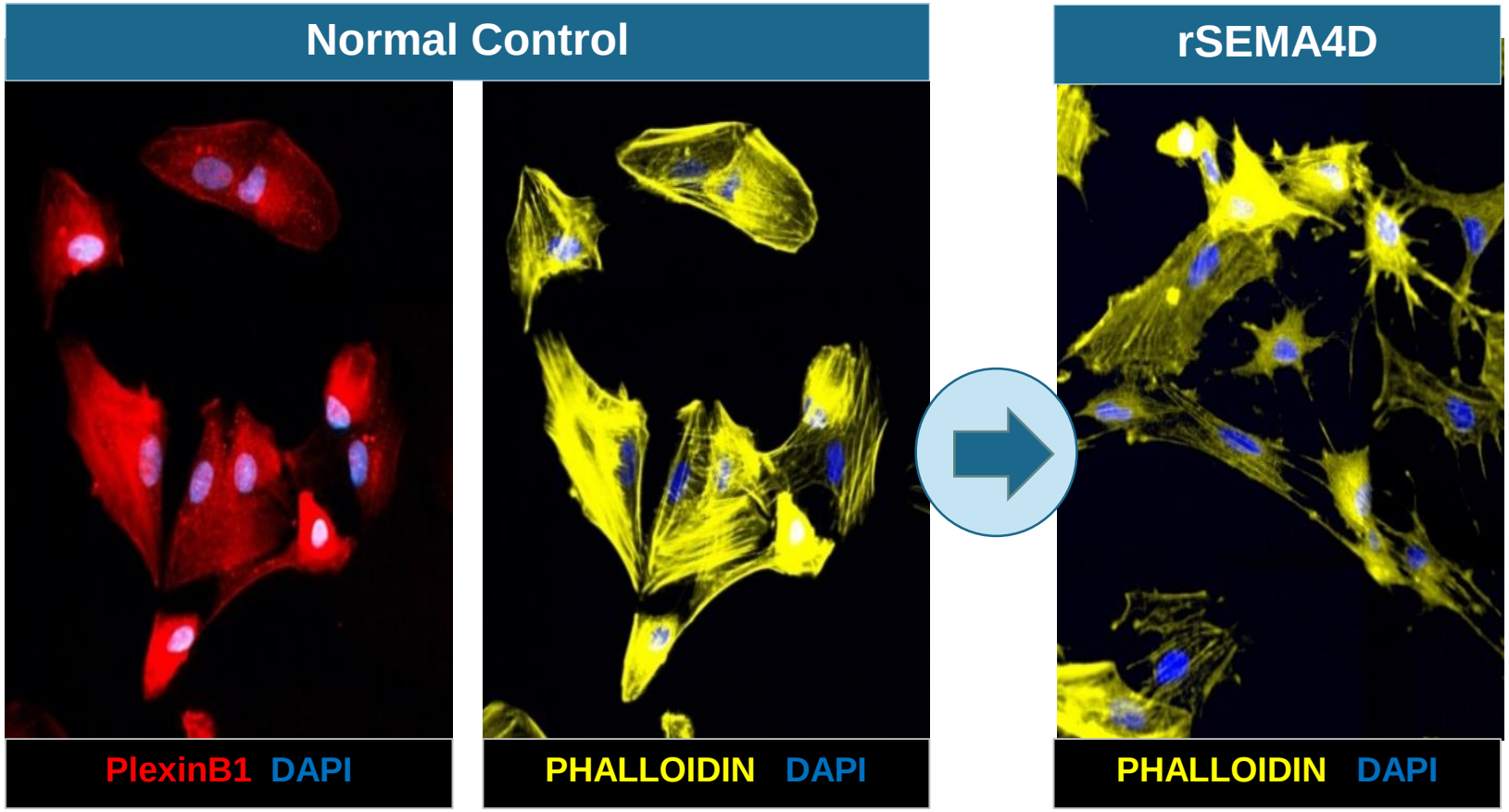


- **SEMA4D expression is upregulated in HD mice as disease progresses, compared to low expression in WT control.**
  - SEMA4D is upregulated early in disease, prior to onset of symptoms, which occurs ~ 5 months of age in Q175 HD transgenic mice.
- **SEMA4D co-localizes with NeuN+ neurons.**

NeuN/Sema staining of retrosplenial cortex region of Q175 knock-in mouse model of HD and age-matched wild type (WT) littermate controls. Representative images are shown from analysis of 3 mice/time-point. M = months of age.

SEMA4D triggers collapse of actin cytoskeleton

A



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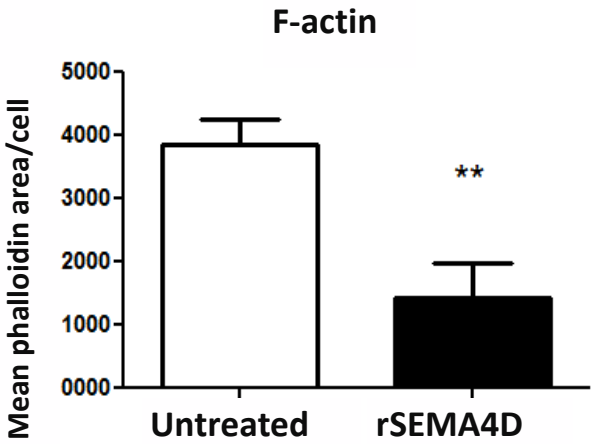
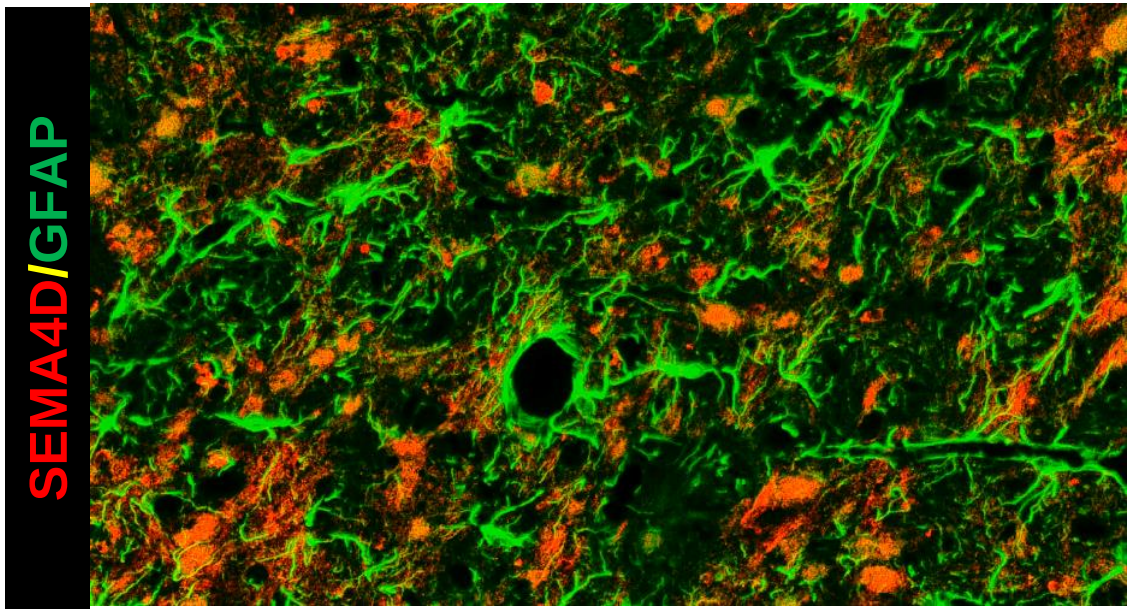


SEMA4D+ neurons are in close proximity to astrocytes

Q175 transgenic mouse model of HD

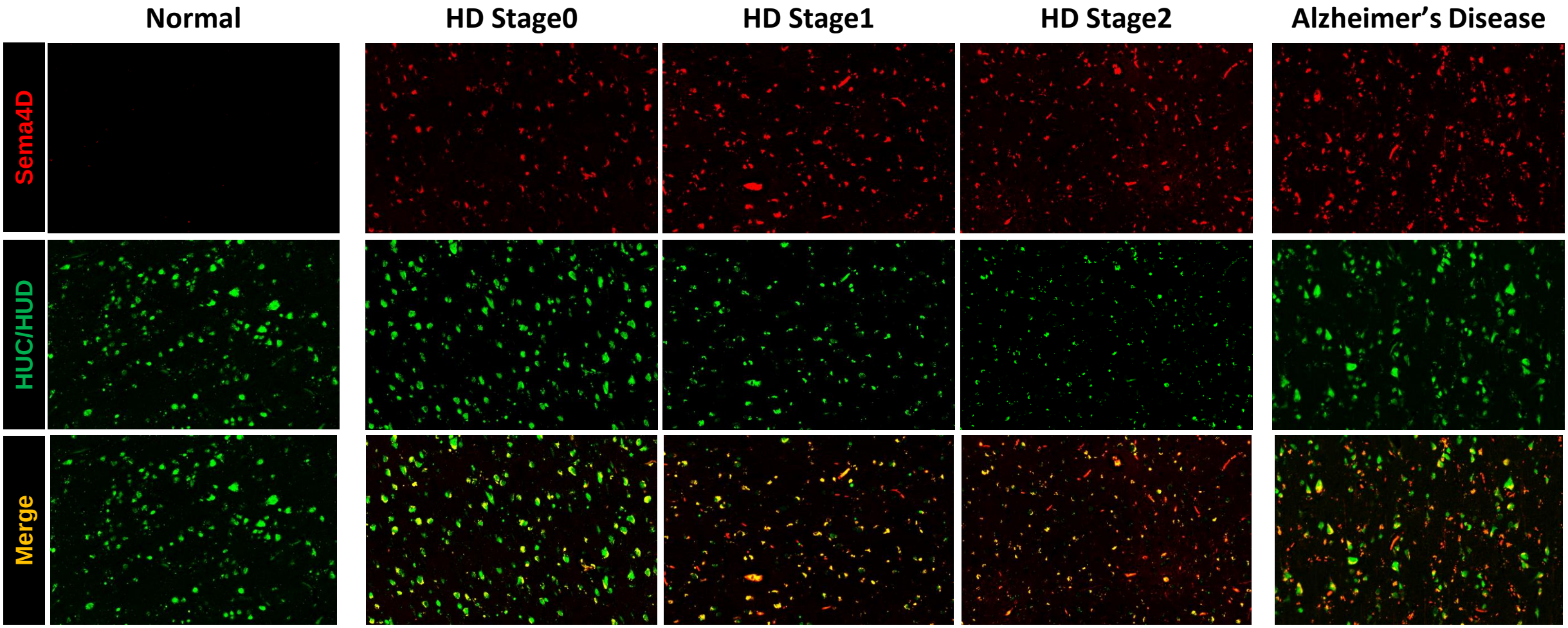
HD-9.3M



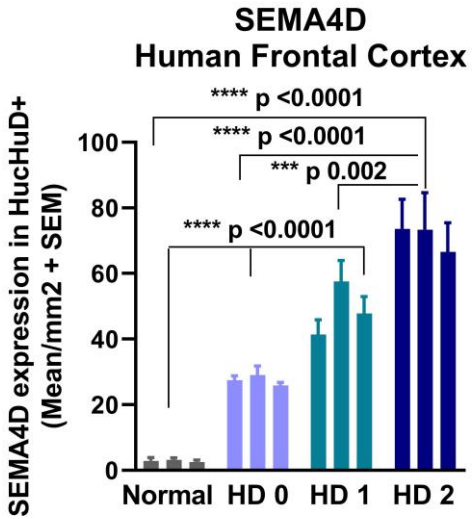
GFAP/SEMA4D staining of caudoputamen region of Q175 knock-in HD mice. Representative image (20X) is shown.

