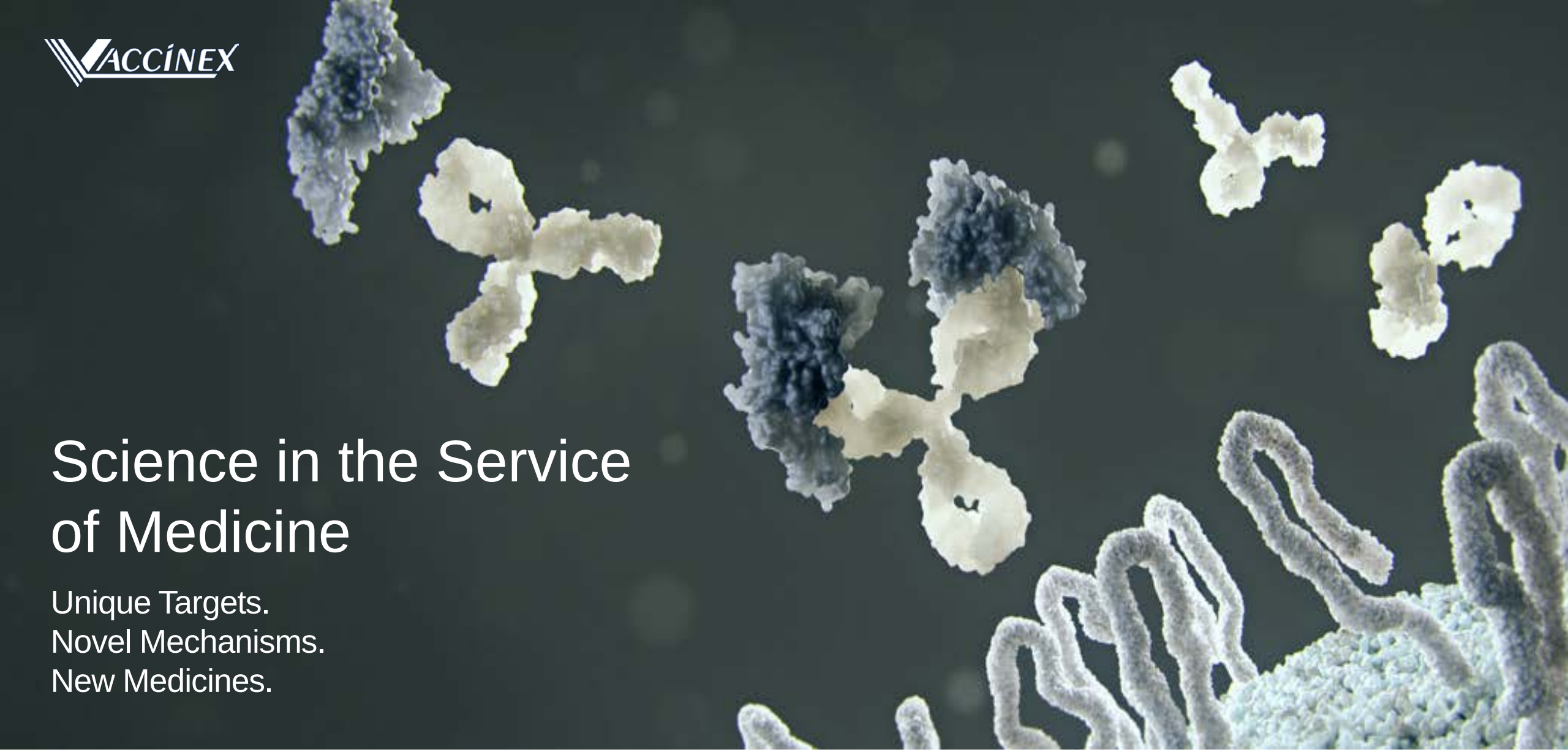


Science in the Service of Medicine

Unique Targets.
Novel Mechanisms.
New Medicines.

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

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.

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

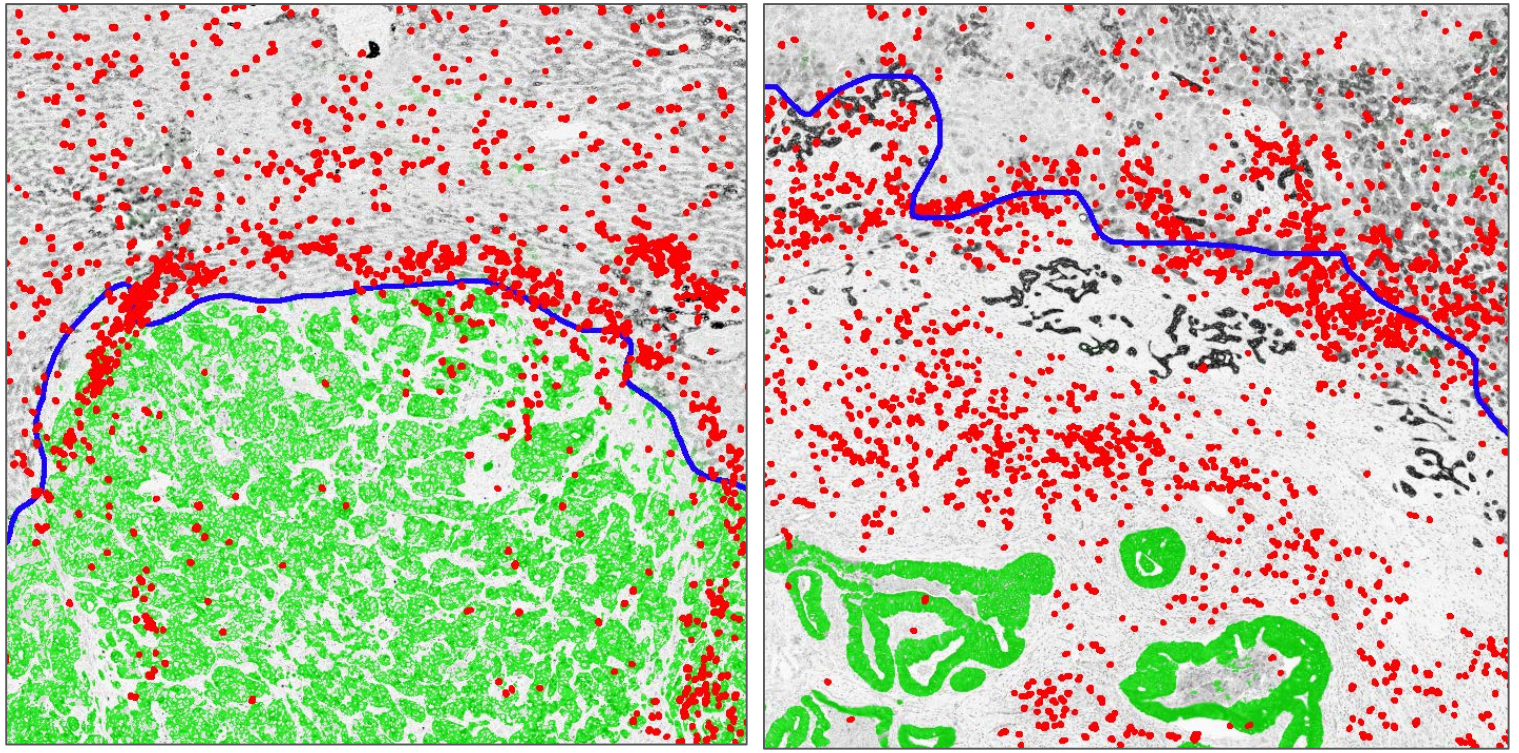
T cells are trapped at margin and are largely excluded from tumor bed

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

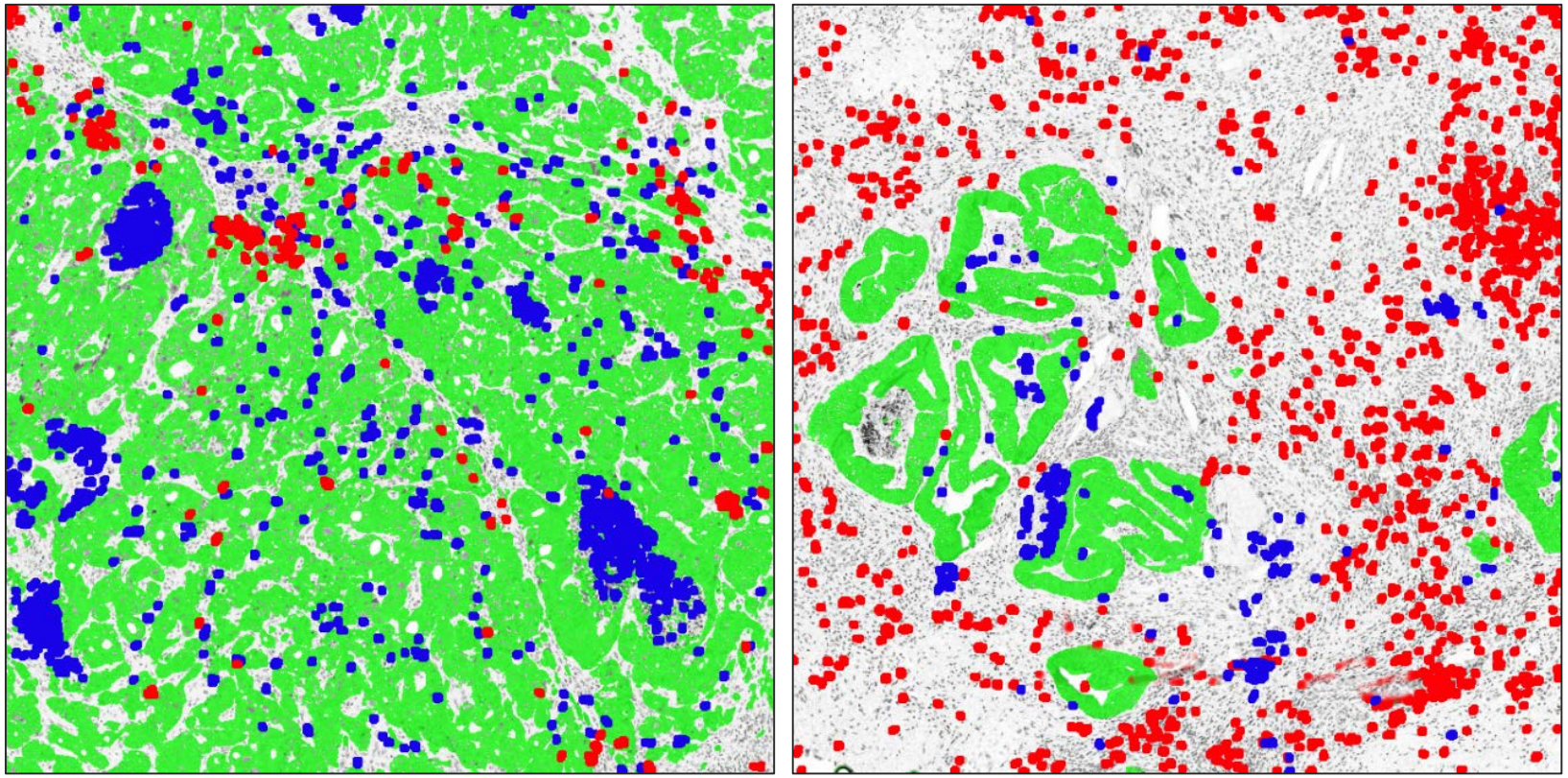
Patients received neoadjuvant chemo therapy before immunotherapy and surgery

