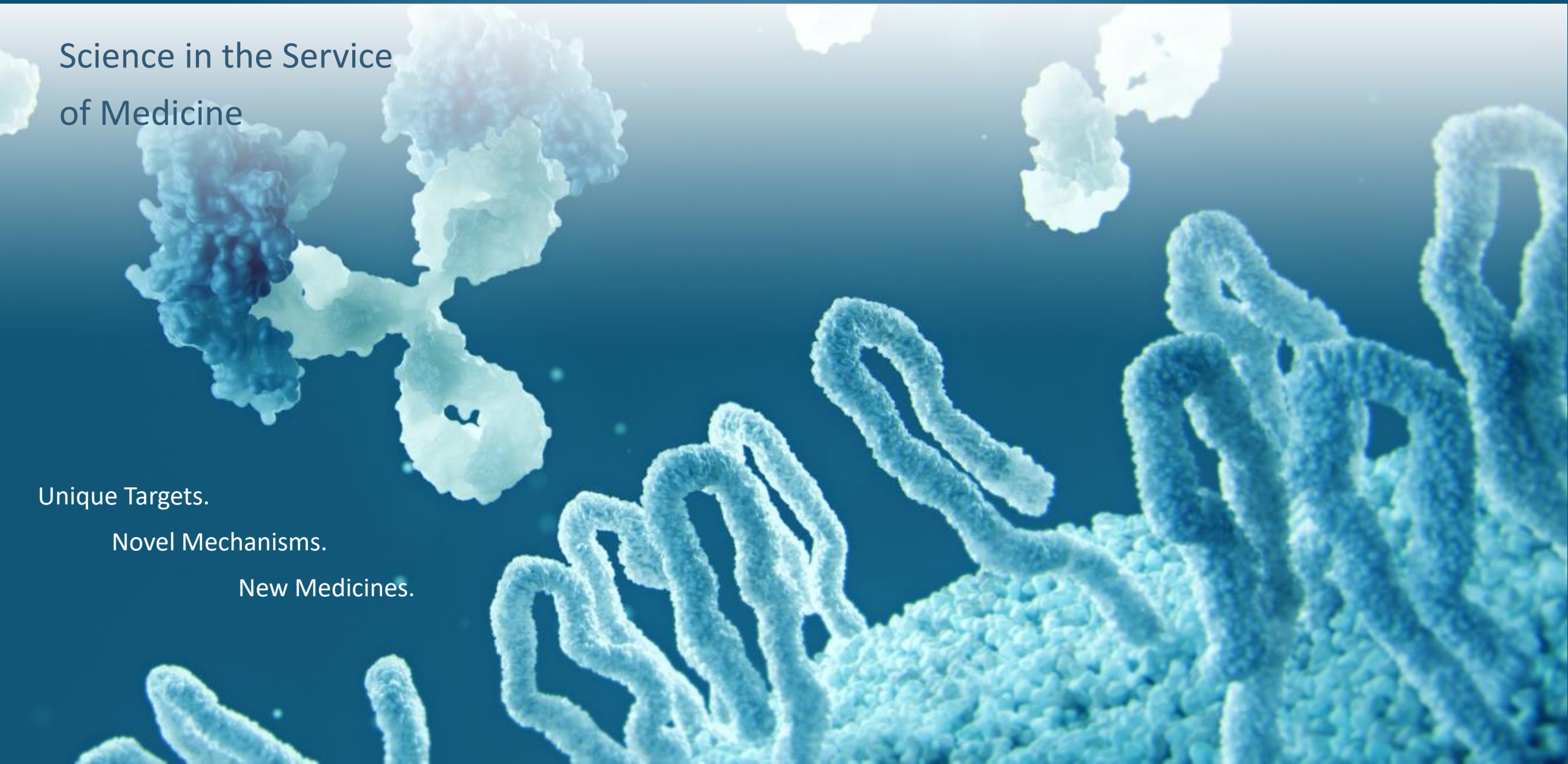
VX15 (pepinemab) Antibody Treatment for Cancer and Neurodegenerative Disease



Science in the Service of Medicine

Unique Targets.

Novel Mechanisms.

New Medicines.

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.

Vaccinex, Inc Corporate Summary

Vaccinex, Inc. (Nasdaq: VCNX) is a publicly traded clinical-stage biotechnology company engaged in the discovery and development of targeted biotherapeutics to treat serious diseases with unmet medical needs, including neurodegenerative diseases, cancer and autoimmune disorders.

Novel mechanistic approach	Lead program, **VX15 (pepinemab),** is a humanized monoclonal antibody that binds to and blocks a unique target, **Semaphorin 4D (SEMA4D)** an important biological effector that inhibits immune activity in tumors and promotes chronic inflammation in brain during slowly progressive neurodegenerative diseases including Huntington's and Alzheimer's.