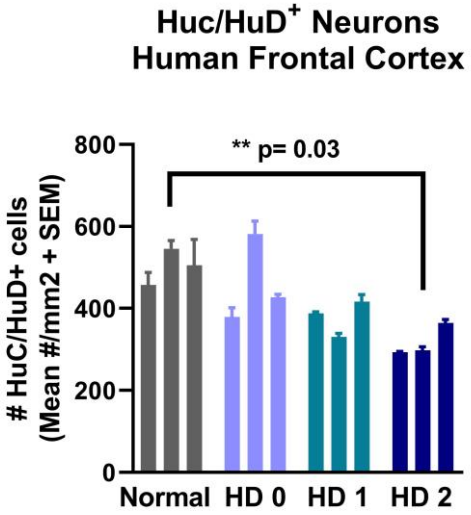
SEMA4D is upregulated in neurons during Human HD and AD disease progression

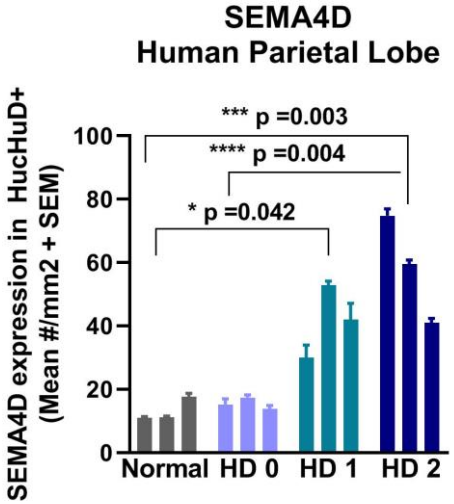
Frontal Lobe

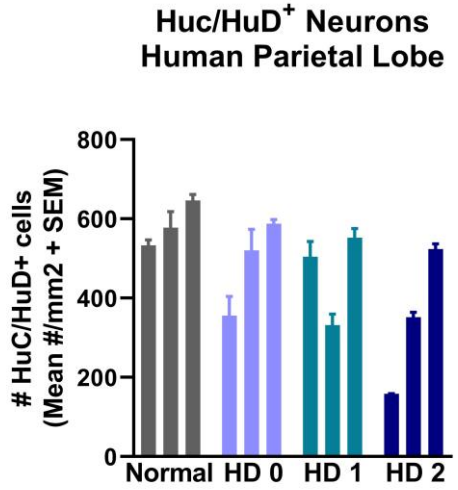


SEMA4D Expression is Increased and Neuronal Survival is Reduced During HD Progression

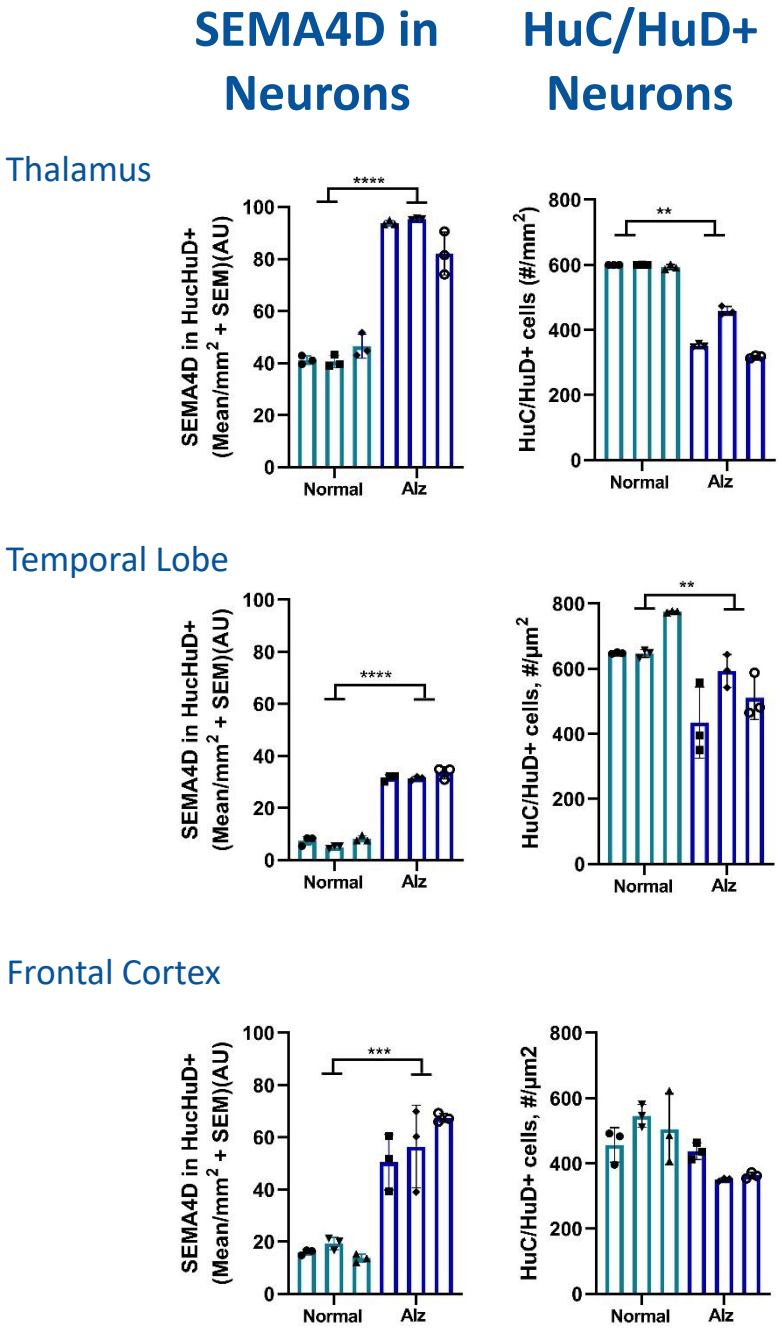








SEMA4D Expression is Increased and Neuronal Survival is Reduced During Alzheimer's Progression



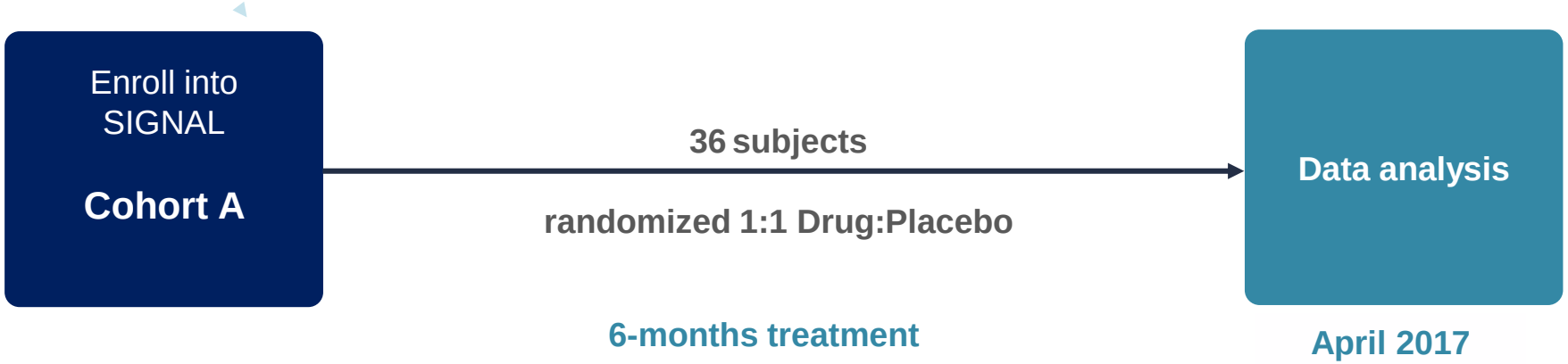
Treatment Rationale: SEMA4D Blocking Antibody will prevent inflammatory transformation of astrocytes that aggravate brain damage in HD

- Blocking SEMA4D signaling prevents collapse of the cell cytoskeleton
- This should preserve normal astrocyte functions and prevent transition to inflammatory activity

- **BIOMARKER: Glucose transport in brain is one of several important normal astrocyte functions that are known to be compromised in HD and AD and can be measured with FDG-PET**

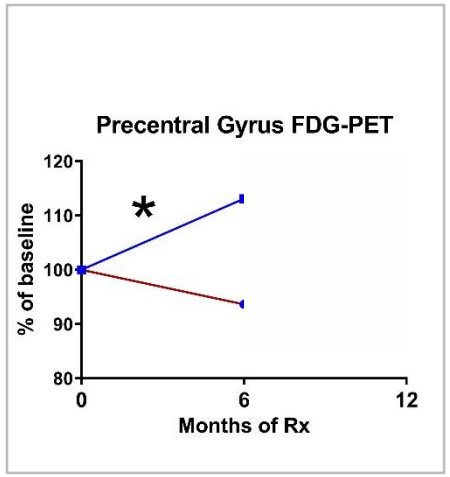
Huntington's Disease Phase 2 Clinical Trial Design

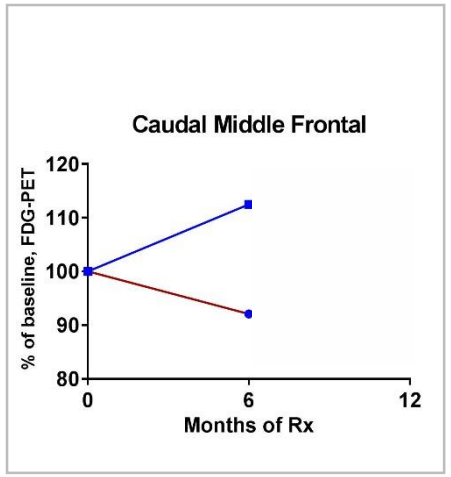
Provided important preliminary data to determine required sample size and treatment duration for a potentially pivotal Cohort B study

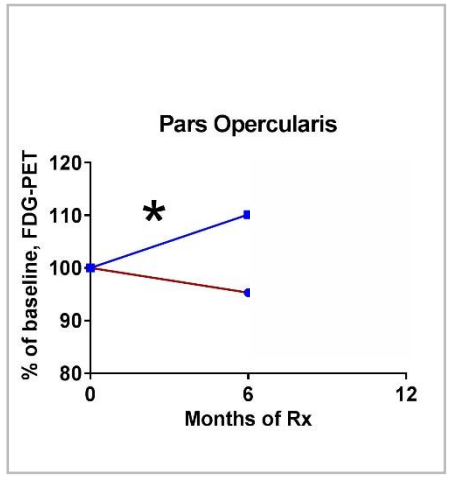


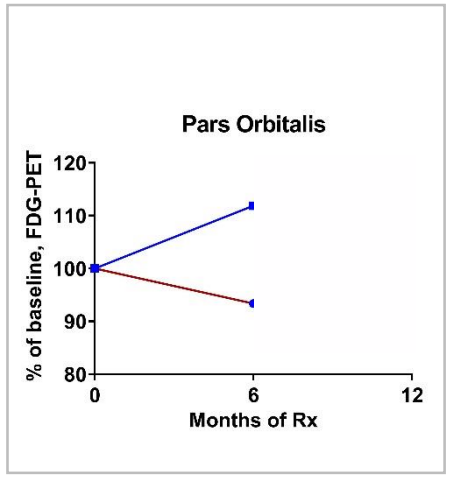
Disclaimer: VX15 (pepinemab) is under clinical investigation for the treatment of Huntington's disease and has not been demonstrated to be safe and effective for this indication. There is no guarantee that VX15 (pepinemab) will be approved for the treatment of Huntington's disease by the U.S. Food and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

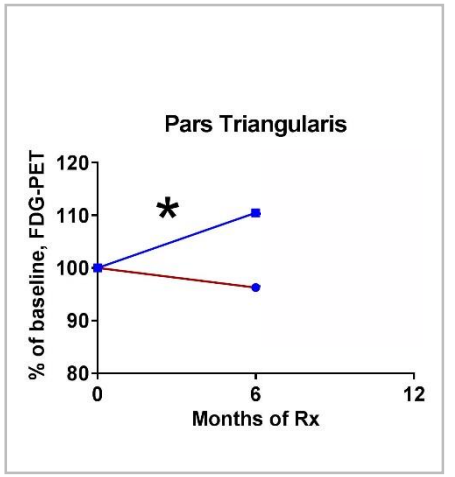
FDG-PET, a Measure of Brain Metabolic Activity, Declines During Natural Course of Disease but is Increased in Response to Treatment