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

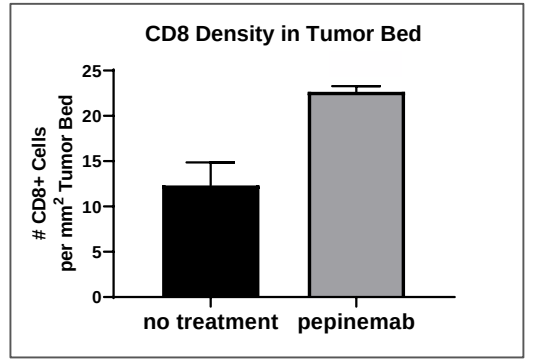
MSS Colorectal cancer metastasis to liver – neoadjuvant/"window of opportunity" study

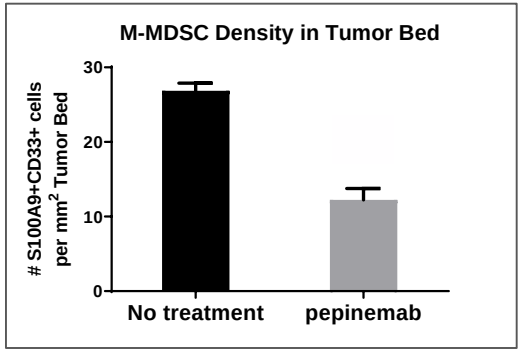
Winship Cancer Institute, Emory University

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+)

Phase 1b/2 CLASSICAL- Lung Study Design

Combination Trial of Pepinemab with Avelumab in NSCLC

Sponsored by: VACCINEX

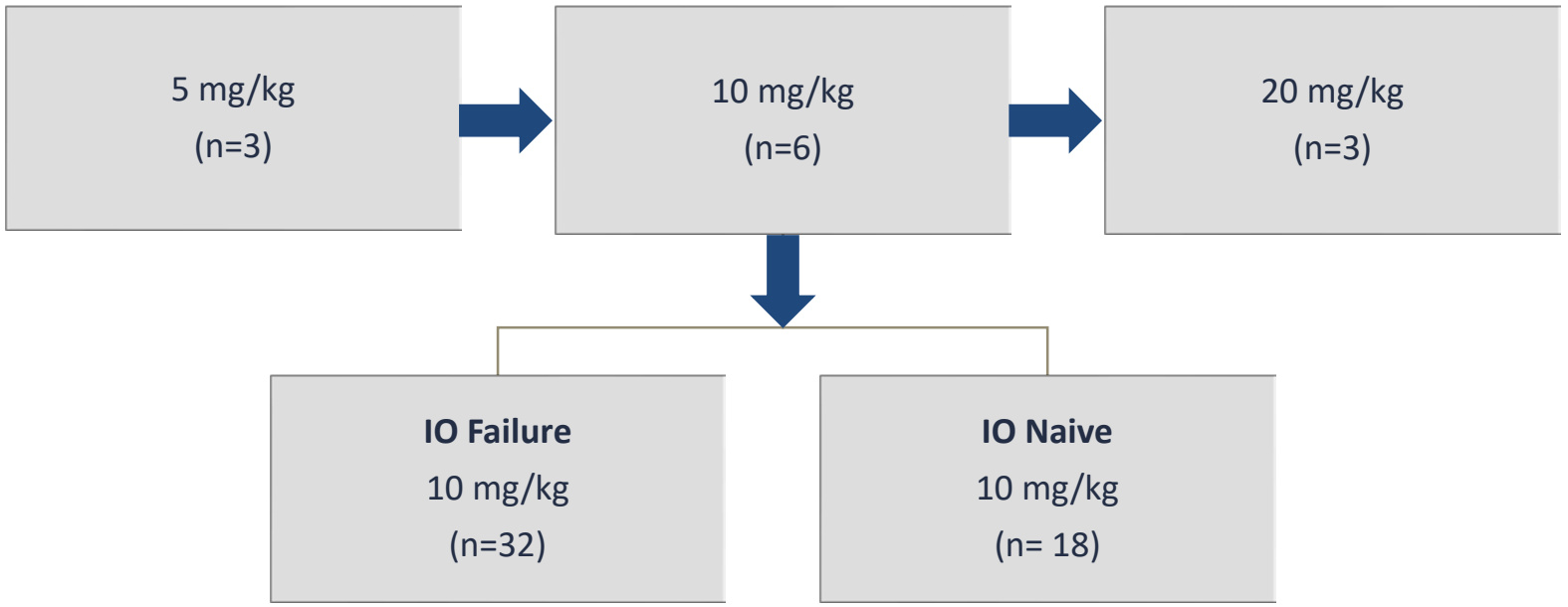
Co-funded by: MERCK

Phase 1b

Dose Escalation
IO Naïve
(n=12)

Phase 2

Dose Expansion
(n=50)