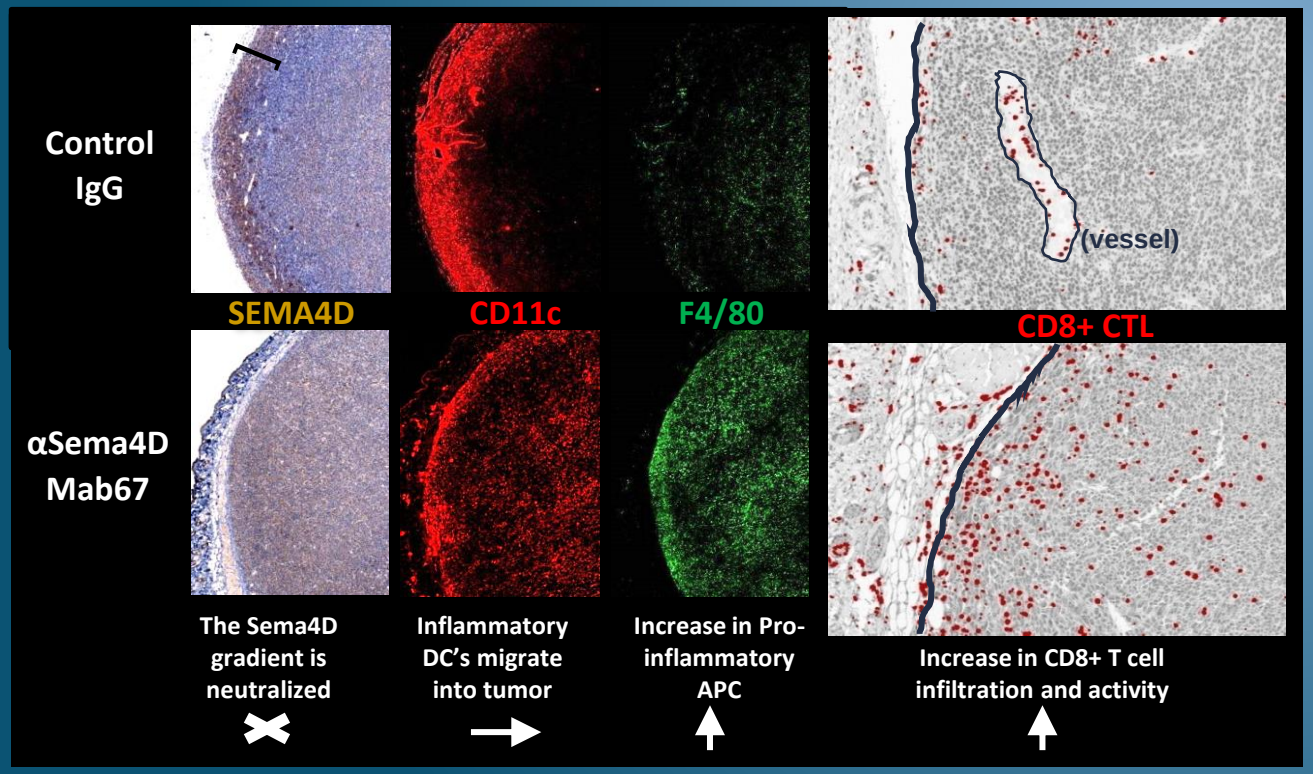
Advanced clinical programs for cancer	• **NSCLC and HNSCC**–completed Phase 1/2 study of pepinemab in combination with avelumab (EMD Serono) in Non-Small Cell Lung Cancer (NSCLC) and currently initiating new proof of concept trial in combination with Keytruda (Merck) in Head & Neck Cancer (HNSCC)
	  • Combination appears to increase objective responses to checkpoint inhibitor in PD-L1 negative and low NSCLC by a factor of 2 or more
	  • Pepinemab alters tumor microenvironment by inceasingCD8+ cytotoxic T cells and reducing Myeloid Derived Suppressor Cells (MDSC)
	  • HNSCC is of special importance because SEMA4D is highly overexpressed and has been shown to induce high levels of MDSC

Advanced clinical programs for neurodegenerative disease	• **Huntington's and Alzheimer's Disease (HD ands AD)**– completed mid-stage phase 2 clinical trial with encouraging results indicating:
	  • Cognitive benefit to patients
	  • Reduced brain atrophy and loss of metabolic activity in key brain regions
	  • Currently exploring pharma collaboration in HD and AD

Proprietary drug discovery platform for multi-pass membrane receptors	• Active collaborations with two major pharma and multiple biotech partners to employ unique capability for selection of high value antibodies against hard to target multi-pass membrane receptors • Sustainable engine for value creation through pipeline expansion and strategic collaborations

Preclinical *In vivo* efficacy of VX15 (anti-SEMA4D antibody)

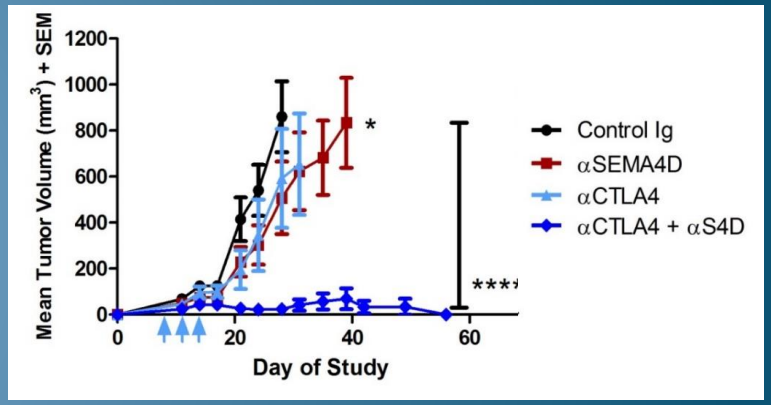
SEMA4D antibody neutralizes the SEMA4D barrier at the tumor boundary. This effectively "opens the gates" of the tumor to the immune system which increases T cell infiltration and reduces immune suppression.