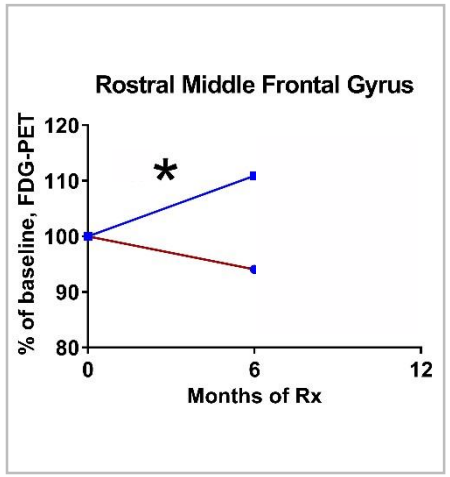


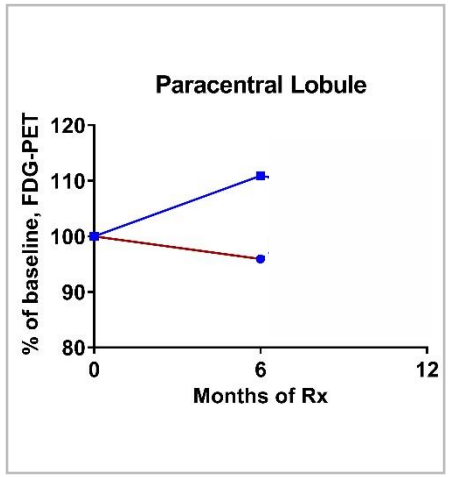


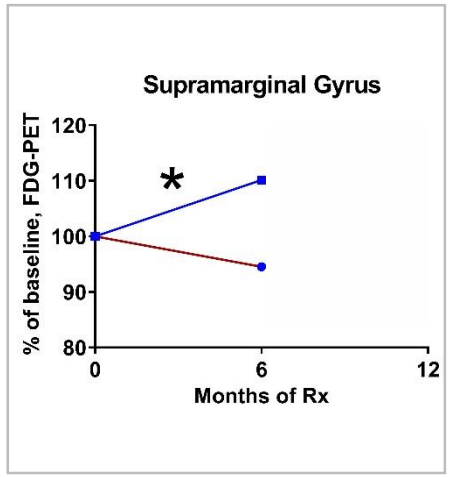


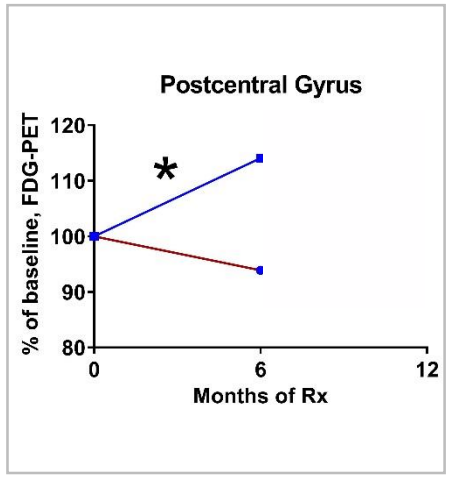


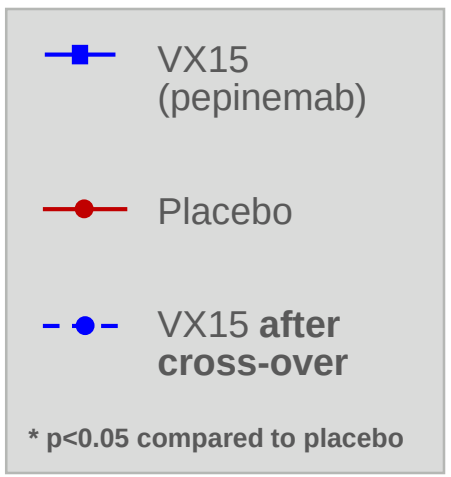




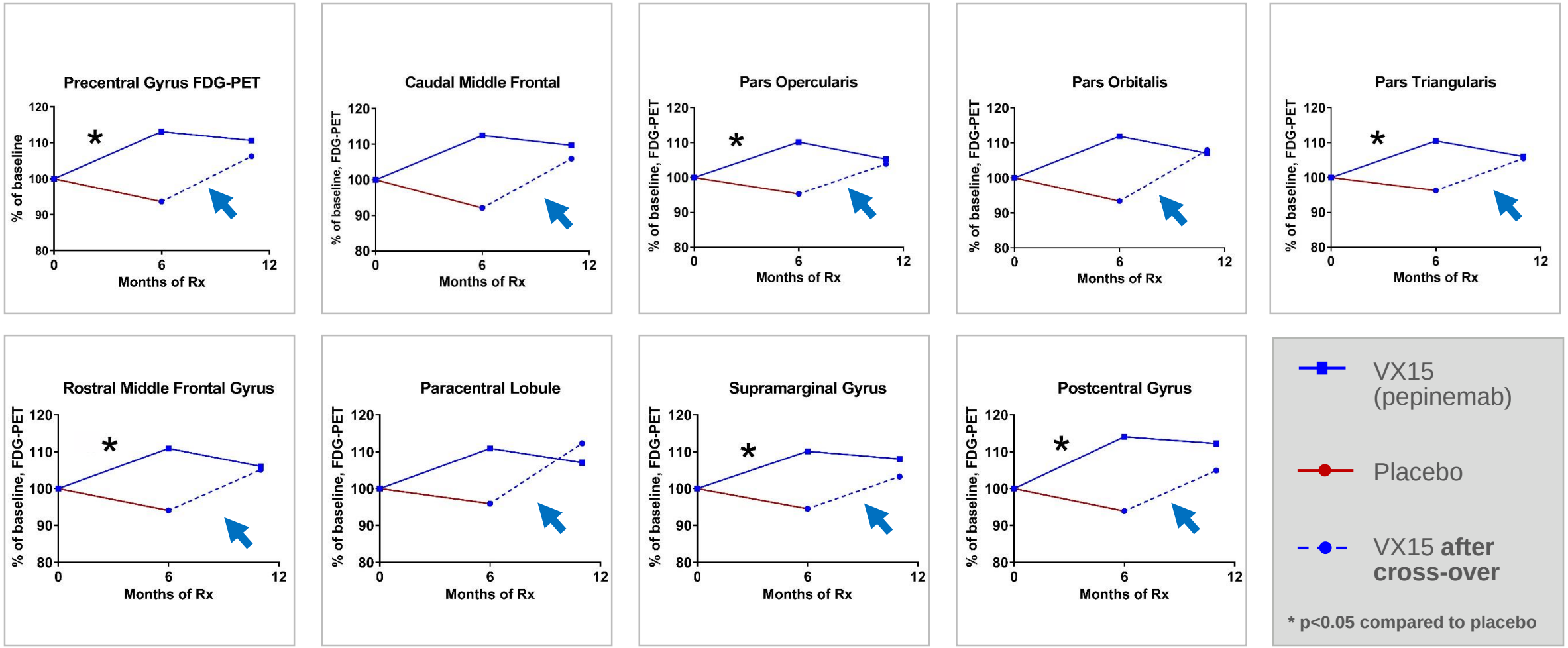








FDG-PET, a Measure of Brain Metabolic Activity, Declines During Natural Course of Disease but is Increased in Response to Treatment



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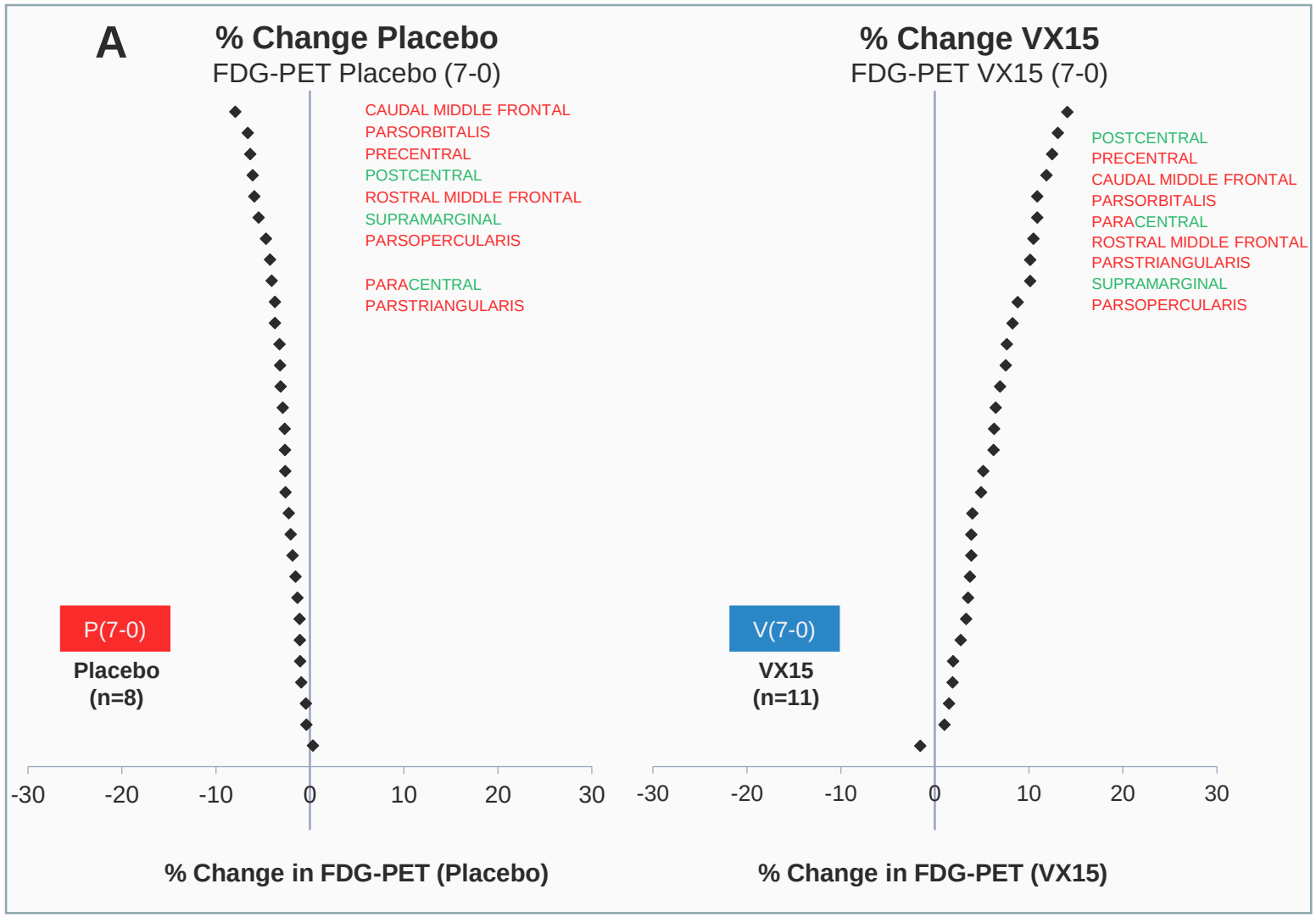
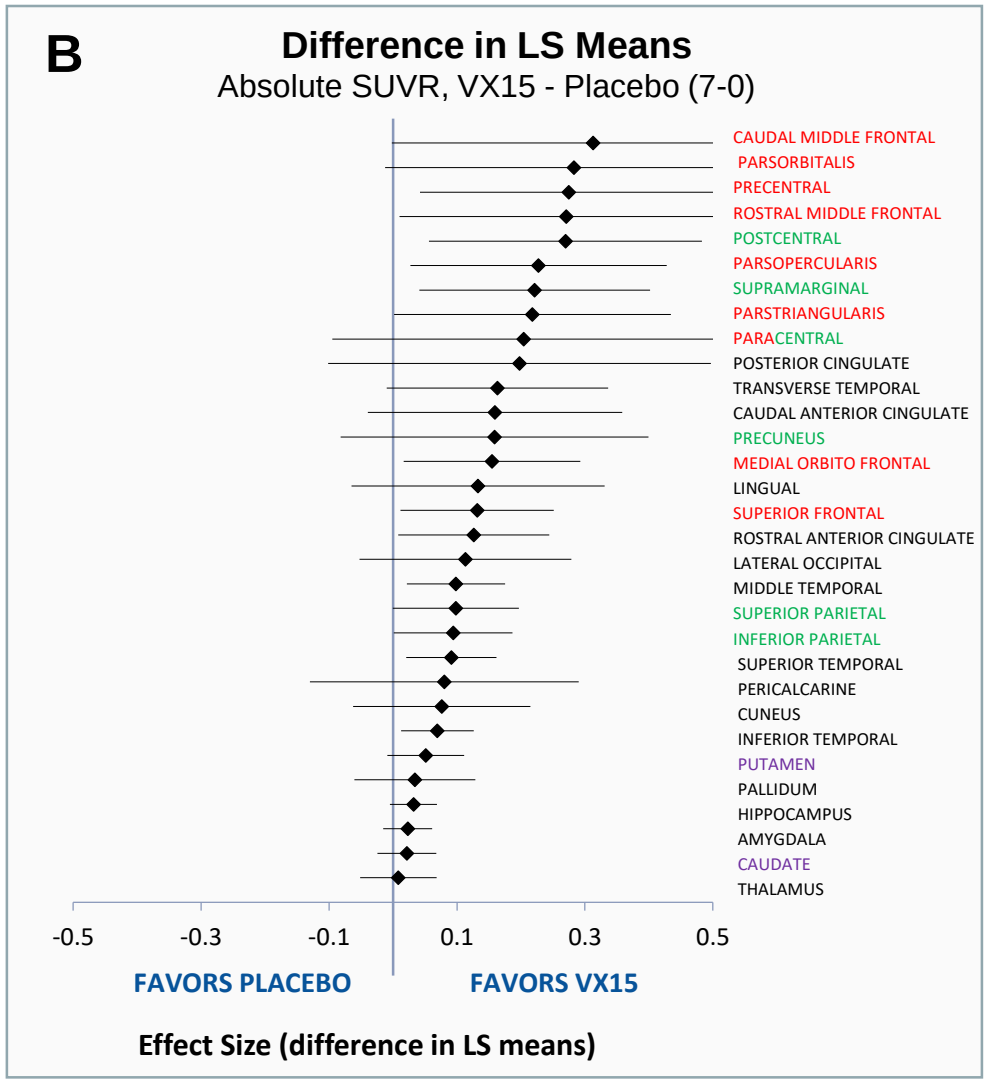
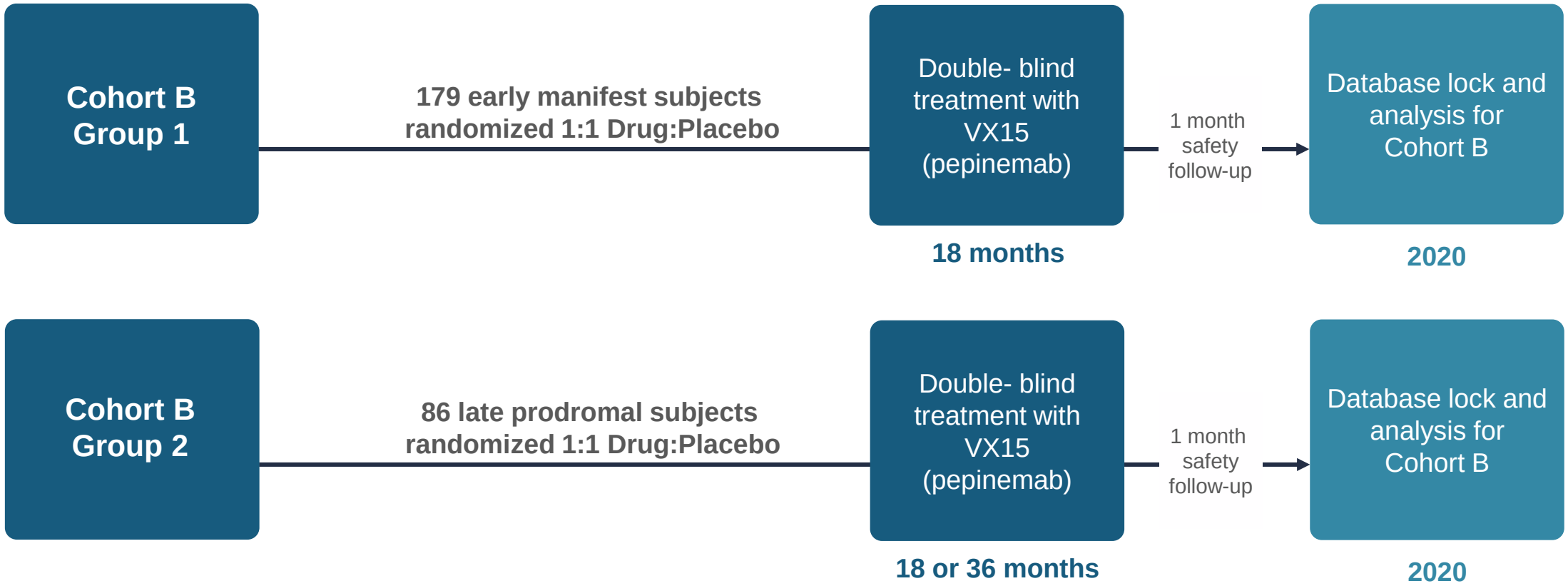