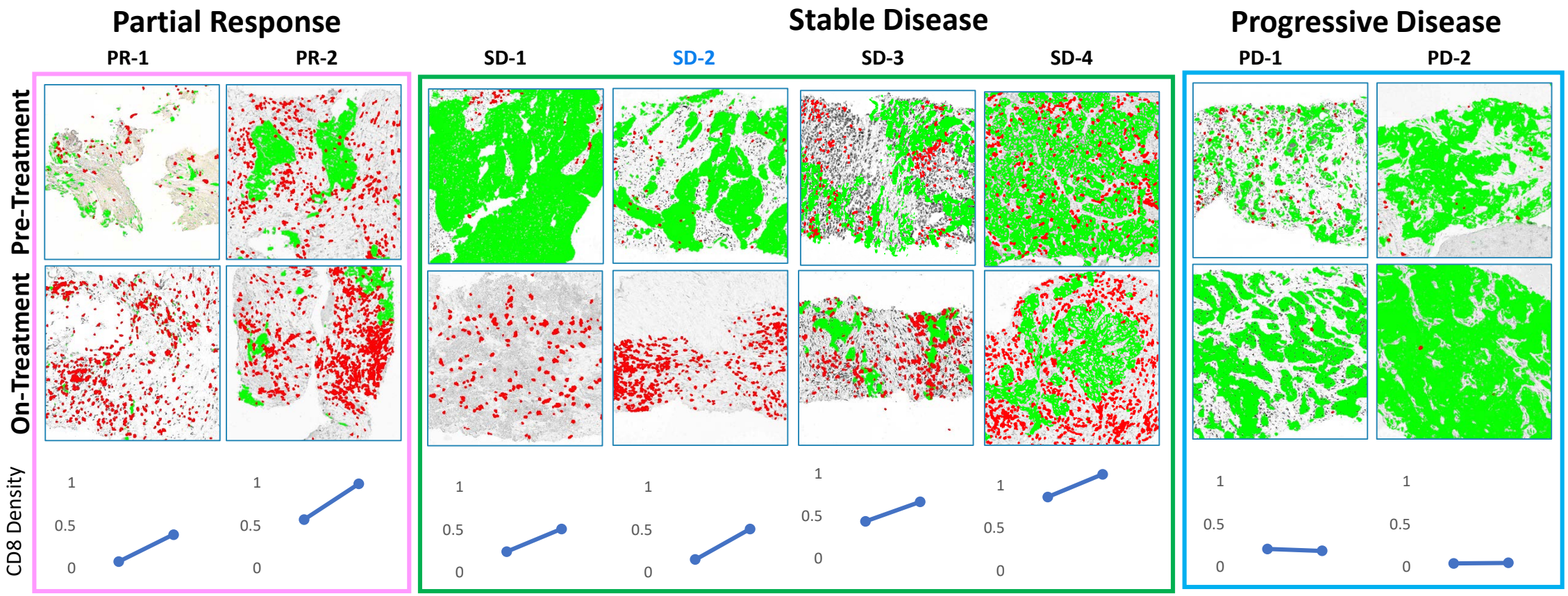
pepinemab
+
10 mg/kg
avelumab
Q2W

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

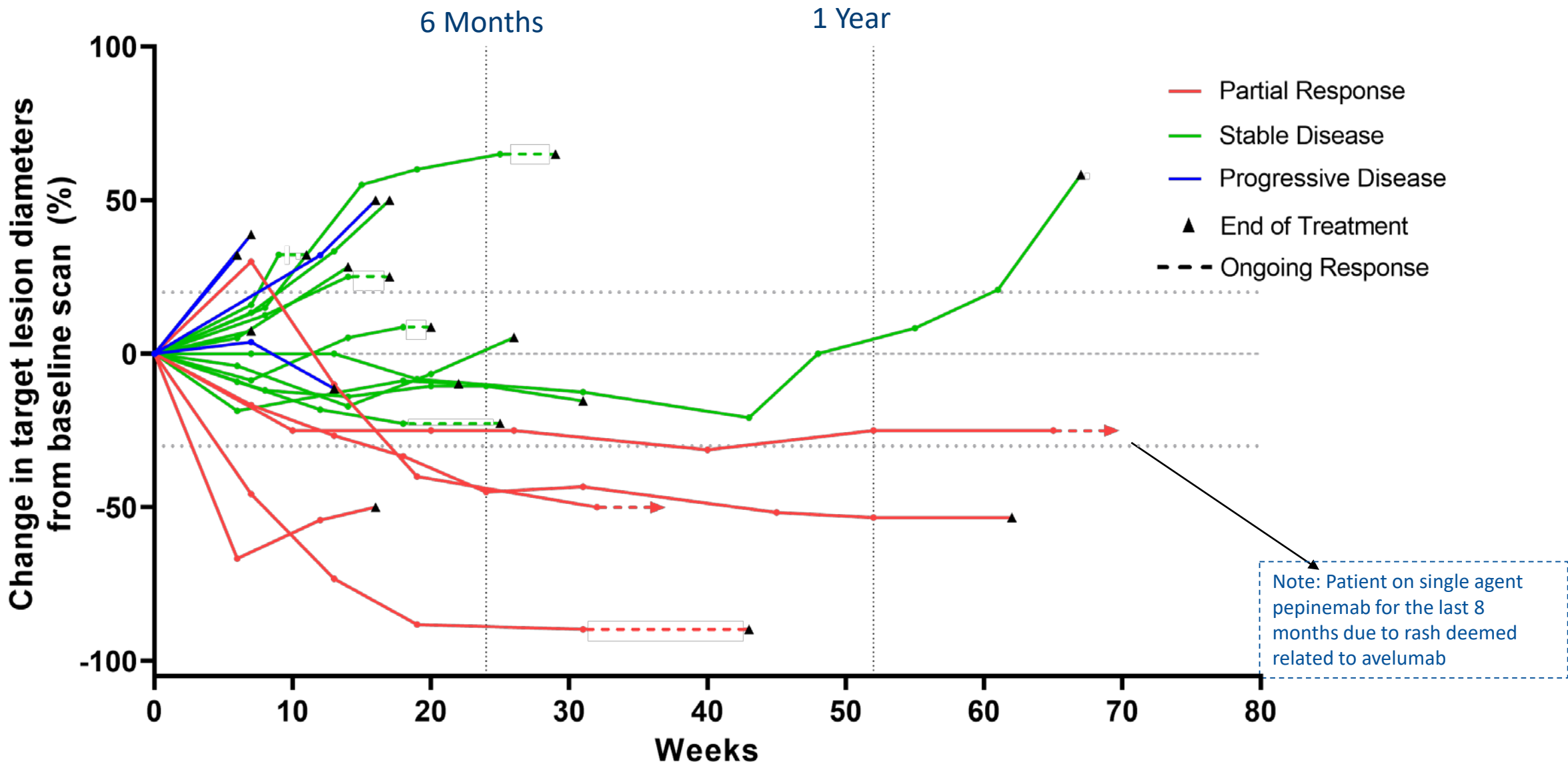
Combination immunotherapy in NSCLC following immunotherapy failure

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

PD-L1 Subpopulations in Evaluable IO Naïve Subjects

CLASSICAL-Lung vs. Historical Javelin Solid Tumor

CLASSICAL-Lung (PD-L1 %) **[22 Subjects]**	**Negative <1%**	**≥80%**
Subpopulation size (%)	8/22 (36.4%)	1/22 (4.5%)

Javelin-Lung (PD-L1 %) **[142 Subjects]**	**Negative <1%**	**≥80%**
Subpopulation size (%)	20/142(14%)	41/142(28.9%)

NOTE: Significantly higher PD-L1 <1% and lower PD-L1 ≥80% subpopulations enrolled in CLASSICAL-Lung than in Javelin-Lung. This reflects shift in available population following Keutruda approval.

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

Objective Response Based on PD-L1 Status in Evaluable IO Naïve Subjects

CLASSICAL-Lung vs. Historical Javelin Solid Tumor

CLASSICAL-Lung (PD-L1 %) **[22 Subjects]**	**Negative <1%**	**1-49%**	**50-79%**	**≥80%**
OR (%)	2/8 (25%)	2/10 (20%)	1/3 (33.3%)	0/1 (0%)

Javelin-Lung (PD-L1 %) **[142 Subjects]**	**Negative <1%**	**1 to 49%**	**50 to 79%**	**≥80%**
OR (%)	2/20 (10%)	9/68(13.2%)	2/13 (15.4%)	9/41 (22.0%)

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

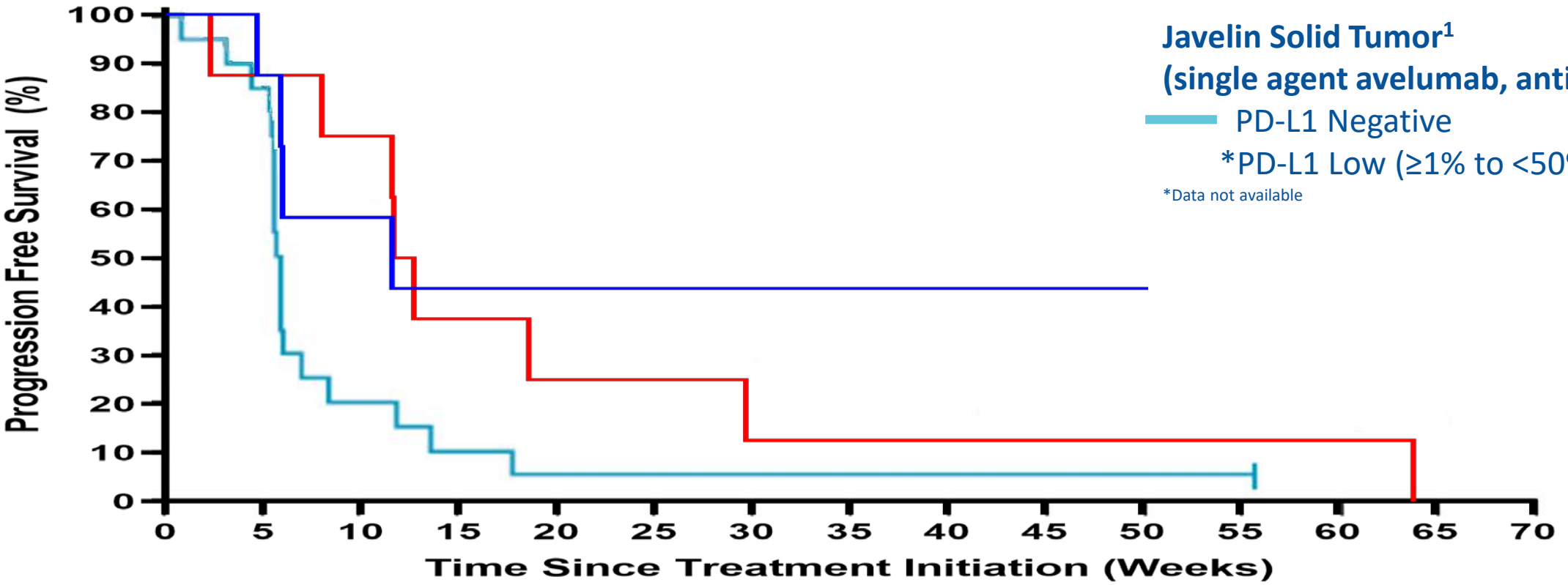
Progression Free Survival in ION Subjects

CLASSICAL-Lung vs. Historical Javelin Solid Tumor

CLASSICAL-Lung
(combination pepinemab and avelumab)
- PD-L1 Negative
- PD-L1 Low (≥1% to <50%)

Javelin Solid Tumor[1]
(single agent avelumab, anti-PD-L1)
- PD-L1 Negative
- *PD-L1 Low (≥1% to <50%)