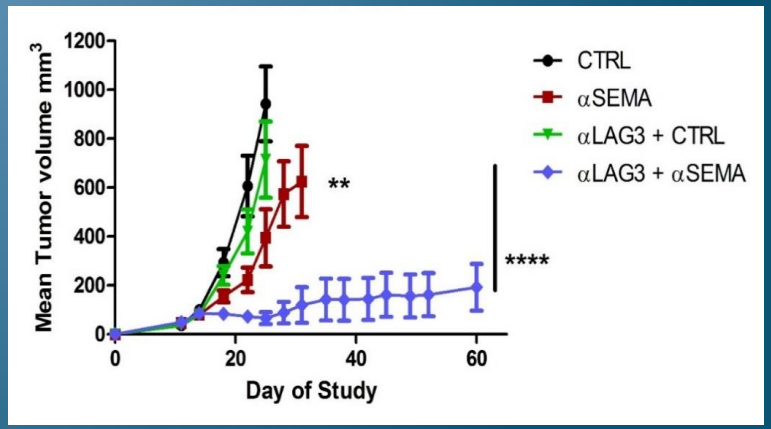
Preclinical Model - Colon26

Evans EE et al. Cancer Immunol Research 2015;3(6): 689-701

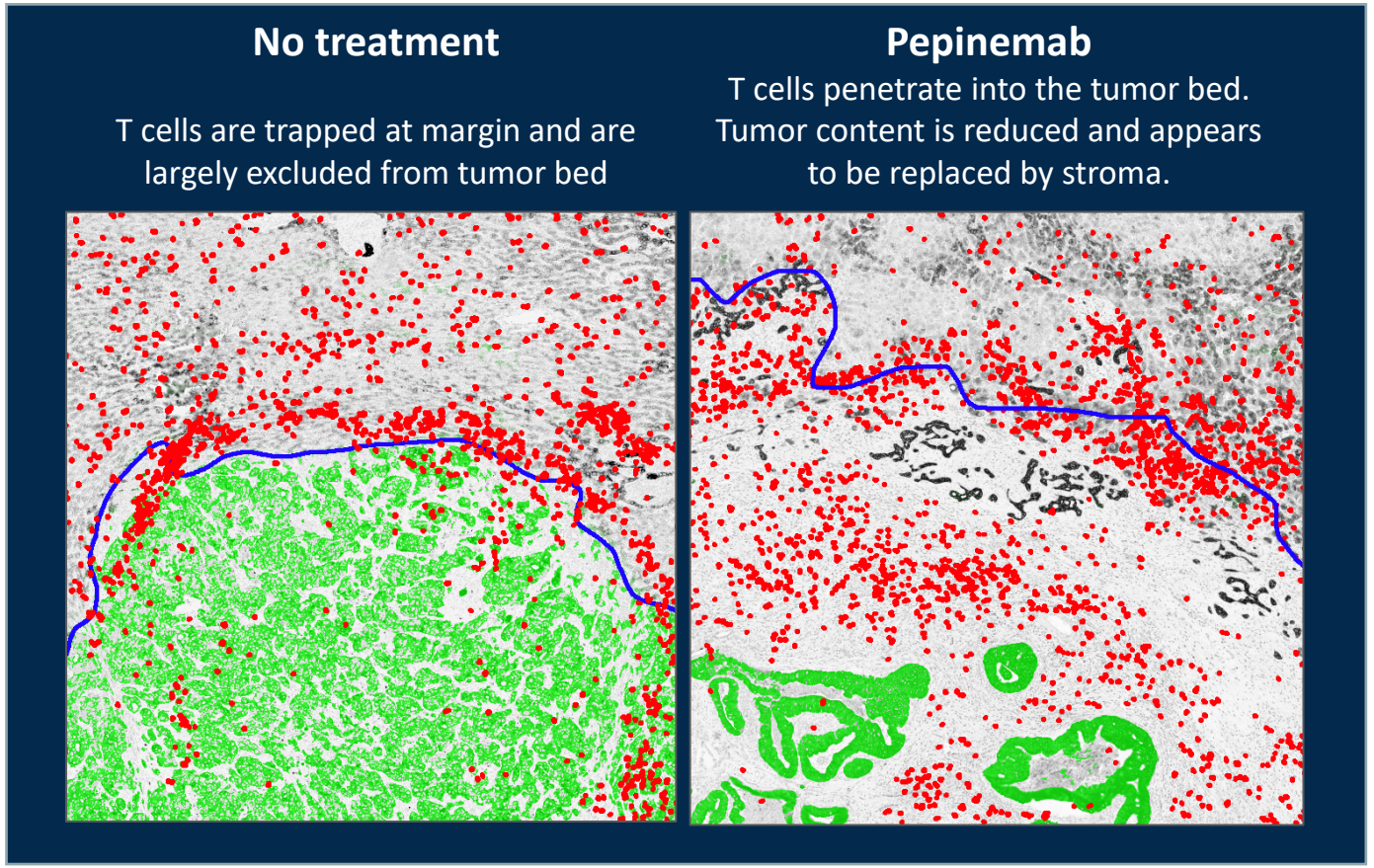
anti-CTLA-4 Combination: Colon26



anti-LAG3 Combination: Colon26



Pepinemab rapidly promotes T cell infiltration into tumor bed



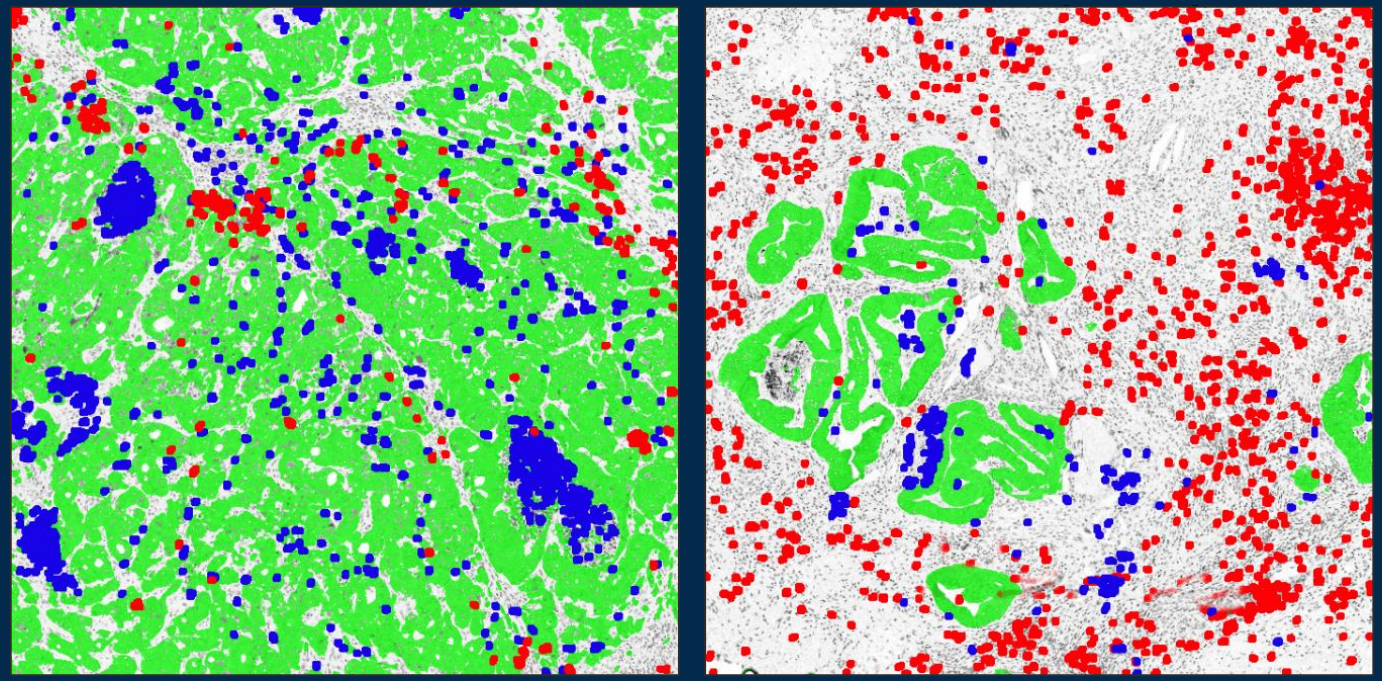
Patients received neoadjuvant chemotherapy before immunotherapy and surgery