frontal lobe (red)
parietal lobe (green)

Huntington's Disease Pivotal Clinical Trial Design: Cohort B

Orphan Drug and **Fast Track** Designation by the FDA Division of Neurology Products



Enrollment complete: Last patient last visit July, 2020
Topline Data expected October, 2020

Many current intervention strategies in diseases of the brain focus on a unique disease-associated biomarker. Most have failed.

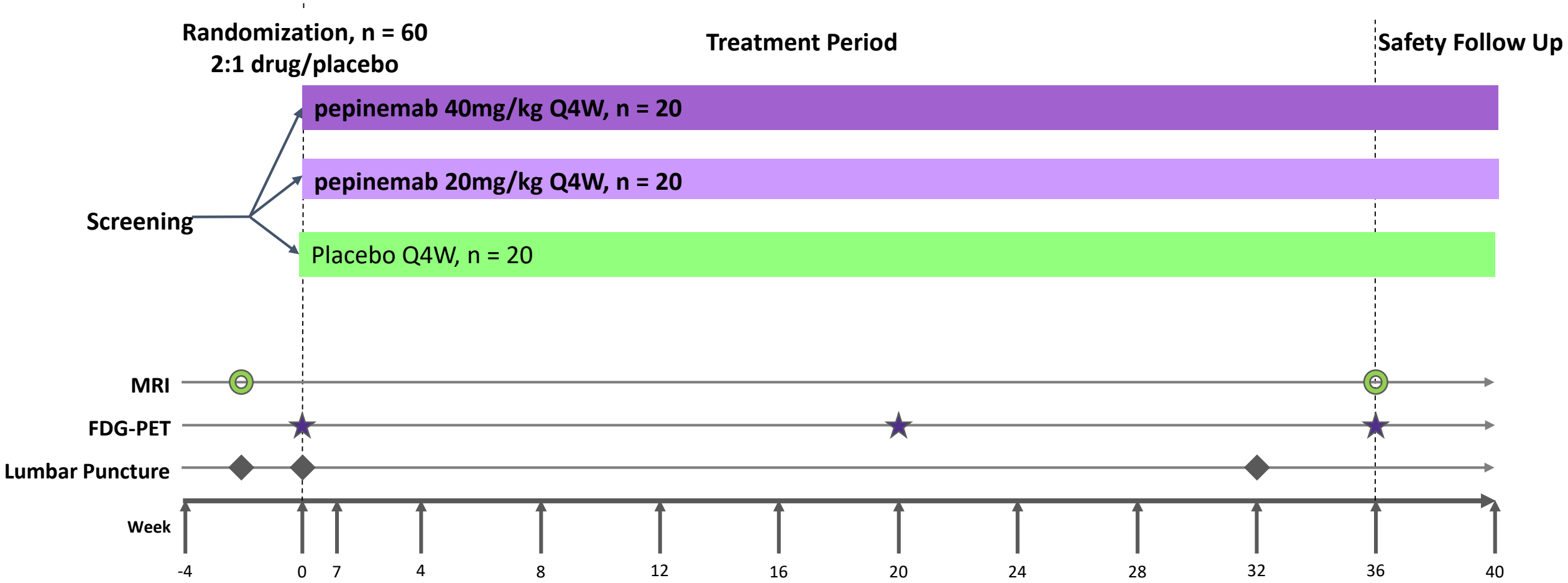
What if we target a *common* pathology – the cause of disease?

- For example, in Alzheimer's Disease, Aβ and Tau targeted therapies have been disappointing

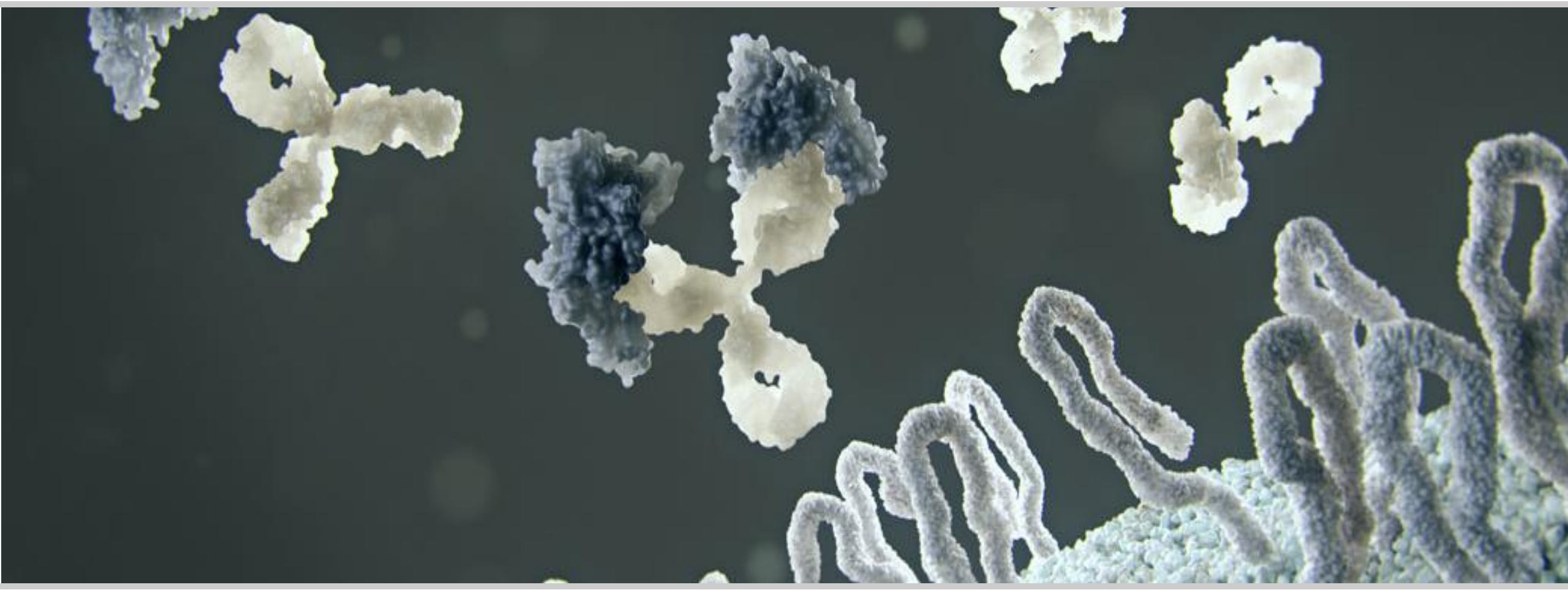
Antibodies to Aβ amyloid	Vaccinex's Novel Target
• Bapineuzumab -> mild Aβ reduction • Crenezumab -> halted Aβ accumulation • Gantenerumab -> Aβ plaque clearance • **Most have not had significant disease modifying effects** • Aducanumab -> Aβ plaque clearance. High doses may be beneficial, but controversial.	• Neurons under stress during the course of underlying disease progression upregulate semaphorin 4D (SEMA4D) • Astrocytes express high affinity plexin-B1 receptors for SEMA4D which triggers inflammatory transformation • Vaccinex's pepinemab anti-SEMA4D antibody blocks its activity and prevents loss of normal astrocyte functions and the chronic inflammation that follows

- **Increasing interest in novel approaches and new targets to address underlying pathology and common pathways affecting neurodegeneration**
  - **This strategy may be broadly applicable across many CNS diseases**