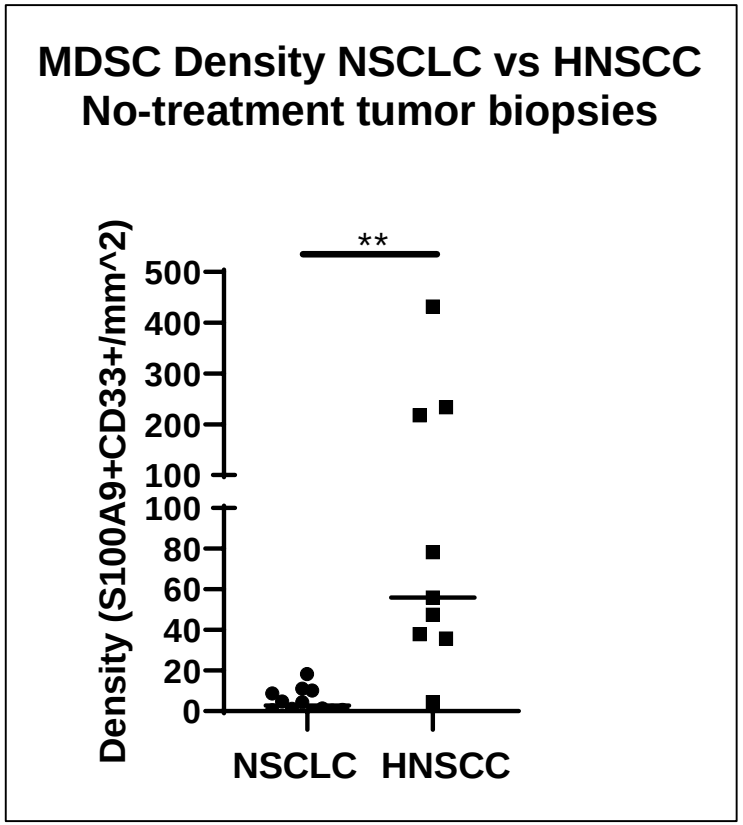
*Data not available

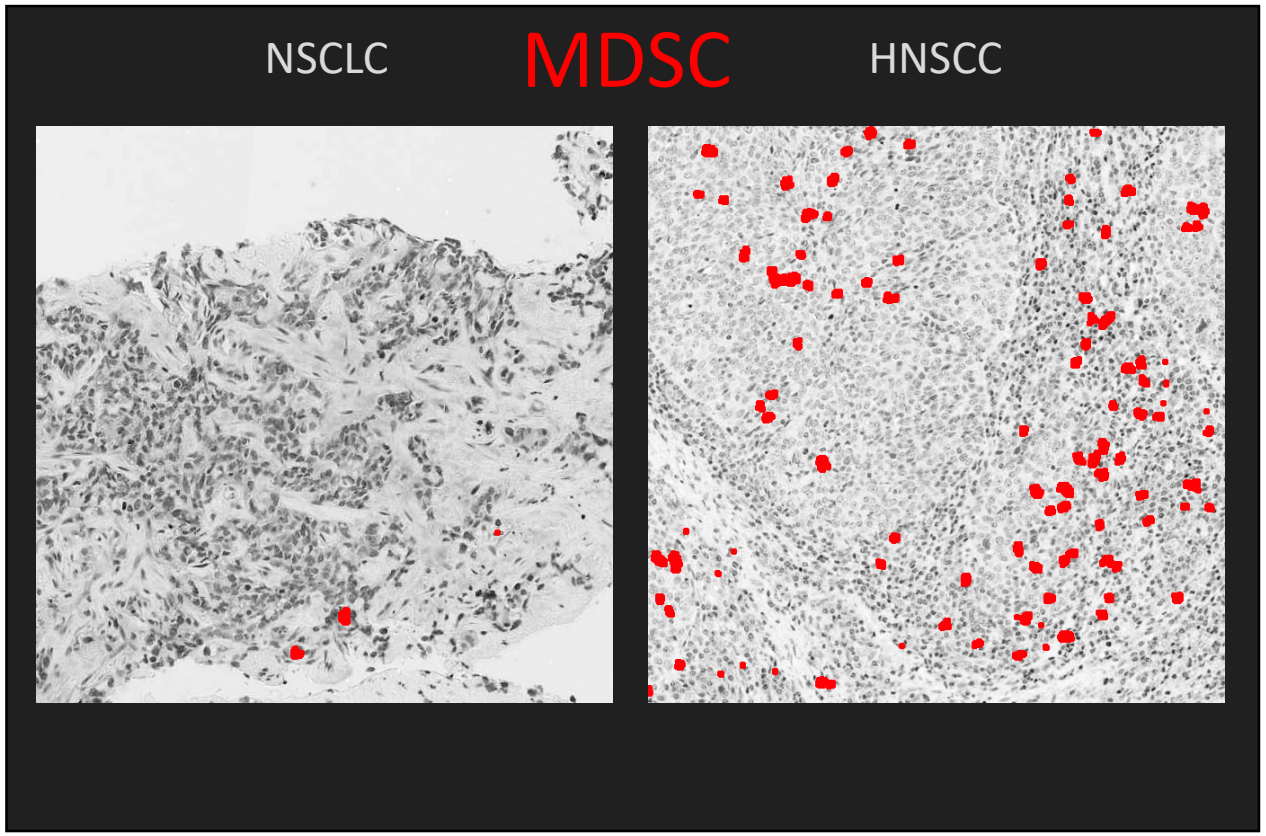


1. Gulley JL, Rajan A, Spigel DR, et al. Avelumab for patients with previously treated metastatic or recurrent non-small-cell lung cancer (JAVELIN Solid Tumor): dose-expansion cohort of a multicentre, open-label, phase 1b trial. *Lancet Oncol* 2017; published online March 31. http://dx.doi.org/10.1016/S1470-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

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]

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

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

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

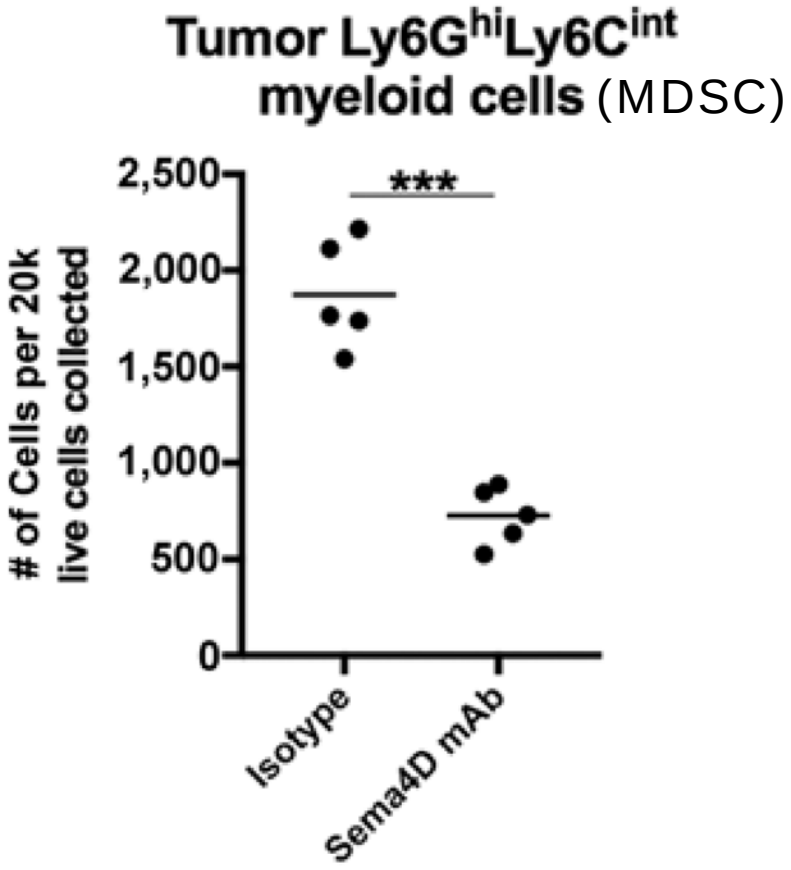
The Journal of Immunology

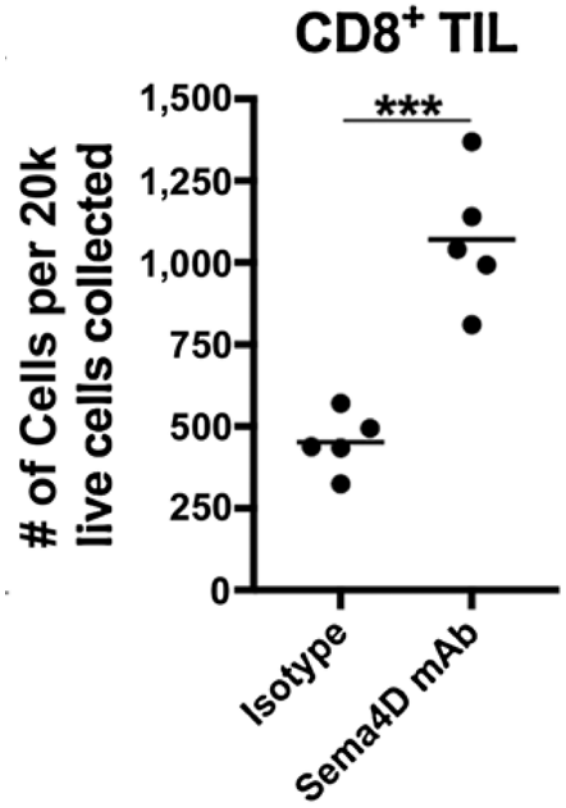
Human Head and Neck Squamous Cell Carcinoma–Associated Semaphorin 4D Induces Expansion of Myeloid-Derived Suppressor Cells

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

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



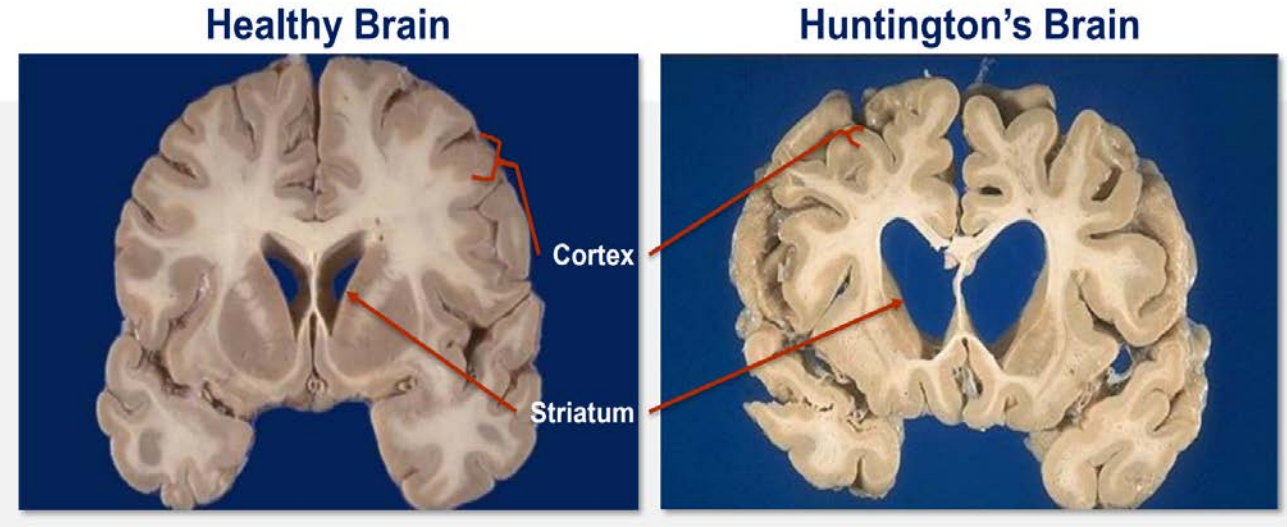


Clavijo PE et al. 2019 . Cancer Immunol Res. 7(2): 282-291

Huntington’s Disease (HD)

HD is an autosomal dominant neurodegenerative disease caused by mutation in a single gene