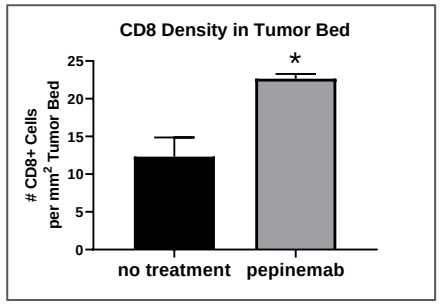
MSS Colorectal cancer metastasis to liver – neoadjuvant/"window of opportunity" study
Winship Cancer Institute, Emory University

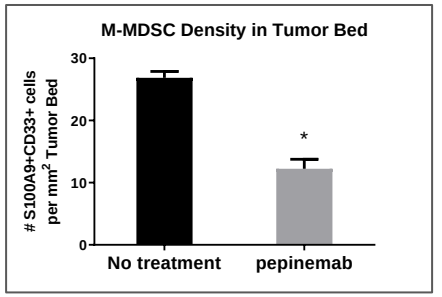
Increased ratio of cytotoxic T cells: myeloid derived suppressor cells following treatment with pepinemab

No treatment
Low CD8+ T cells
High Tumor content and MDSC

Pepinemab
High CD8+ T cells
Low tumor content and MDSC







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

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

Patients received neoadjuvant chemotherapy before immunotherapy and surgery

MSS Colorectal cancer metastasis to liver – neoadjuvant/"window of opportunity" study
Winship Cancer Institute, Emory University

Phase 1b/2 CLASSICAL-Lung Combination Trial of Pepinemab with Avelumab in patient with advanced NSCLC

Sponsored by: VACCINEX

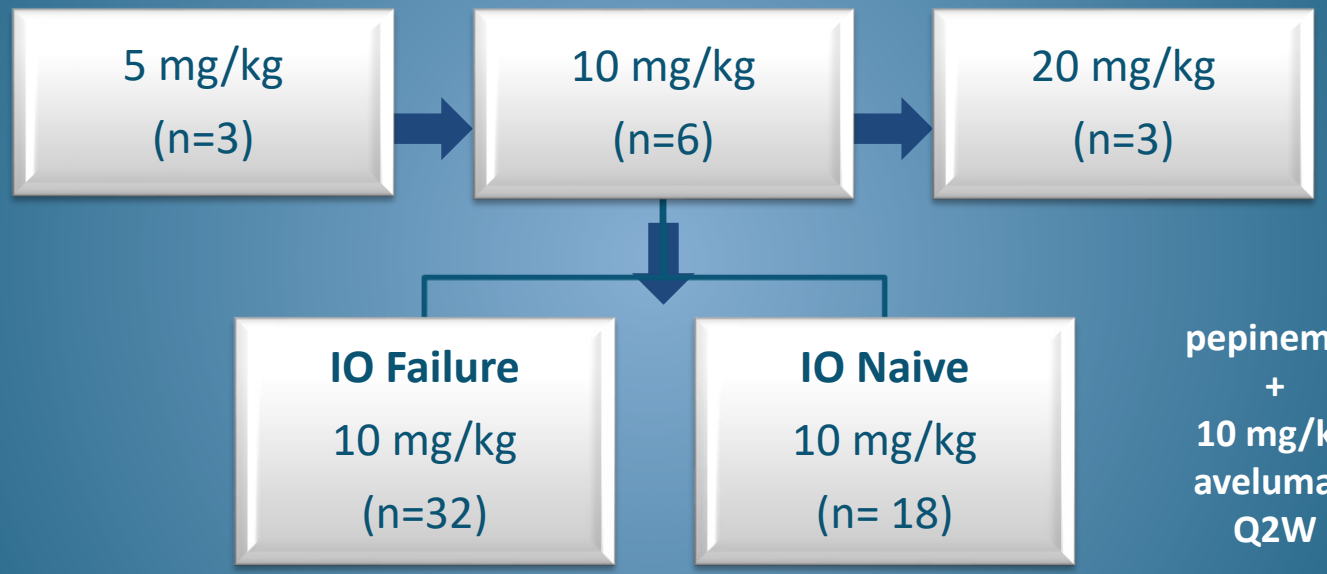
Co-funded by: MERCK

Phase 1b

Dose Escalation IO Naïve (n=12)

Phase 2

Dose Expansion (n=50)