Alzheimer's Disease Trial

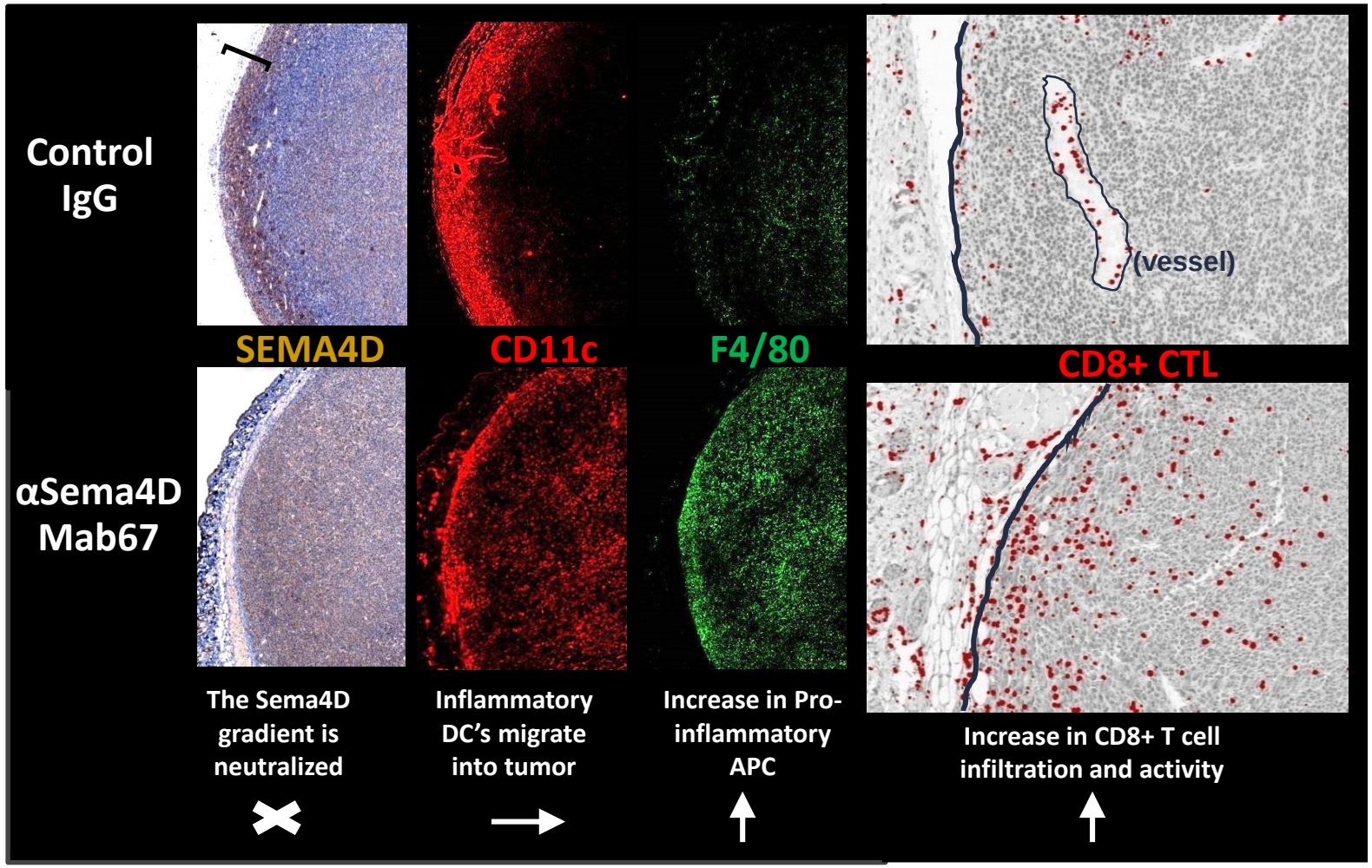


Program funding from Alzheimer's Association and Alzheimer's Drug Discovery Foundation (ADDF)



Combination Immunotherapy for Cancer

SEMA4D antibody neutralizes the SEMA4D barrier and "opens the gates" of the tumor to the immune system, increasing T cell infiltration while reducing immune suppression



Immune suppression

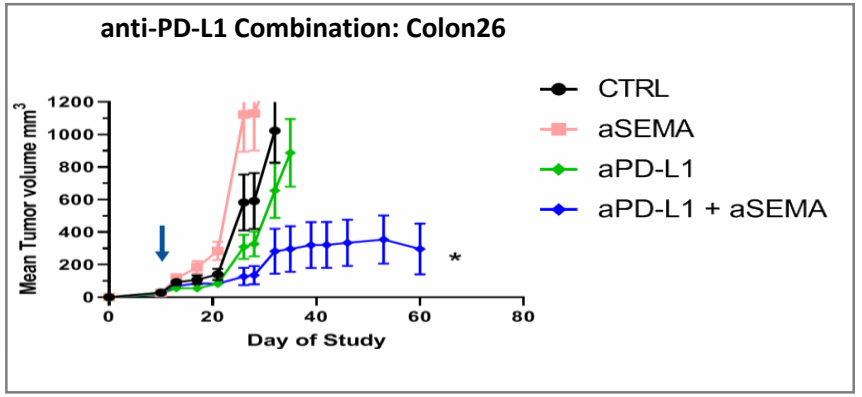
PEPI

SEMA4D barrier
Tregulatory, exhaustion
MDSC, M2 TAM, PD-L1
CXCL1, CCL2

Anti-tumor activity

PEPI

"Killer" T cells
DC, M1 APC
IFNγ, CXCL10



Preclinical Model - Colon26

Evans EE et al. Cancer Immunol Research 2015;3(6): 689-701
http://www.ncbi.nlm.nih.gov/pubmed/25614511

Pepinemab rapidly promotes T cell infiltration into tumor bed

MSS Colorectal cancer metastasis to liver – neoadjuvant/"window of opportunity" study

Winship Cancer Institute, Emory University

No treatment

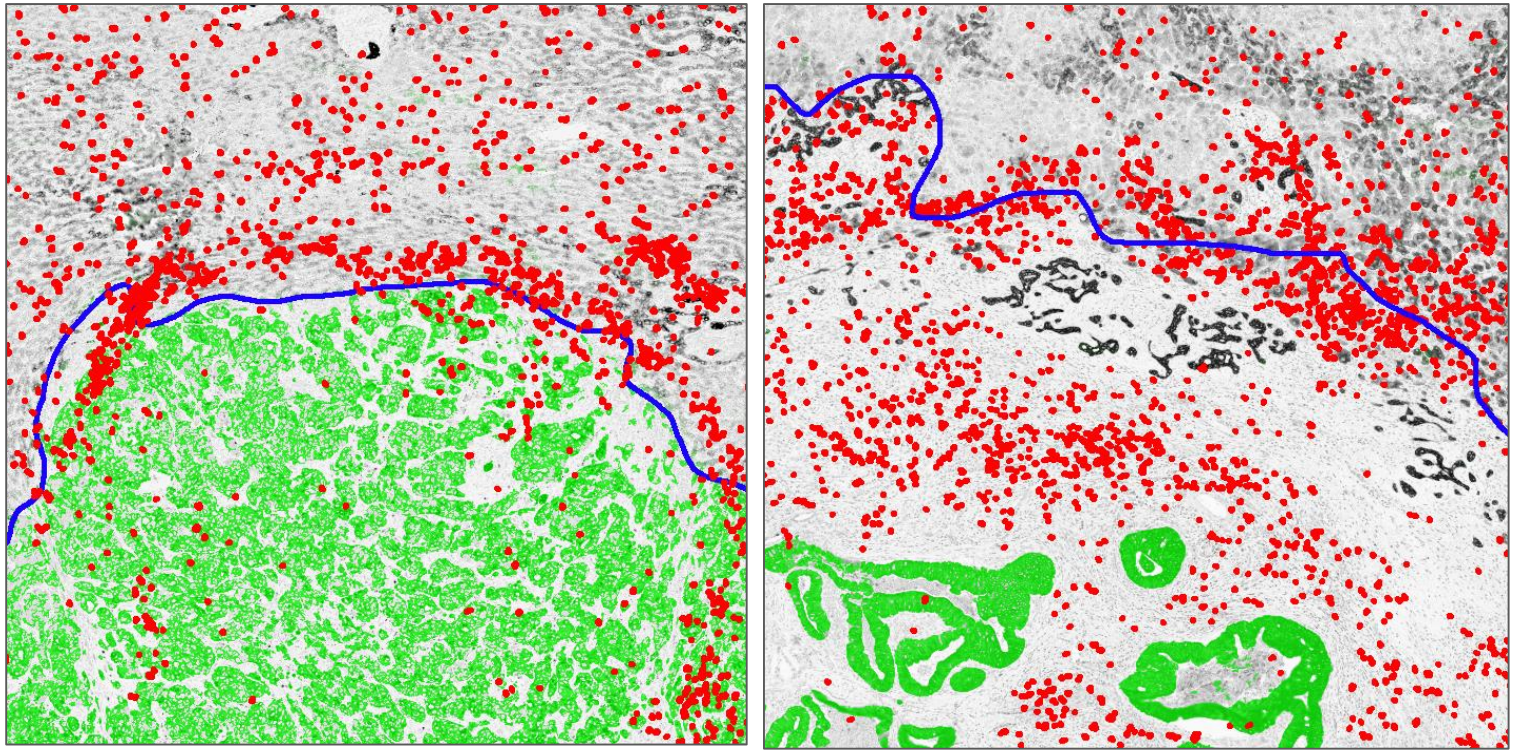
T cells are trapped at margin and are largely excluded from tumor bed

Pepinemab

T cells penetrate into the tumor bed. Tumor content is reduced and appears to be replaced by stroma.

Normal liver

Tumor Bed



CD8+ T cells
Margin of tumor bed
Tumor nodules

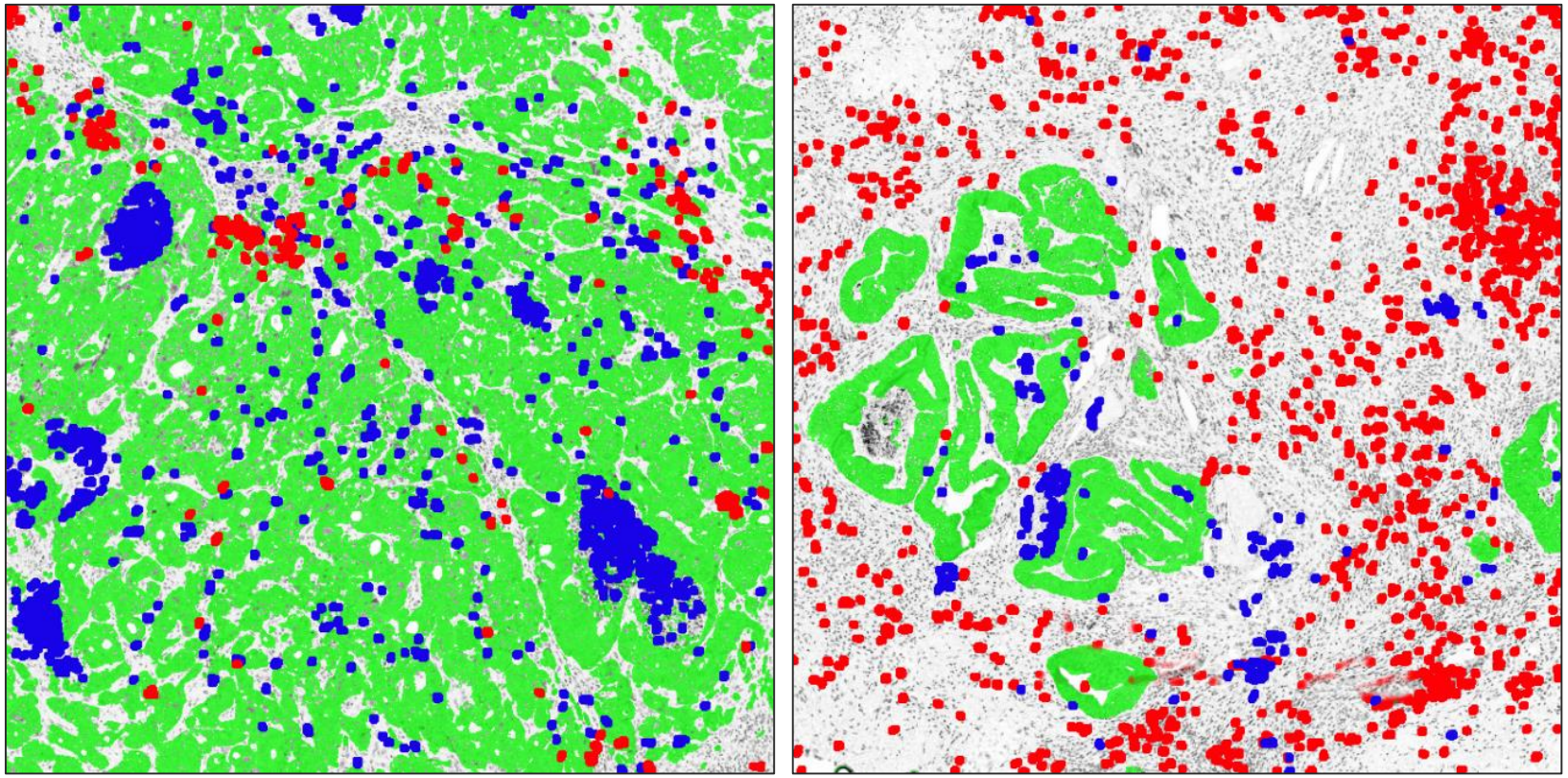
Patients received neoadjuvant chemo therapy before immunotherapy and surgery