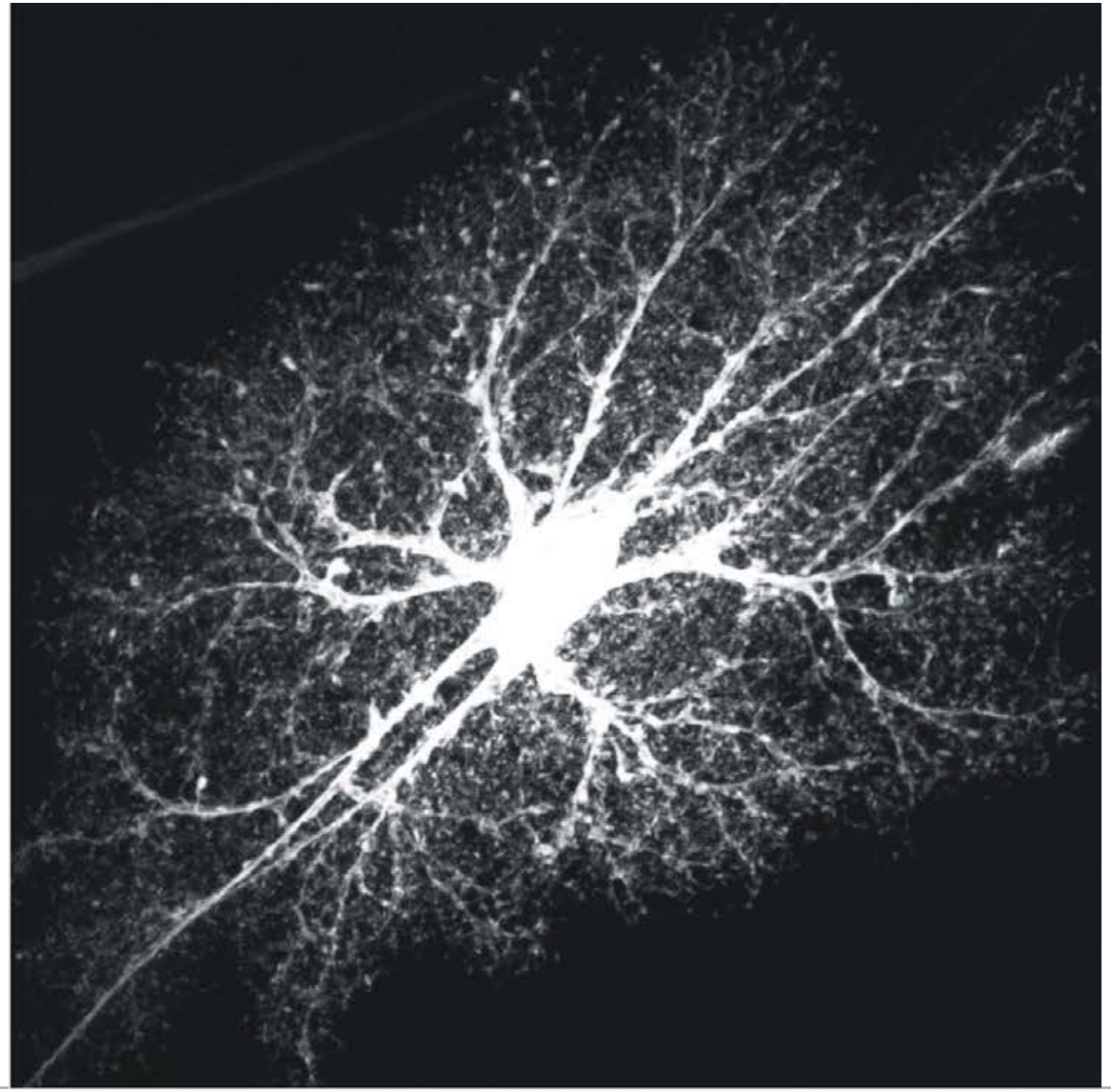
- Neuronal degeneration and severe atrophy is observed in multiple brain regions
- Symptoms usually appear between the ages of 30 to 50



Estimated patient population ~30,000 manifest disease and 100,000 pre-manifest with inherited mutation (prodromal) in the U.S. Similar number in EU 5

There are currently no approved treatments to alter the course of HD

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

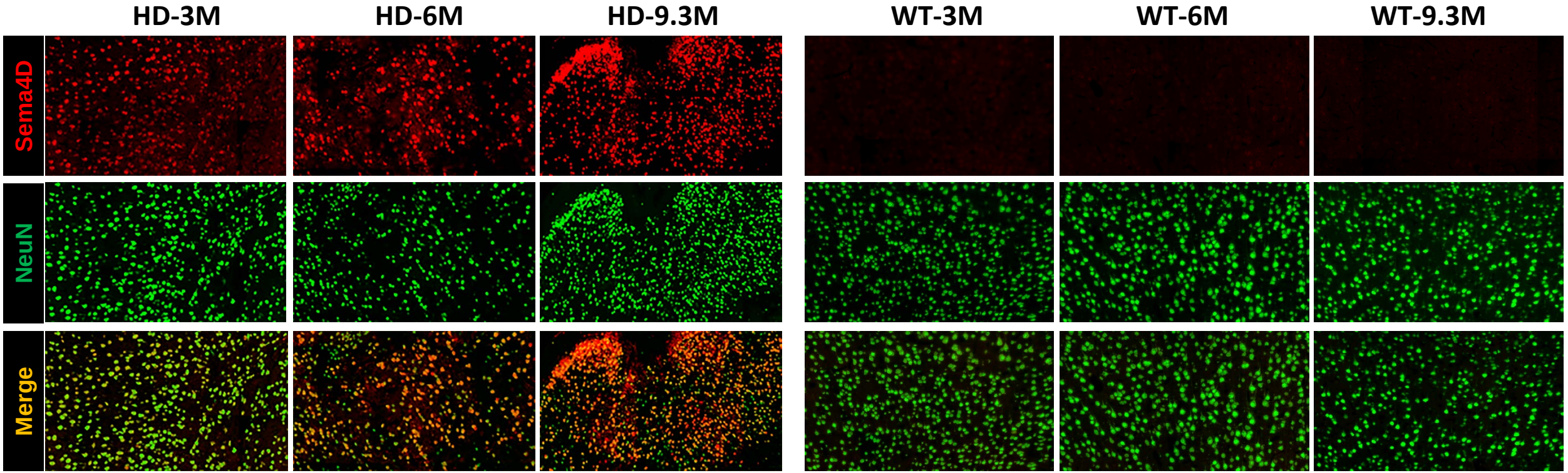
- **CNS damage triggers a dramatic change in astrocyte morphology and function**
  - this is beneficial in the context of acute focal injury such as stroke
  - but becomes maladaptive in broad chronic injury such as that caused by mHTT aggregates in HD or Aβ amyloid/Tau fibrils in AD

How do astrocytes recognize and respond to damage?

- SEMA4D is upregulated on neurons during underlying Huntington’s disease progression
- Astrocytes express high levels of receptors for SEMA4D
- SEMA4D triggers collapse of the astrocyte cytoskeleton which results in loss of normal astrocyte functions and gain of inflammatory activity

SEMA4D is progressively upregulated in NeuN+ neurons of HD mice

Q175 transgenic mouse model of HD



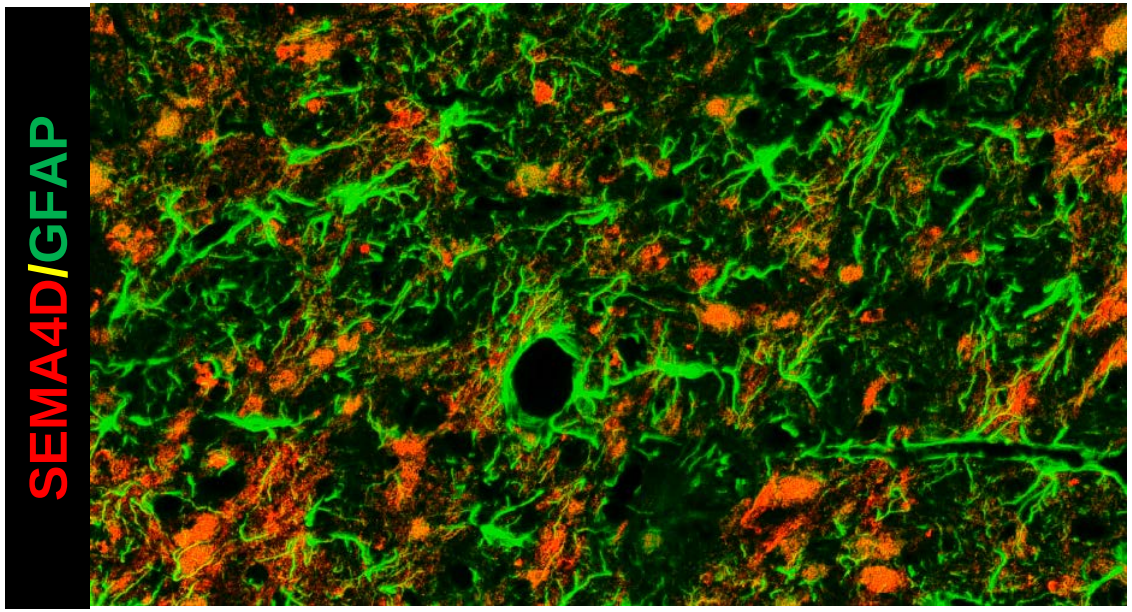
- **SEMA4D expression is upregulated in HD mice as disease progresses, compared to low expression in WT control.**
  - SEMA4D is upregulated early in disease, prior to onset of symptoms, which occurs ~ 5 months of age in Q175 HD transgenic mice.
- **SEMA4D co-localizes with NeuN+ neurons.**

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+ neurons are in close proximity to astrocytes