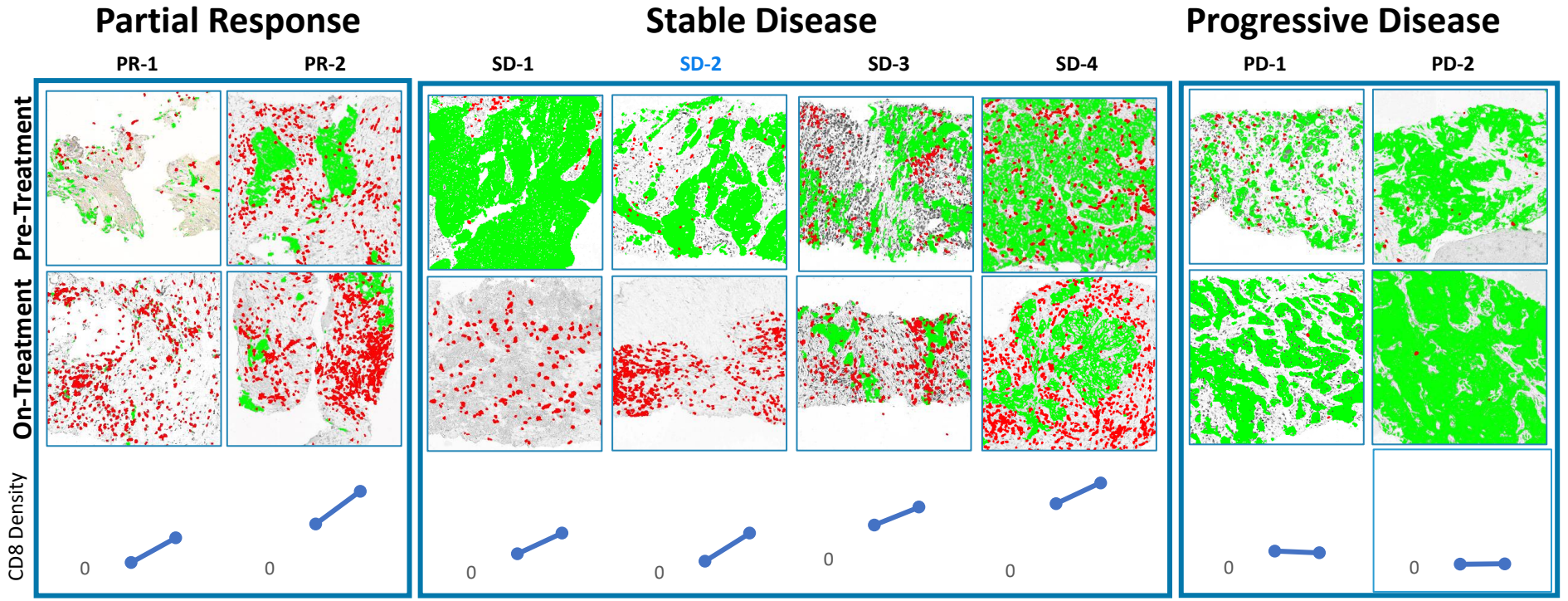


pepinemab + 10 mg/kg avelumab Q2W

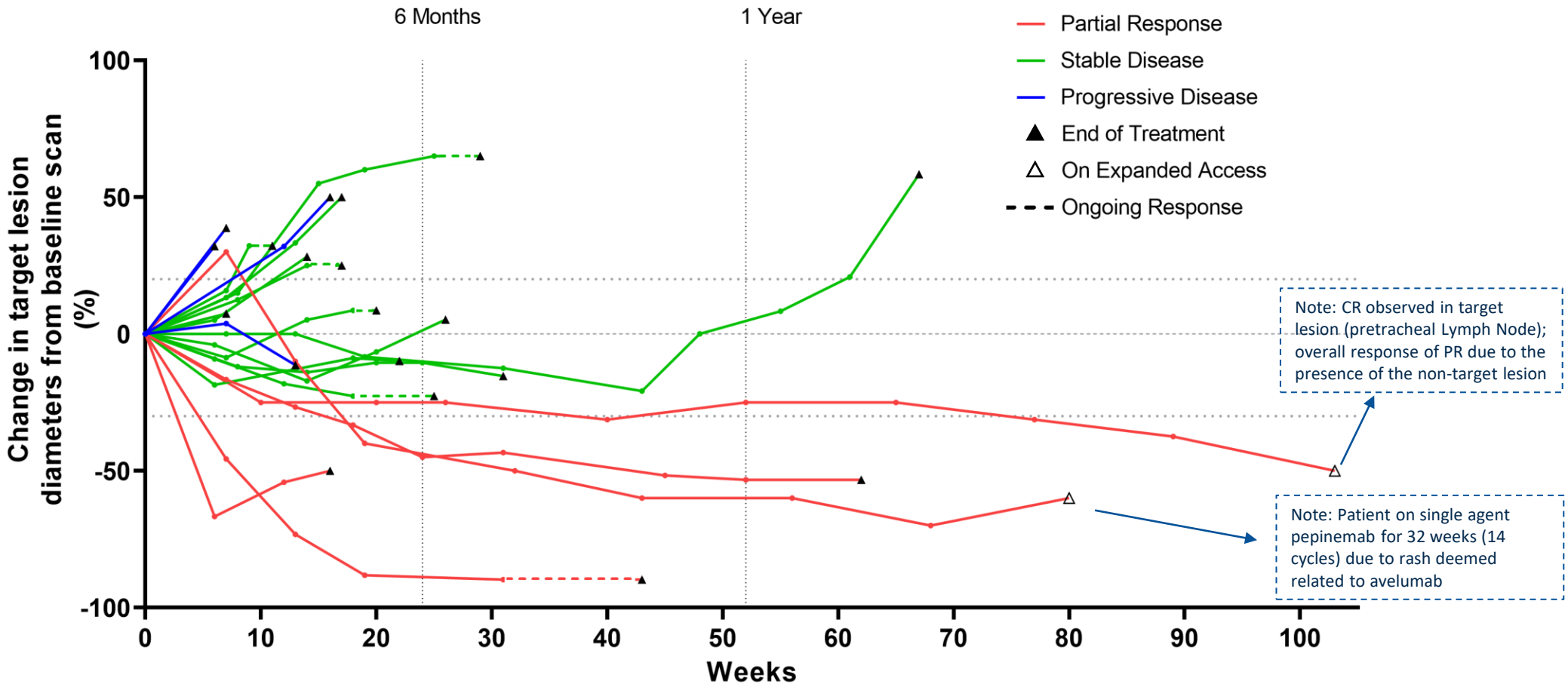
Study Objectives

- 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

Phase 1b/2 CLASSICAL- Increase in CD8+ T cell infiltration, decrease in tumor burden



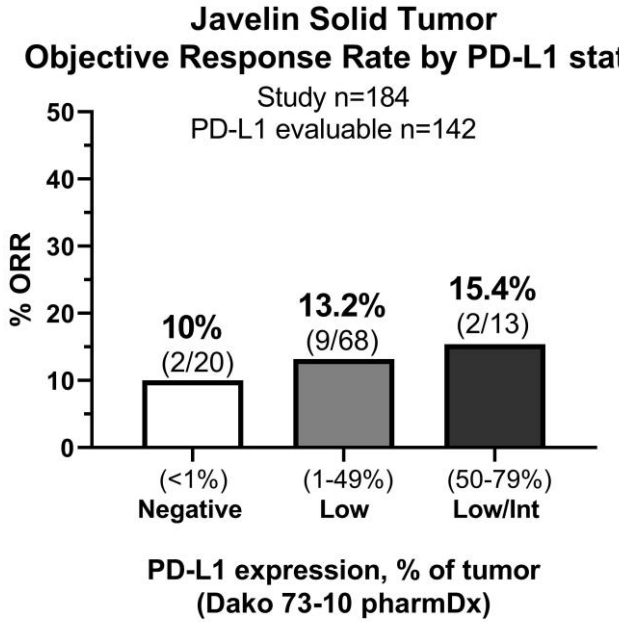
Phase 1b/2 CLASSICAL-Lung Percent Change in Target Lesion Diameter by weeks (IO Naïve)