Reduced MDSC and high CD8+ T cells following treatment with pepinemab

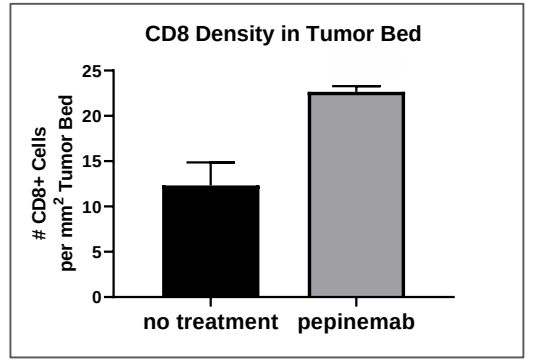
MSS Colorectal cancer metastasis to liver – neoadjuvant/"window of opportunity" study

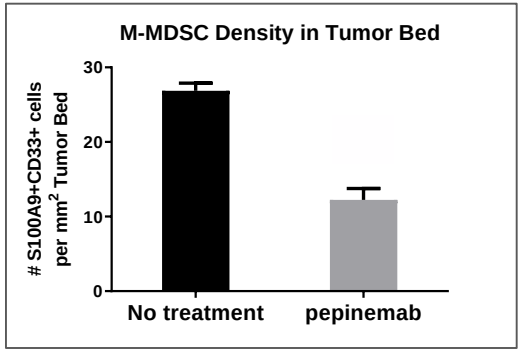
Winship Cancer Institute, Emory University

No treatment **Pepinemab**



Patients received neoadjuvant chemo therapy before immunotherapy and surgery





Density was determined from entire tumor bed (n= 2 sections/patient).

M-MDSC (S100A9+CD33+)
CD8+ T cells
Tumors (Cytokeratin+)

Sponsored by:

Co-funded by:

Phase 1b/2 CLASSICAL- Lung Study Design

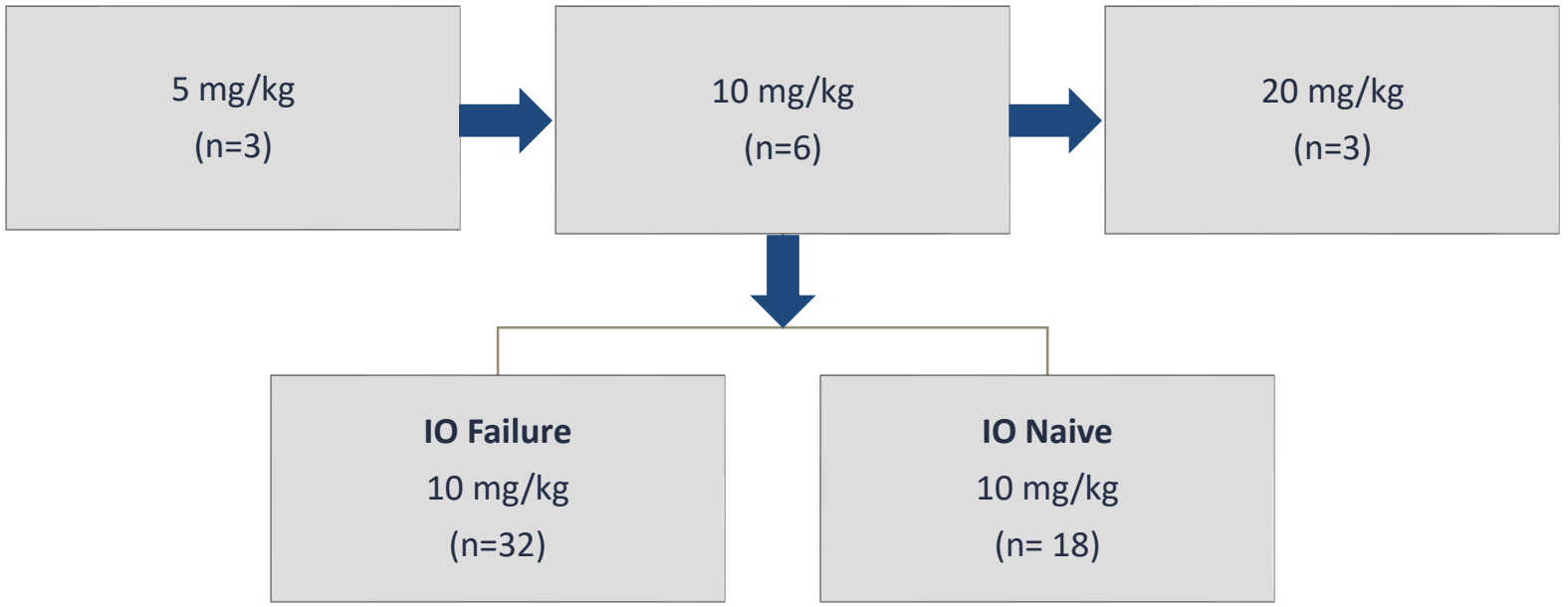
Combination Trial of Pepinemab with Avelumab in NSCLC

Phase 1b

Dose Escalation
IO Naïve
(n=12)

Phase 2

Dose Expansion
(n=50)



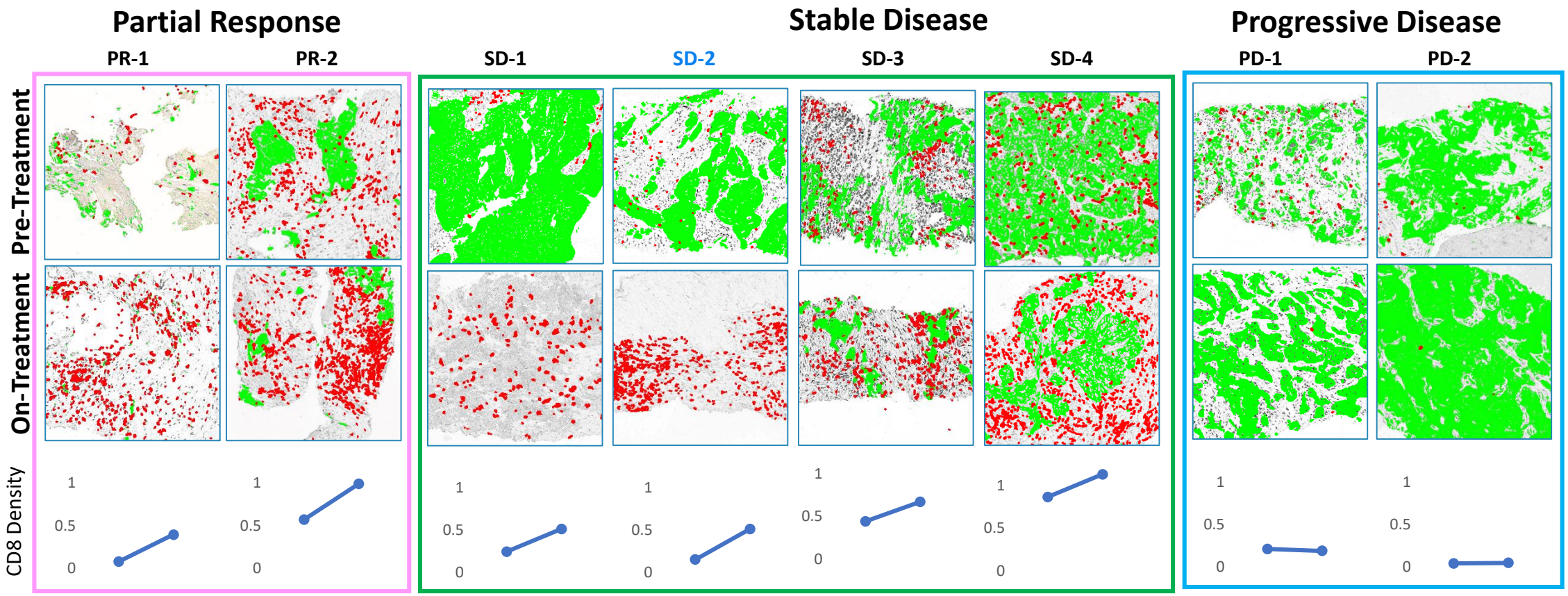
pepinemab
+
10 mg/kg
avelumab
Q2W

Study Objectives

- The primary objective is safety, tolerability, and identification of the RP2D for dose expansion.
- Secondary objectives include evaluation of efficacy, immunogenicity, and PK/PD, and an exploratory objective is to identify candidate biomarkers of activity

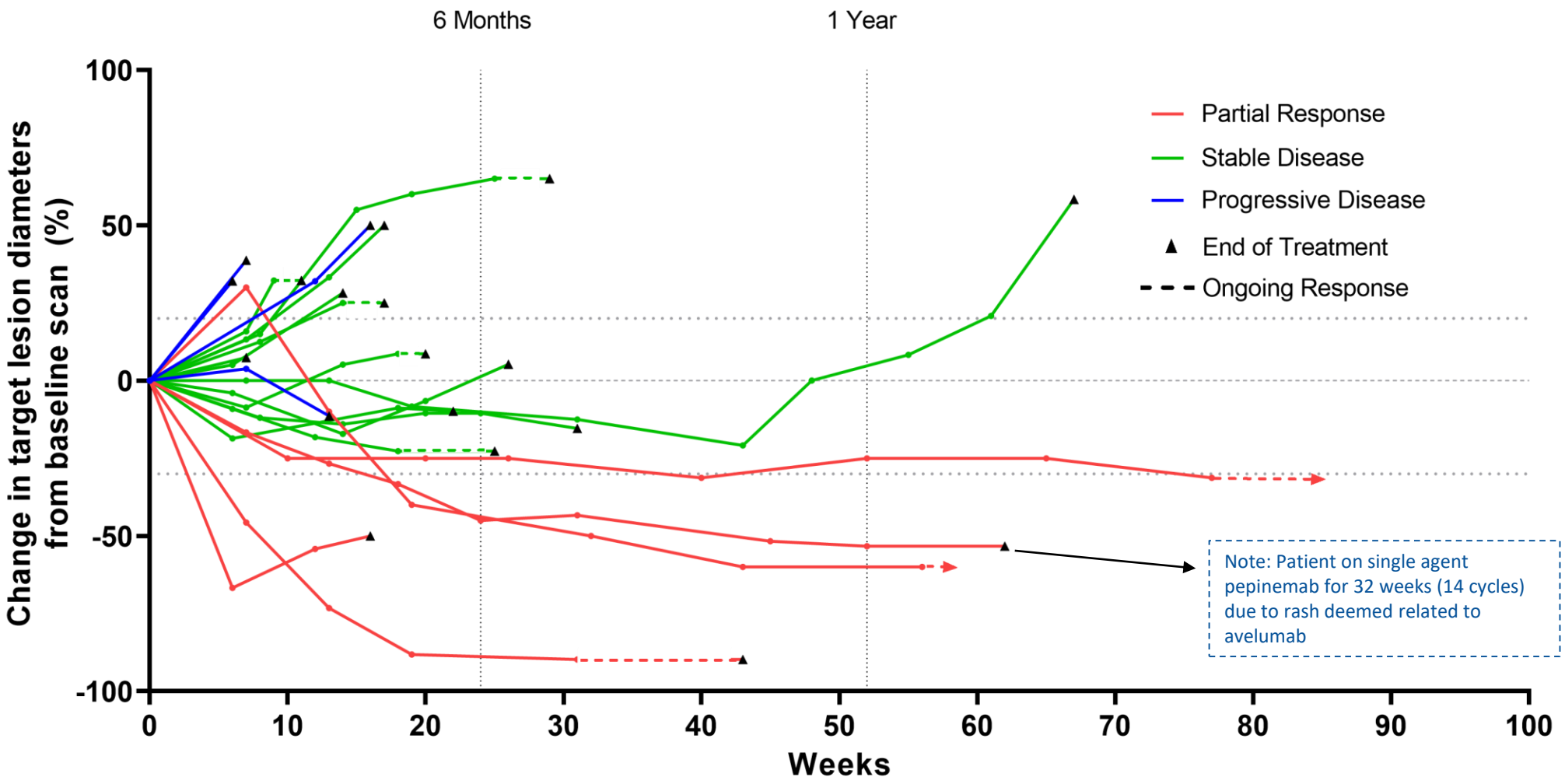
Combination immunotherapy in NSCLC following immunotherapy failure