Q175 transgenic mouse model of HD

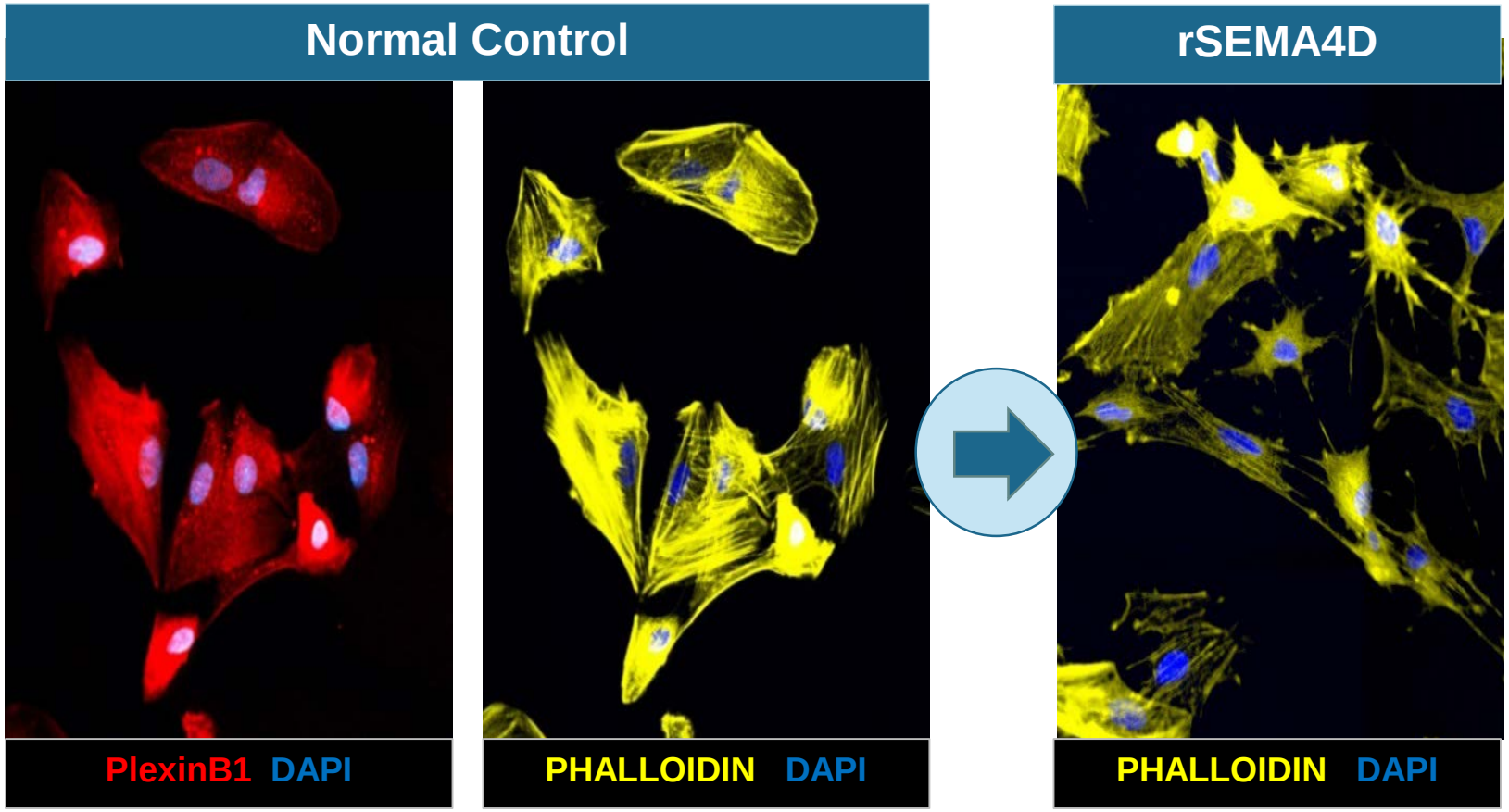
HD-9.3M



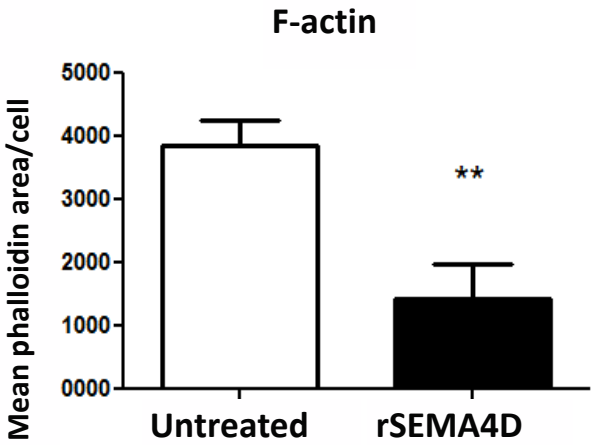
GFAP/SEMA4D staining of caudoputamen region of Q175 knock-in HD mice. Representative image (20X) is shown.

SEMA4D triggers collapse of actin cytoskeleton

A

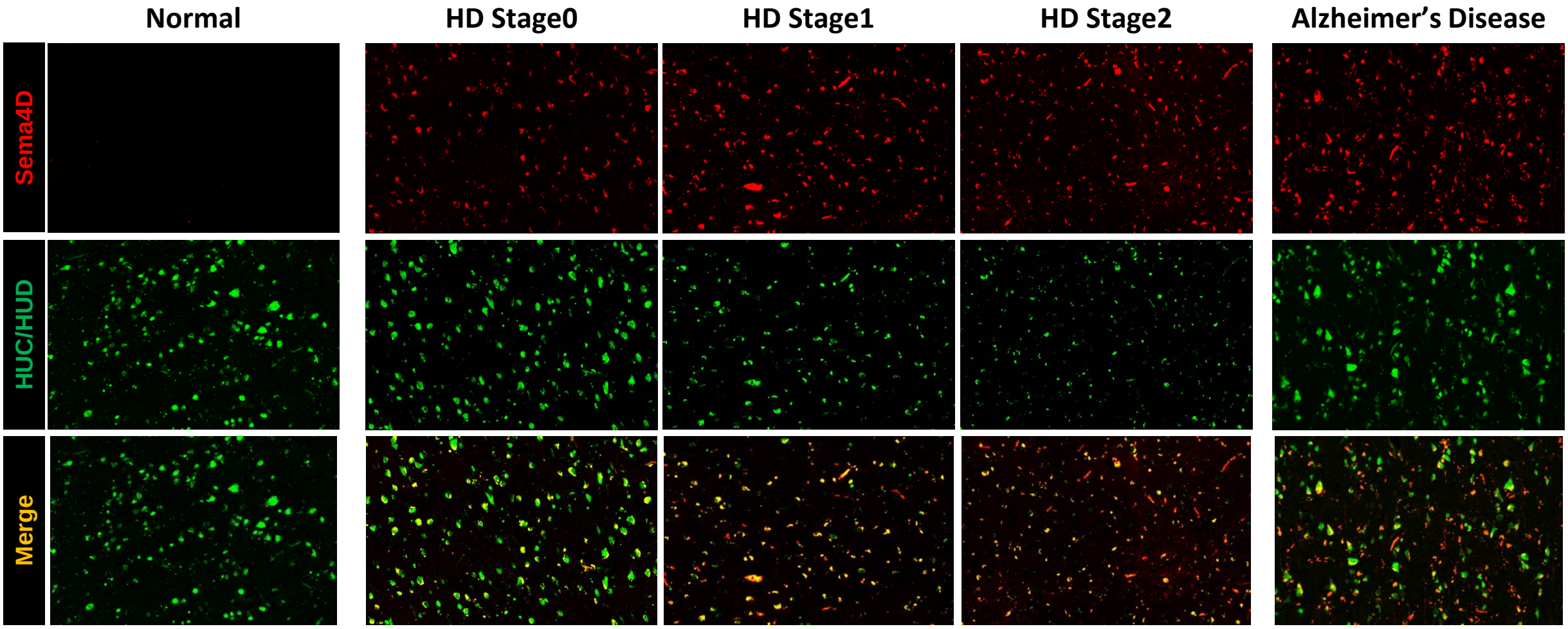


B

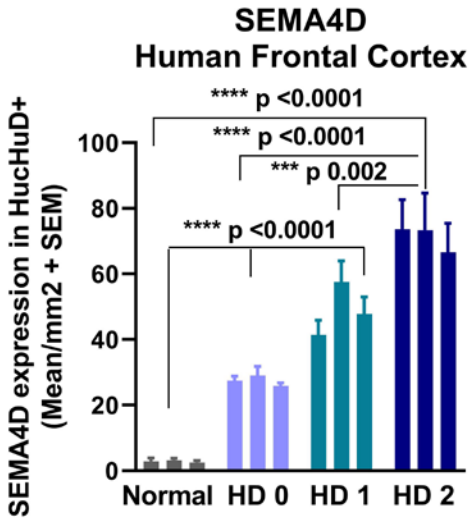


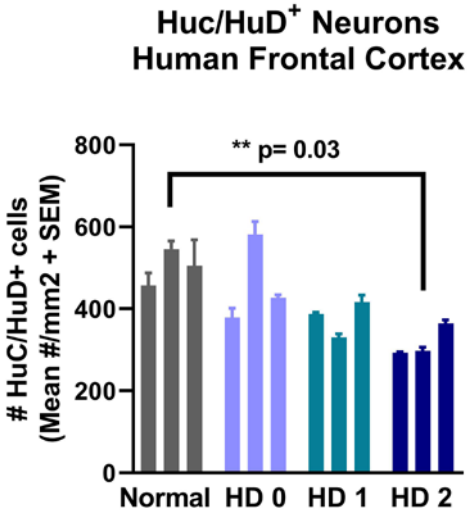
SEMA4D is upregulated in cortical neurons during Human HD Progression