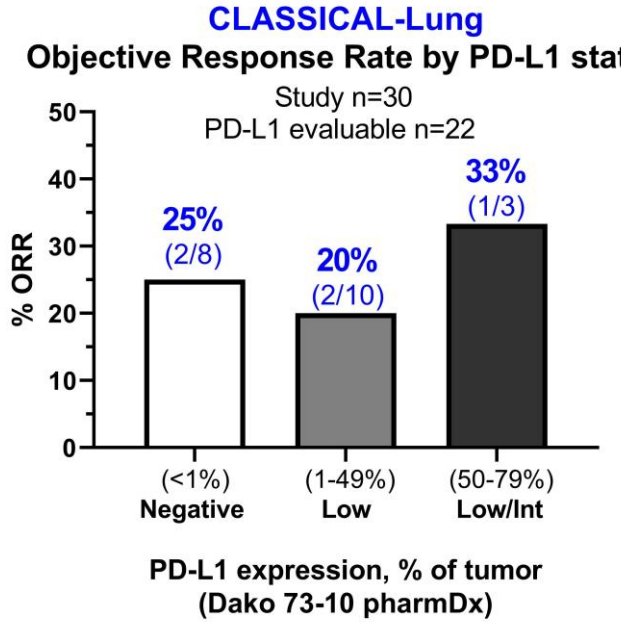


Lines are color-coded based on best overall response

Phase 1b/2 CLASSICAL-Lung Objective Response Rate by PDL-1 Status (IO Naïve)

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





1. Calculated from data published in:

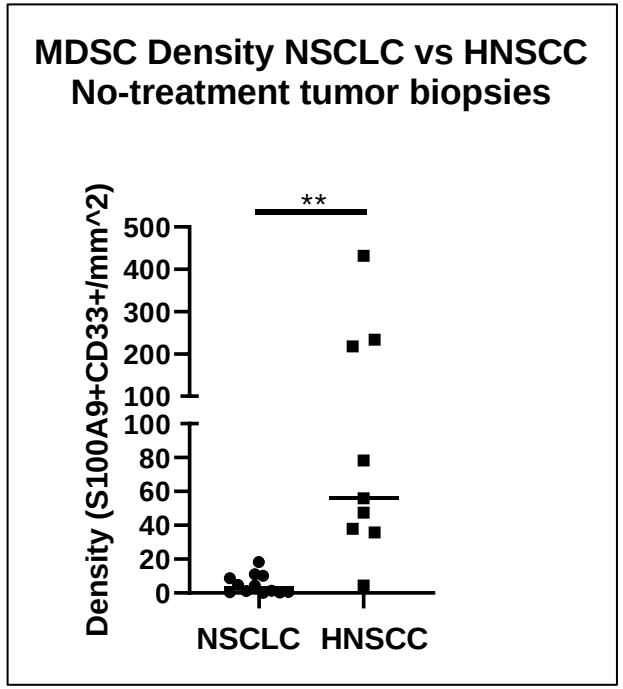
Gulley JL, Rajan A, Spigel DR, et al. Avelumab for patients with previously treated metastatic or recurrent non-small-cell lung cancer (JAVELIN Solid Tumor): dose-expansion cohort of a multicentre, open-label, phase 1b trial. *Lancet Oncol* 2017; published online March 31. http://dx.doi.org/10.1016/S1470-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

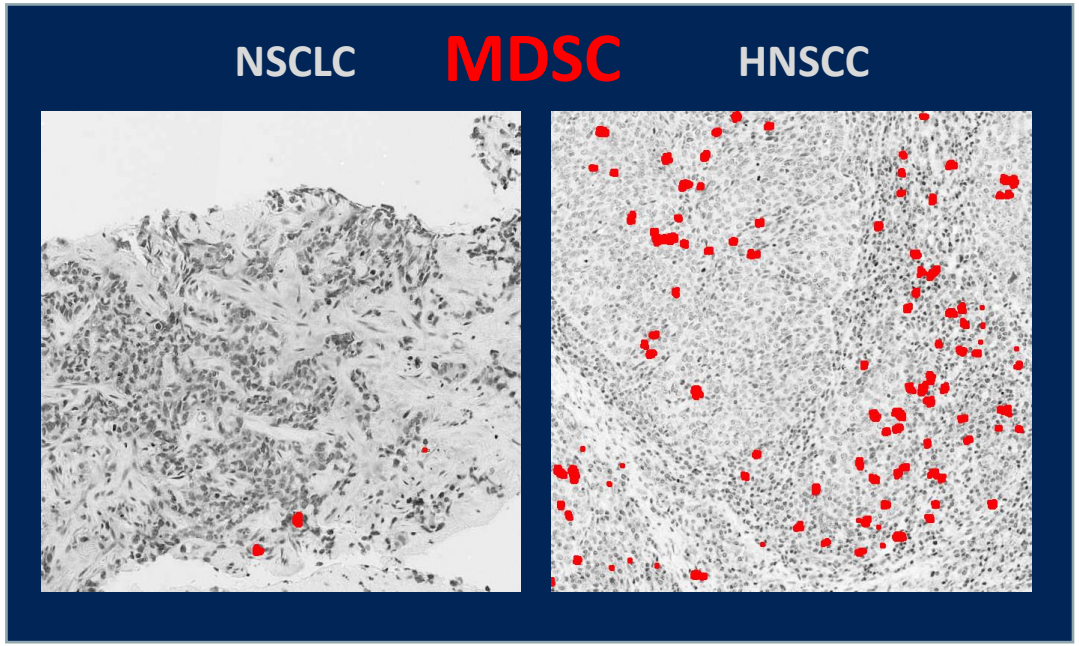
Gulley JL, Rajan A, Spigel DR, et al. Exposure Response and PD-L1 expression analysis of second-line avelumab in patients with advanced NSCLC: data from the JAVELIN Solid tumor trial: Abstract No. 9086. Presented at 53rd ASCO Annual Meeting; Jun 2-6, 2017

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.