Increase in CD8+ T cell infiltration, decrease in tumor burden



Tumor (Cytokeratin+)
CD8+ T cells
Pembrolizumab refractory

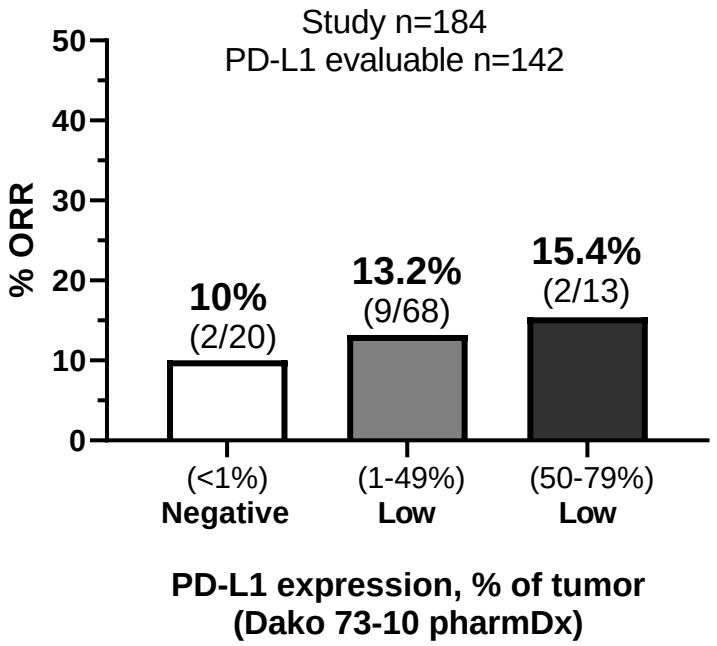
Percent Change in Target Lesion Diameter by Weeks (IO Naïve)



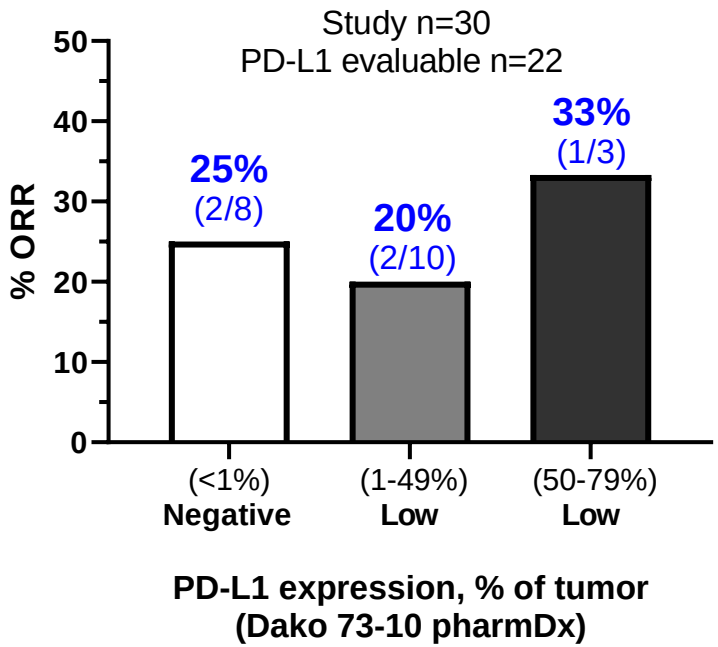
Lines are color-coded based on best overall response

Combination therapy achieved a higher response rate in difficult to treat PD-L1-low population, compared to historical data in IO naïve patients with avelumab

Javelin Solid Tumor[1]
Objective Response Rate by PD-L1 status



CLASSICAL-Lung [2]
Objective Response Rate by PD-L1 status



1. Calculated from data published in:

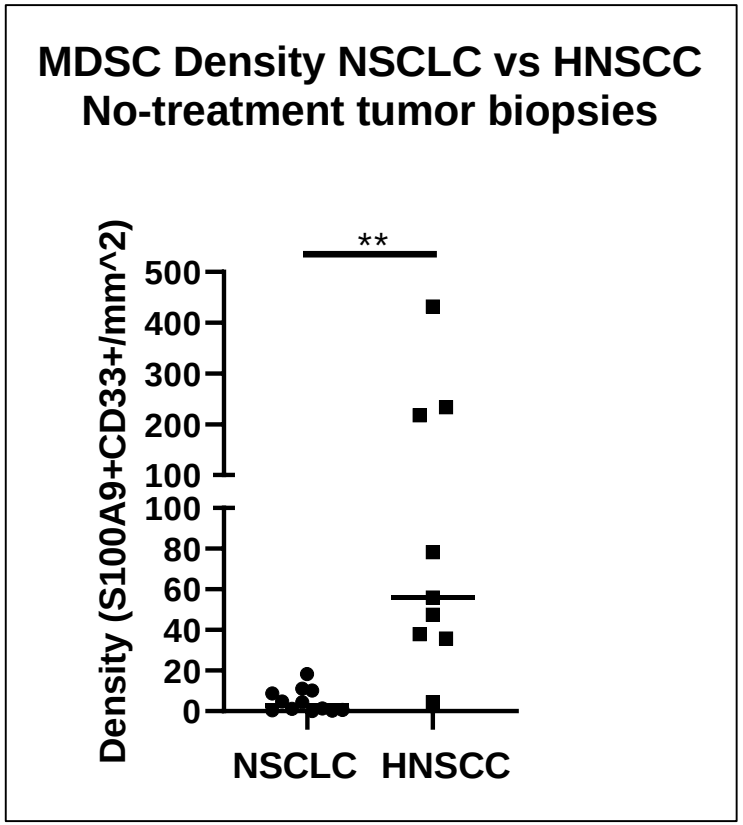
Gulley JL, Rajan A, Spigel DR, et al. Avelumab for patients with previously treated metastatic or recurrent non-small-cell lung cancer (JAVELIN Solid Tumor): dose-expansion cohort of a multicentre, open-label, phase 1b trial. *Lancet Oncol* 2017; published online March 31. http://dx.doi.org/10.1016/S1470- 2045(17)30240-1.

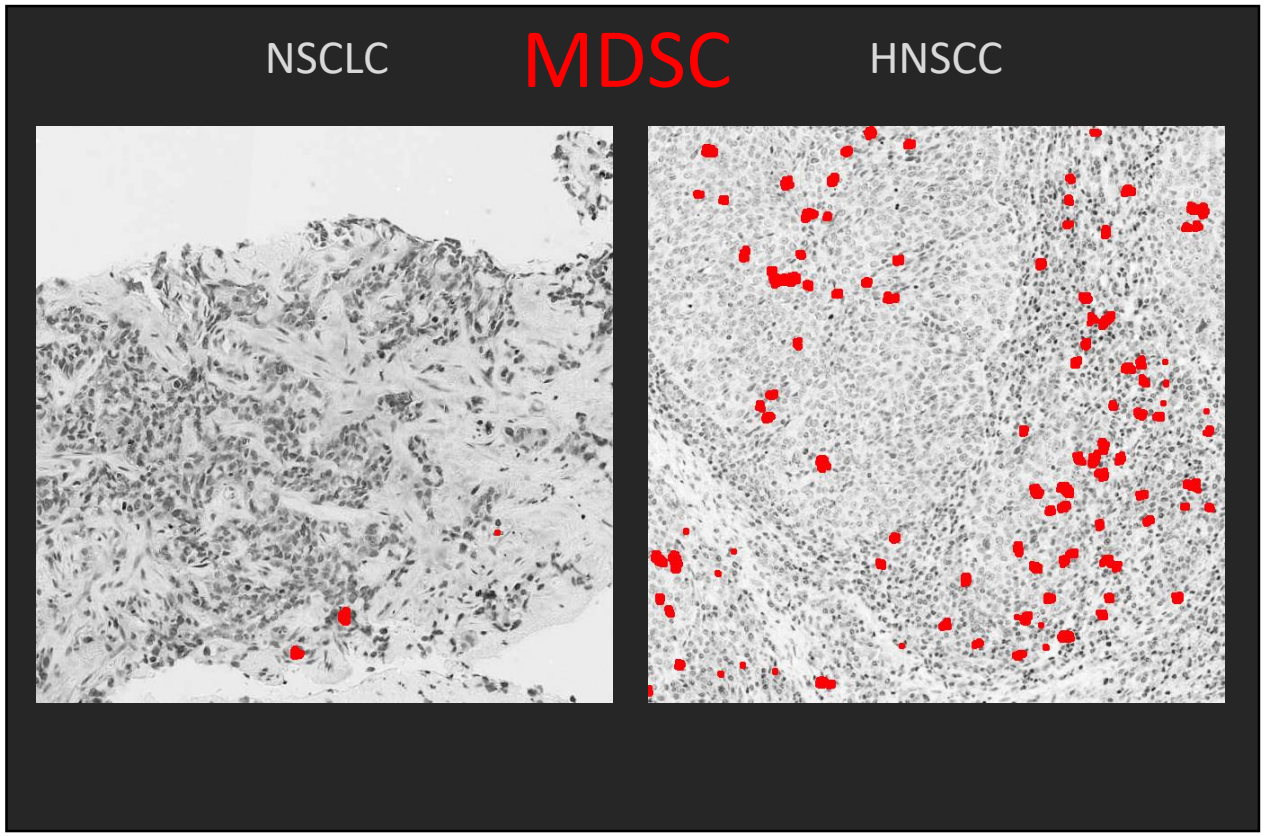
Gulley JL, Rajan A, Spigel DR, et al. Exposure Response and PD-L1 expression analysis of second-line avelumab in patients with advanced NSCLC: data from the JAVELIN Solid tumor trial: Abstract No. 9086. Presented at 53rd ASCO Annual Meeting; Jun 2-6, 2017

2. 27% (8/30) subjects did not have PD-L1 status reported and 9.5% (2/21) subjects were non-evaluable for post dose scans (included in ORR calculation) due to withdrawal prior to first scan. Note that a score of 80% in Merck KGaA 73-10 assay employed here is equivalent to a score of 50% in The 22C3 assay employed by US Merck.