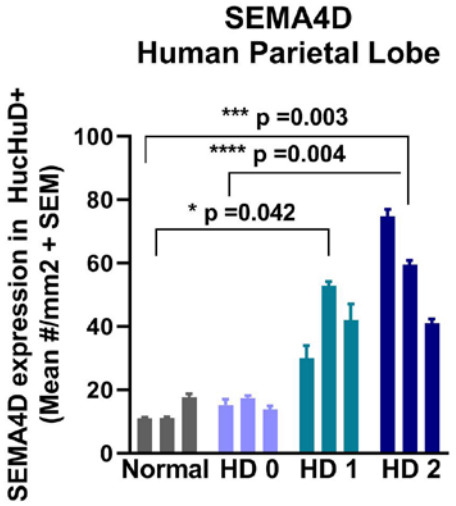
Frontal Lobe

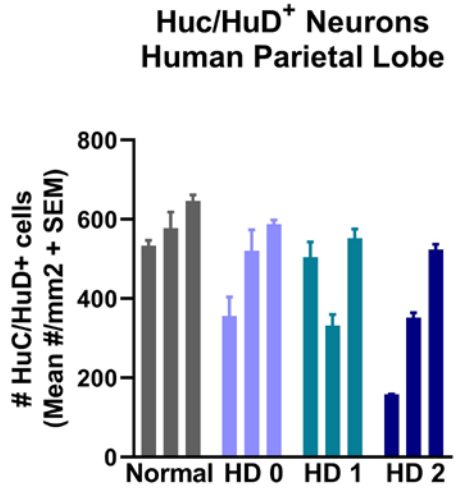


Changes in SEMA4D and Neuronal HuC/HuD Marker Expression with HD Progression









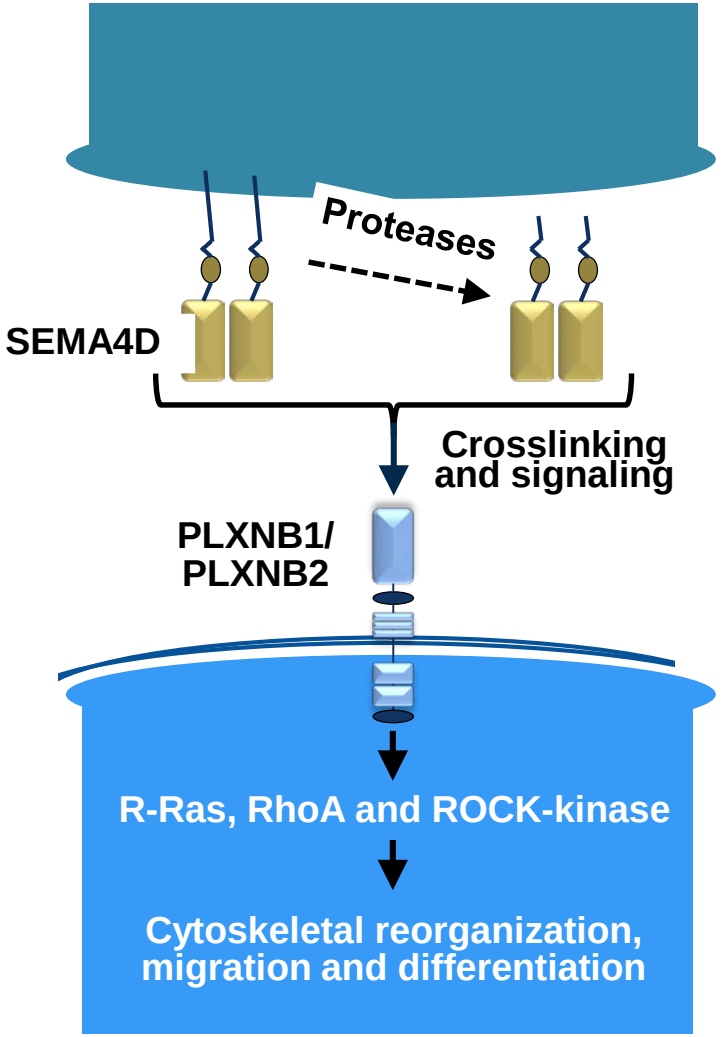
Semaphorin 4D (SEMA4D) Mechanism of Action Neurology

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 extension and cell migration

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

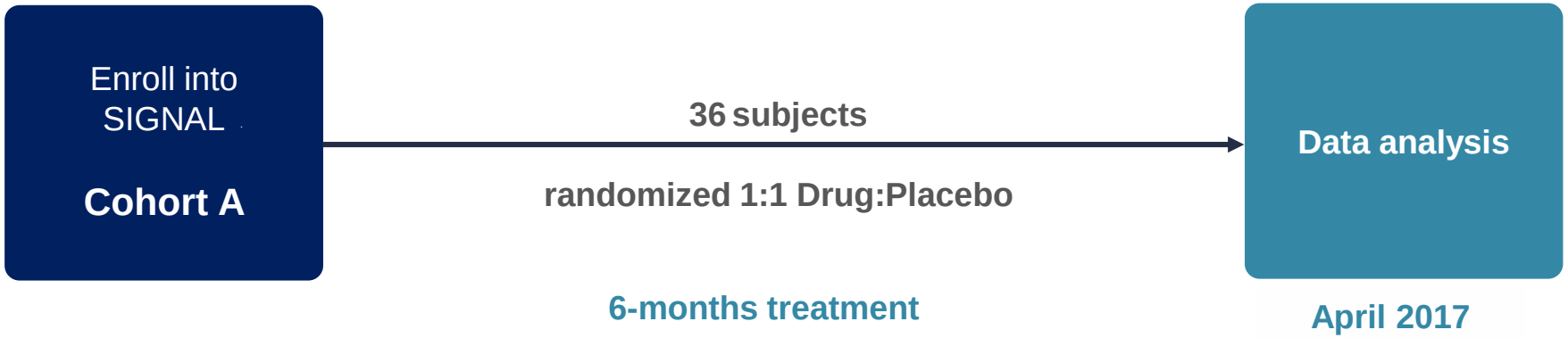
Pepinemab (VX15 antibody) binds to SEMA4D and blocks its signaling activity. This preserves normal astrocyte morphology and function and averts inflammatory transformation



Treatment Rationale: Anti-SEMA4D Antibody can 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
  - Glucose transport in brain is one of several important normal astrocyte functions that are known to be compromised in HD. This should be reflected in treatment outcomes and may be detected by FDG-PET in cortical regions of brain.

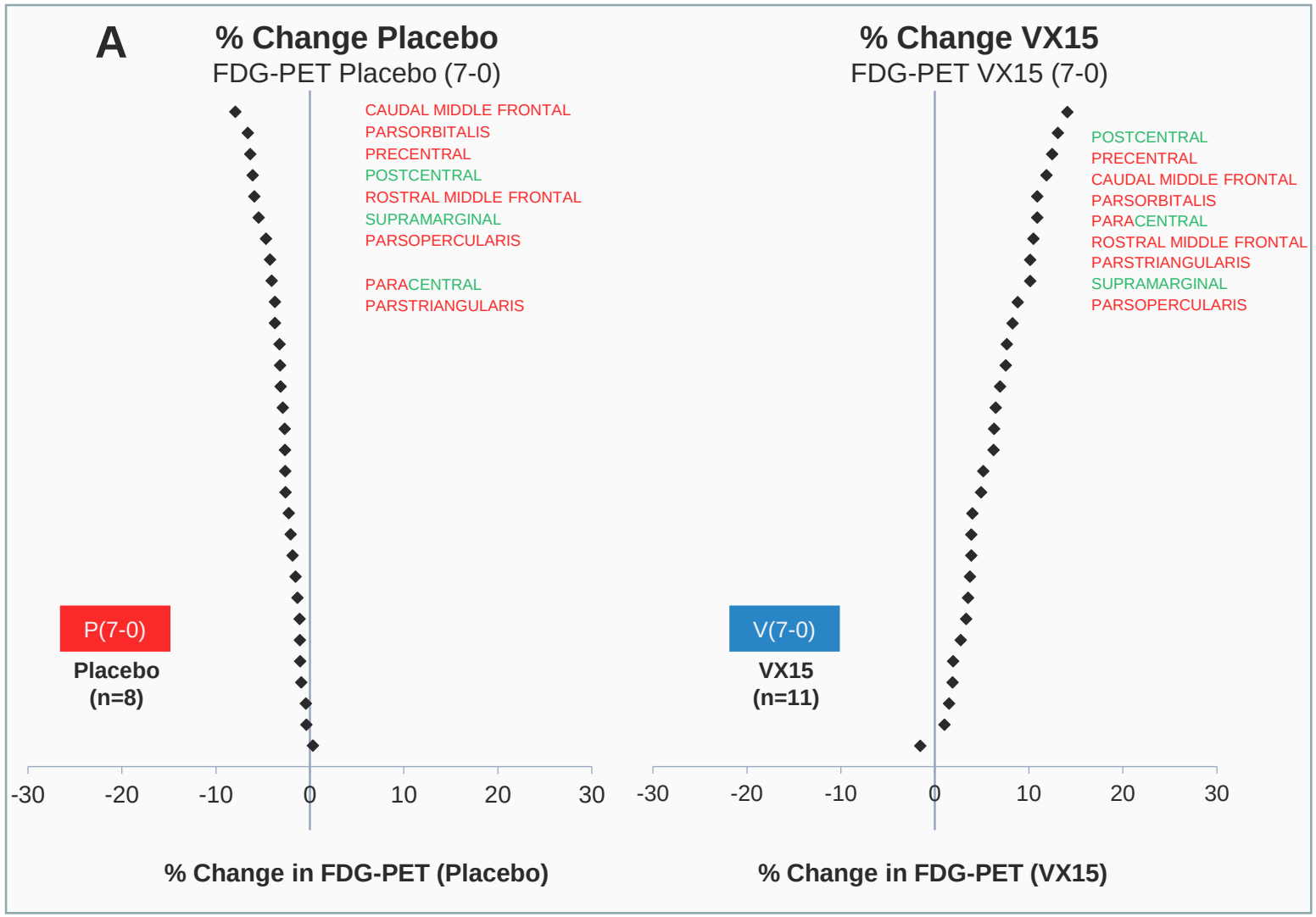
Huntington's Disease Clinical Trial Design: Cohort A