NEXT STEPS: HNSCC

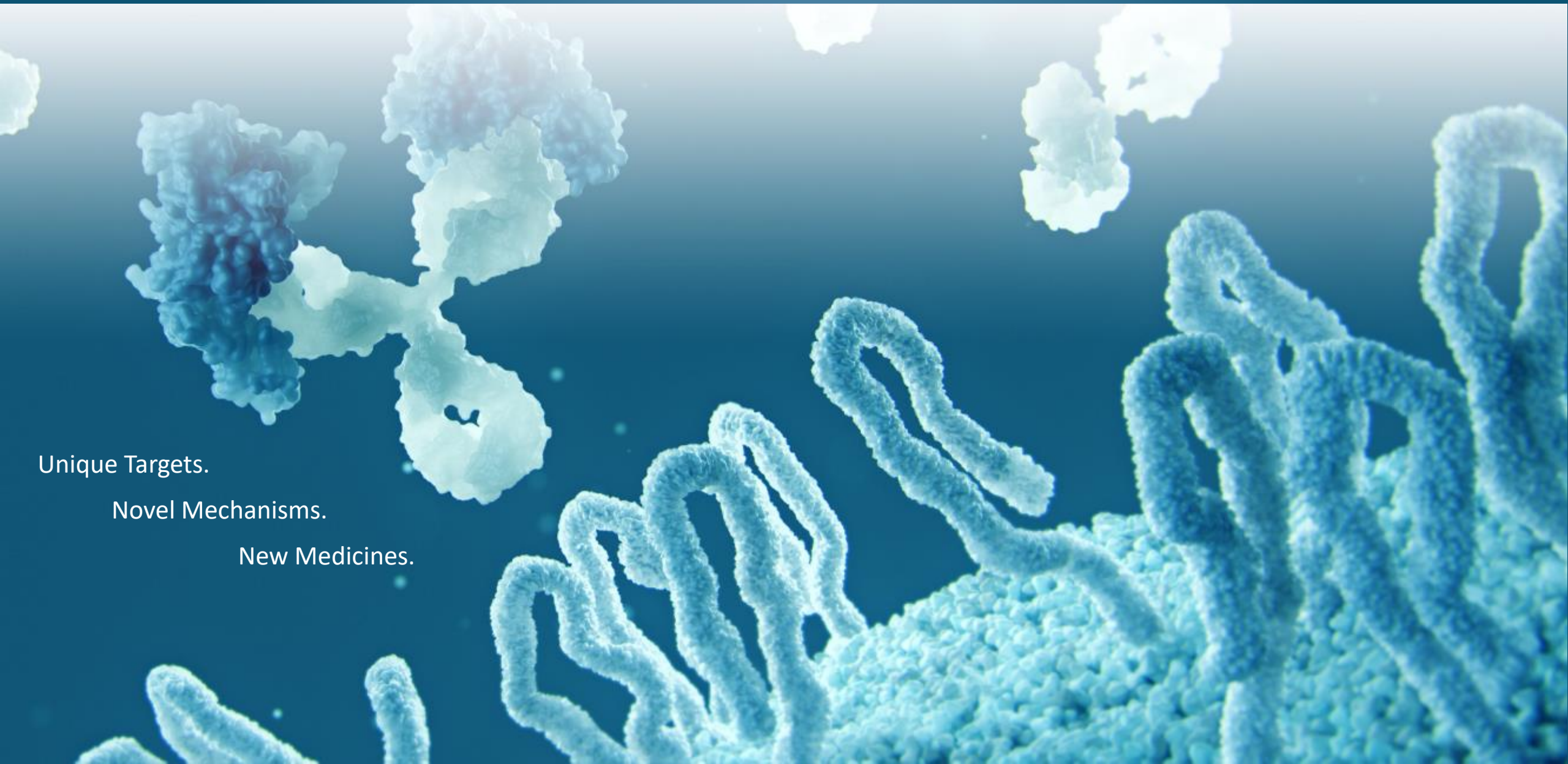
- We have entered into agreement with MSD to initiate a phase 2 study of pepinemab in combination with pembrolizumab in HNSCC, a tumor indication characterized by high levels of SEMA4D that induce and expand MDSC.
- NSCLC have low MDSC content relative to HNSCC, therefore, benefit from only 1 of 2 major pepinemab mechanisms of action.
- MDSC represent an important mechanism of resistance to immune checkpoint therapy





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

SIGNAL Phase 2 Clinical Study



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.