NSCLC have low MDSC content relative to HNSCC

CLASSICAL-NSCLC patients may, therefore, benefit from only 1 of 2 major pepinemab mechanisms of action





- NSCLC: pre-treatment biopsies from CLASSICAL-Lung
- HNSCC: pre-treatment and no treatment biopsies from HNSCC integrated biomarker tria (collaboration at Emory University)

SEMA4D and HNSCC

SEMA4D reported to play a role in invasion and MDSC survival / function in HNSCC

Published OnlineFirst December 4, 2018; DOI: 10.1158/2326-6066.CIR-18-0156

Research Article

Cancer Immunology Research

Semaphorin4D Inhibition Improves Response to Immune-Checkpoint Blockade via Attenuation of MDSC Recruitment and Function

Paul E. Clavijo[1], Jay Friedman[1], Yvette Robbins[1], Ellen C. Moore[1], Ernest Smith[2], Maurice Zauderer[2], Elizabeth E. Evans[2], and Clint T. Allen[1,3]

Published January 6, 2016, doi:10.4049/jimmunol.1501293

The Journal of Immunology

Human Head and Neck Squamous Cell Carcinoma–Associated Semaphorin 4D Induces Expansion of Myeloid-Derived Suppressor Cells

Rania H. Younis,*,†,1 Kyu Lee Han,*,1 and Tonya J. Webb†,‡

www.impactjournals.com/oncotarget/ Oncotarget, 2018, Vol. 9, (No. 13), pp: 11126-11144

Research Paper

Semaphorin 4D in human head and neck cancer tissue and peripheral blood: A dense fibrotic peri-tumoral stromal phenotype

Roshanak Derakhshandeh[1,6], Sonia Sanadhya[1], Kyu Lee Han[1], Haiyan Chen[3], Olga Goloubeva[5,7], Tonya J. Webb[6,7] and Rania H. Younis[1,2,4,7]

[1]Department of Oncology and Diagnostic Sciences, School of Dentistry, University of Maryland Baltimore, Baltimore, Maryland, USA

INTERNATIONAL JOURNAL OF ONCOLOGY 51: 625-632, 2017

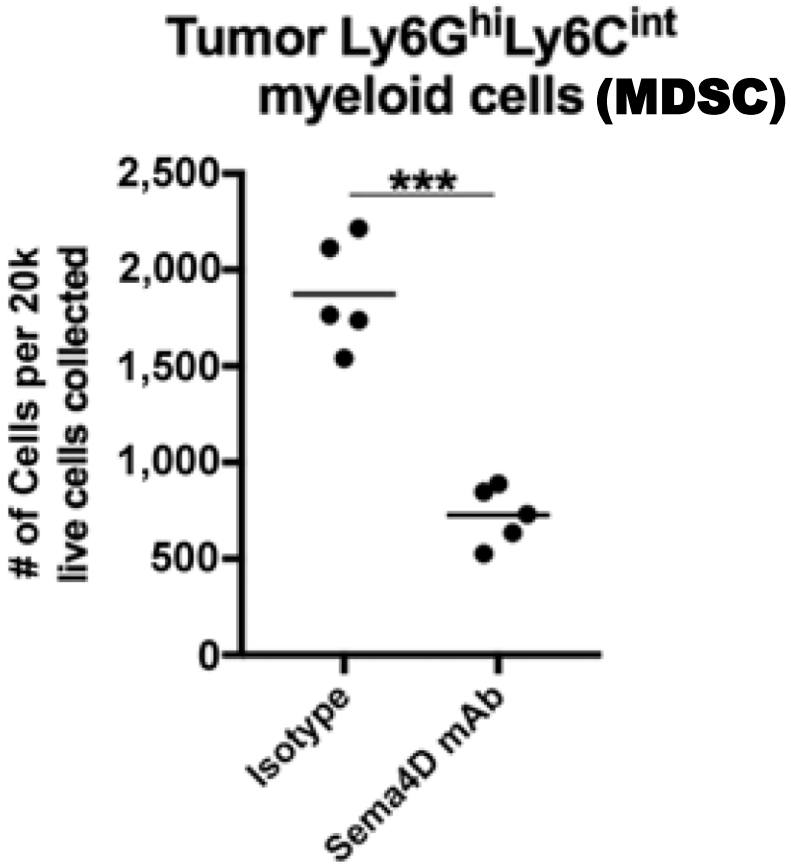
Semaphorin 4D promotes bone invasion in head and neck squamous cell carcinoma

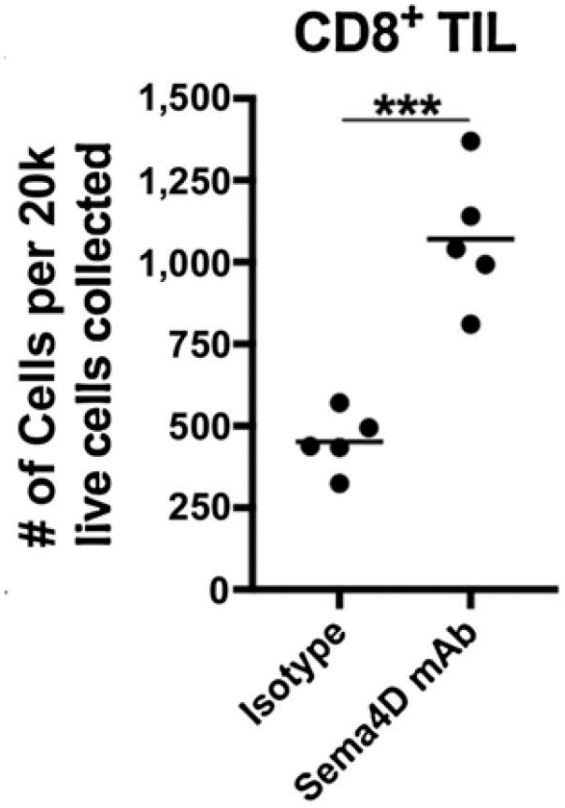
HIROYUKI TAKADA[1], SOICHIRO IBARAGI[1], TAKANORI EGUCHI[2,3], TATSUO OKUI[1], KYOICHI OBATA[1], MASANORI MASUI[1], AYAKA MORISAWA[1], KIYOFUMI TAKABATAKE[4], HOTAKA KAWAI[4], NORIE YOSHIOKA[1], NUR MOHAMMAD MONSUR HASSAN[5], TSUYOSHI SHIMO[1,3], GUO-FU HU[6], HITOSHI NAGATSUKA[4] and AKIRA SASAKI[1]

Departments of [1]Oral and Maxillofacial Surgery, and [2]Dental Pharmacology, Okayama University Graduate School

Depletion of SEMA4D shifts the balance of MDSC and CD8+ tumor cells within HNSCC Tumor Microenvironment

In vivo quantitation of MDSC and T cells in HNSCC animal tumor model



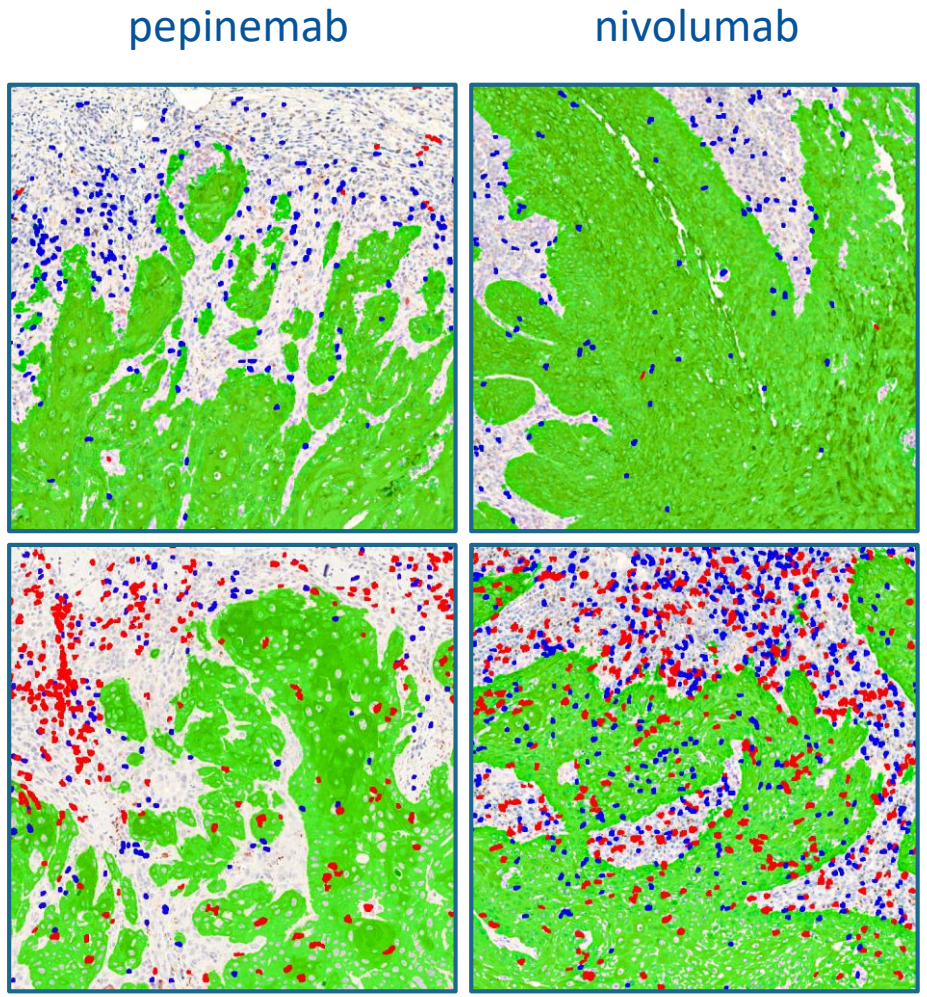


Clavijo PE et al. 2019 . Cancer Immunol Res. 7(2): 282-291

Cytotoxic and regulatory T-Cell populations pre and post pepinemab treatment

HNSCC pre- and post-treatment biopsies

Neoadjuvant/"window of opportunity" study, Winship Cancer Institute, Emory University



- An increase in CD8+ and decrease in FoxP3+ T-cells is evident post pepinemab treatment.
- Nivolumab increases CD8+ but also induces striking increase in FoxP3+ T-cells.

Cytotoxic T cells (CD8+)
Tregulatory (FoxP3+)
Tumors (Cytokeratin+)

Robust Patent Estate

VX15 (pepinemab) US Patents and Patent Applications

Key Composition of Matter Claims	**US No. 8,496,938 issued 7/30/13)** ***Expected Exclusivity to 2030 (before patent term extension)***
Key Additional Method of Use Claims for Treatment of Cancer and Neurodegenerative Diseases	US No. 9,243,9068 issued 1/26/16 US No. 9,249,227 issued 2/2/16 Filed: 2014 – 2015 Expected Exclusivity to 2035 (before patent term extension)

Total Patent Franchise	US	EU
Granted / allowed	26	11
Pending	15	13

Vaccinex Executive Management Team

Maurice Zauderer, Ph.D., *Founder, President & Chief Executive Officer*
Formerly University of Rochester School of Medicine and Columbia University

John E. Leonard, Ph.D., *SVP Development & Officer*
Formerly VP Product Development at IDEC and Biogen-IDEC

Scott E. Royer, CFA, MBA, *Chief Financial Officer*
Formerly CFO, Medical Films Division of CarestreamHealth

Ernest S. Smith, Ph.D., *SVP Research & Chief Scientific Officer*
Formerly University of Rochester School of Medicine

Raymond E. Watkins, *SVP & Chief Operating Officer*
Formerly Director of Operations, Australasia at Life Technologies (Invitrogen).

Vaccinex Board of Directors

Albert D. Friedberg	Chairman, President and CEO of Friedberg Mercantile Group, a Toronto-based commodities and investment management firm he founded in 1971. He served as Chairman of the Toronto Futures Exchange from March 1985 to June 1988.
Chrystyna M. Bedrij	Co-Founder and Principal, Griffin Securities
Jacob B. Frieberg	Principal, The WTF Group.
J. Jeffrey Goater	CEO of Surface Oncology, Formerly, CFO of Voyager Therapeutics.
Bala S. Manian, Ph.D.	Founder (or co-founder) of Quantum Dot Corporation, SurroMed, Biometric Imaging, LumisysInc., Molecular Dynamics and ReaMetrix.
Gerald E. Van Strydonck	Formerly, Managing Partner at PricewaterhouseCoopers.
Barbara Yanni	Formerly, Vice President and Chief Licensing Officer at Merck & Co., Inc.
Maurice Zauderer, Ph.D.	Vaccinex Founder, President and Chief Executive Officer. Formerly, Professor at University of Rochester and at Columbia University.

Vaccinex Corporation

Clinical-stage immunotherapy company focused on the discovery and development of antibody therapies for neurodegenerative diseases and cancer

VCNX (NASDAQ)	
Shares outstanding	16.4M
Market cap	2020 high $137 million 2020 low $60 million
Headquarters	Rochester, NY
Employees	49
IPO (proceeds $40M)	August 2018
PIPE (proceeds $21.3M)	July 2019/Jan 2020
Analysts	Oppenheimer, BTIG, Ladenburg

Anticipated Vaccinex 2020 Milestones

Event	Timing
Near **Topline Clinical Data for Pepinemab in Combination with Avelumab in NSCLC**	April 2020
Interim analysis of combination Window-of-Opportunity studies at Emory University (Melanoma, HNSCC, colorectal and pancreatic cancer)	ASCO 2020
Completion (LPLV) of SIGNAL Cohort B study in Huntington's Disease	July 2020
Expected Topline Clinical Data for SIGNAL Cohort B study in Huntington's Disease	**October 2020**
Estimated enrollment of first patient in Alzheimer's disease phase1 study	H2 2020
Site selection for first line combination immunotherapy in Head & Neck Cancer	H2 2020