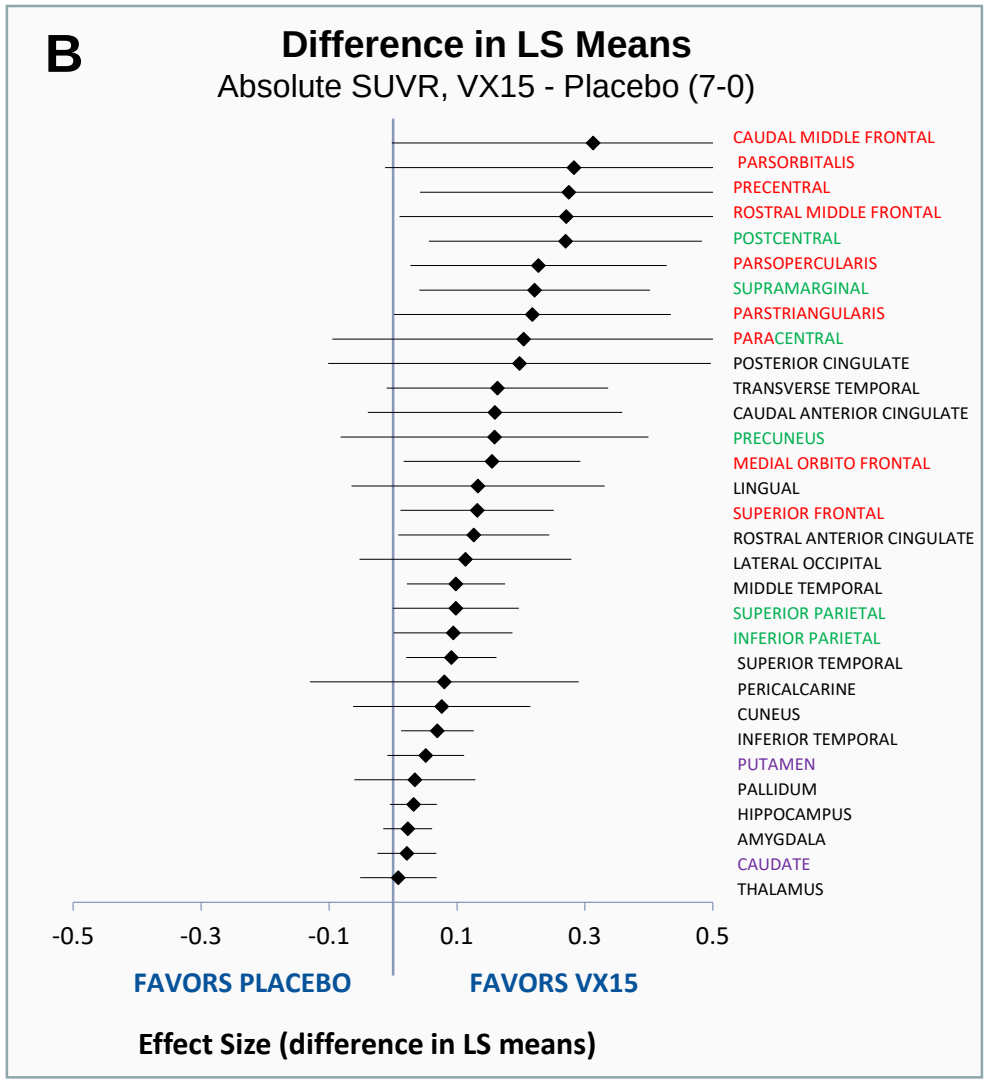


Cohort A provided important data to determine required sample size and treatment duration for potentially pivotal Cohort B study and also identified a biomarker of treatment effect

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.

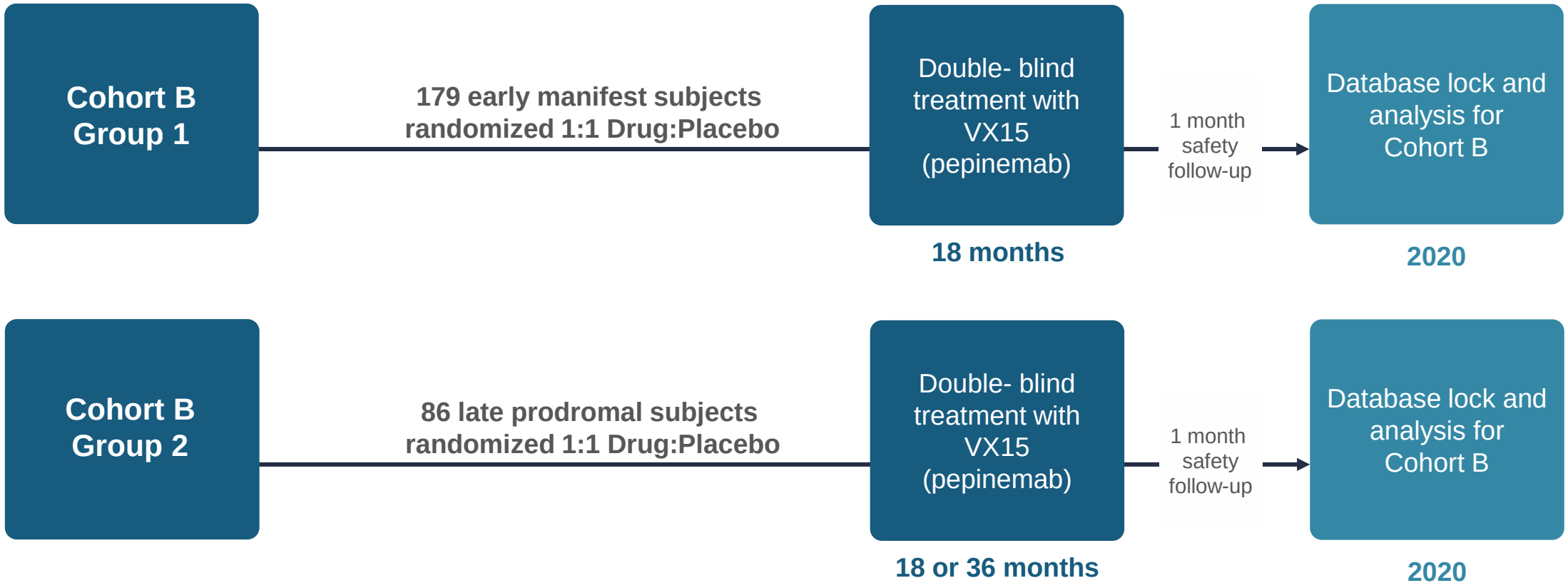
Clinical Treatment effect: FDG-PET biomarker





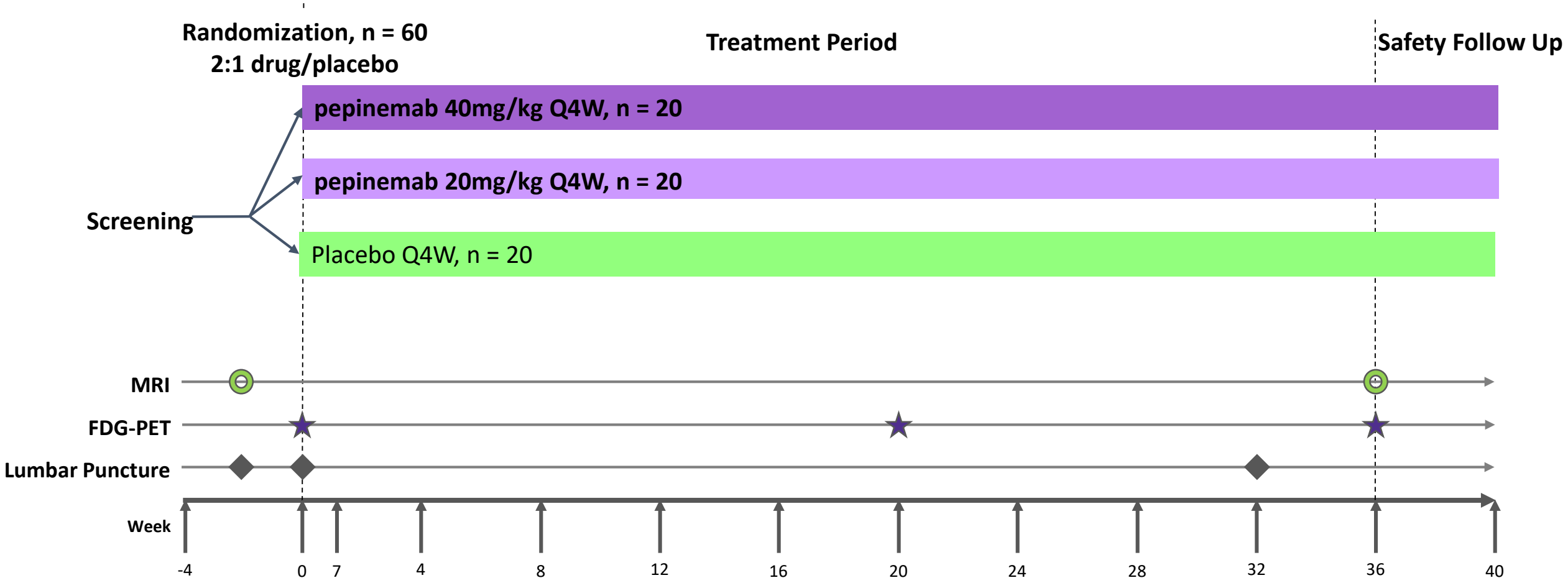
frontal lobe (red)
parietal lobe (green)

Huntington's Disease Clinical Trial Design: Cohort B



Enrollment in Cohort B was completed on December 31, 2018
Last patient last visit anticipated around July, 2020

Alzheimer's Disease Trial



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

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

Anticipated Vaccinex 2020 Milestones

Event	Timing
SUGNAL Cohort A Data in Huntington's Disease submitted for publication	January 2020
Near **Topline Clinical Data for Pepinemab in Combination with Avelumab in NSCLC**	February 2020
Interim analysis of combination Window-of-Opportunity studies at Emory University (Melanoma, HNSCC, colorectal and pancreatic cancer)	ASCO 2020
Estimated enrollment of first patient in Alzheimer's disease phase1 study	July 2020
Estimated **Topline Clinical Data for SIGNAL Cohort B study in Huntington's Disease**	October 2020
Secondary Equity Offering	Q3 2020

Vaccinex Corporation

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

VCNX (NASDAQ)	
52 week High/Low	$12.23/$3.77
Recent Close	$7.50 (30Jan2020)
Shares outstanding	16.4M
Market cap	$123 million
Headquarters	Rochester, NY
Employees	45
IPO (proceeds $40M)	August 2018
PIPE (proceeds $21.3M)	July 2019/Jan 2020
Underwriters and Analysts	Oppenheimer, BTIG, Ladenburg