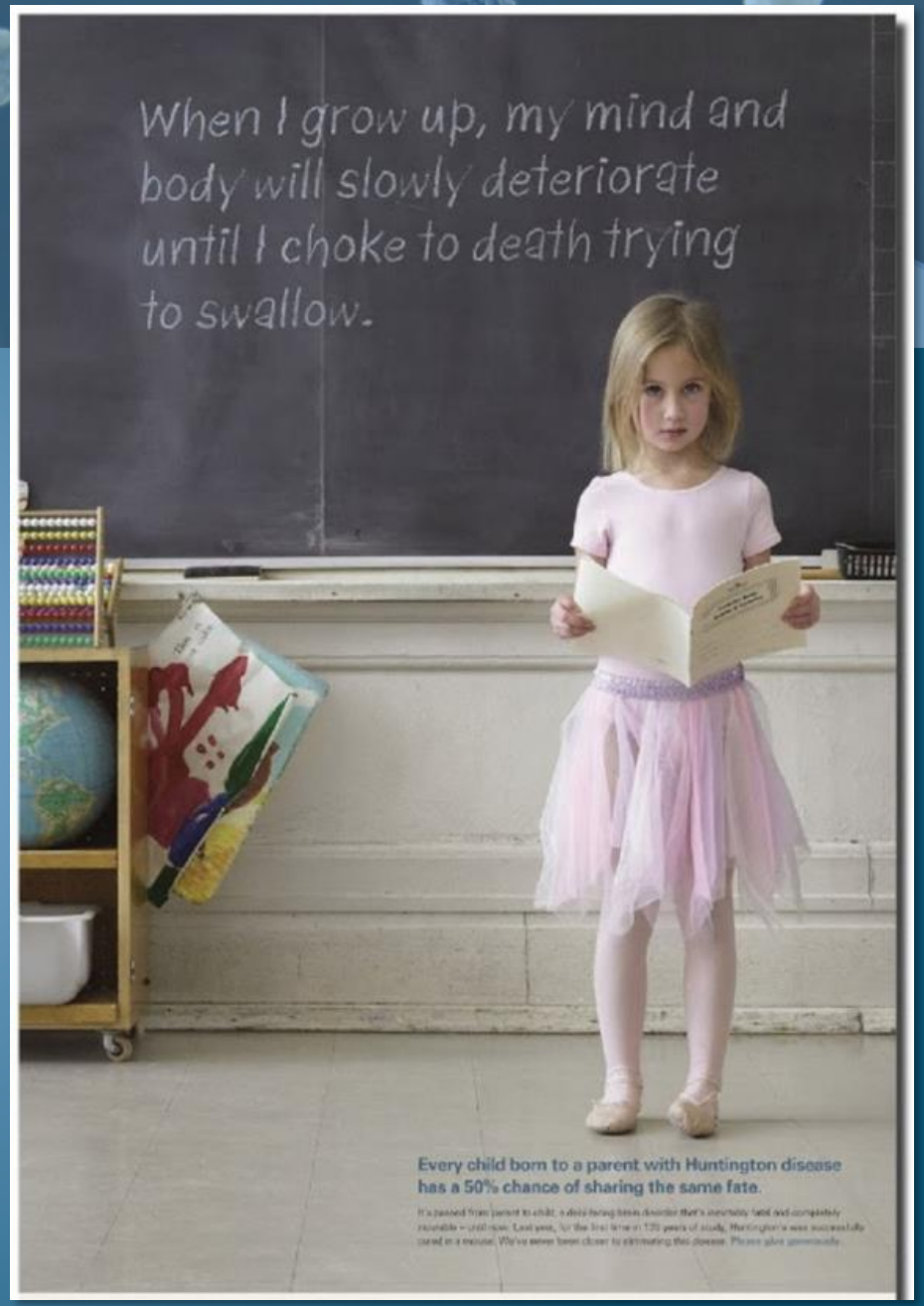


Photo credit: Huntington Society of Canada

Treatment for Huntington's disease is an unmet need

There are currently no approved treatments to alter the course of Huntington's Disease.

Estimated patient population in the US is ~40,000 individuals with manifest disease and >150,000 with pre-manifest disease (they have the inherited (prodromal) mutation).

The estimated population in the EU is similar to the US.

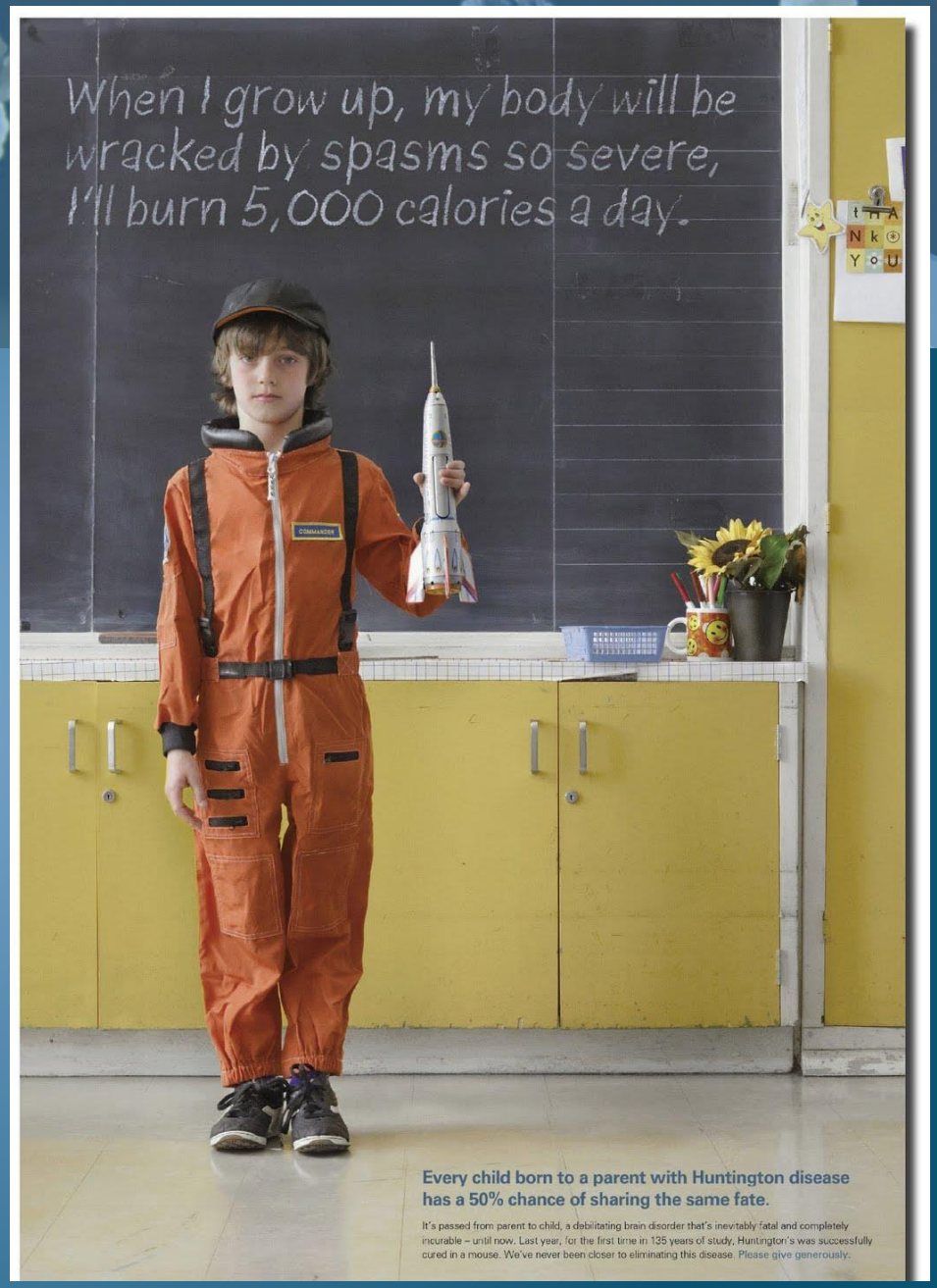
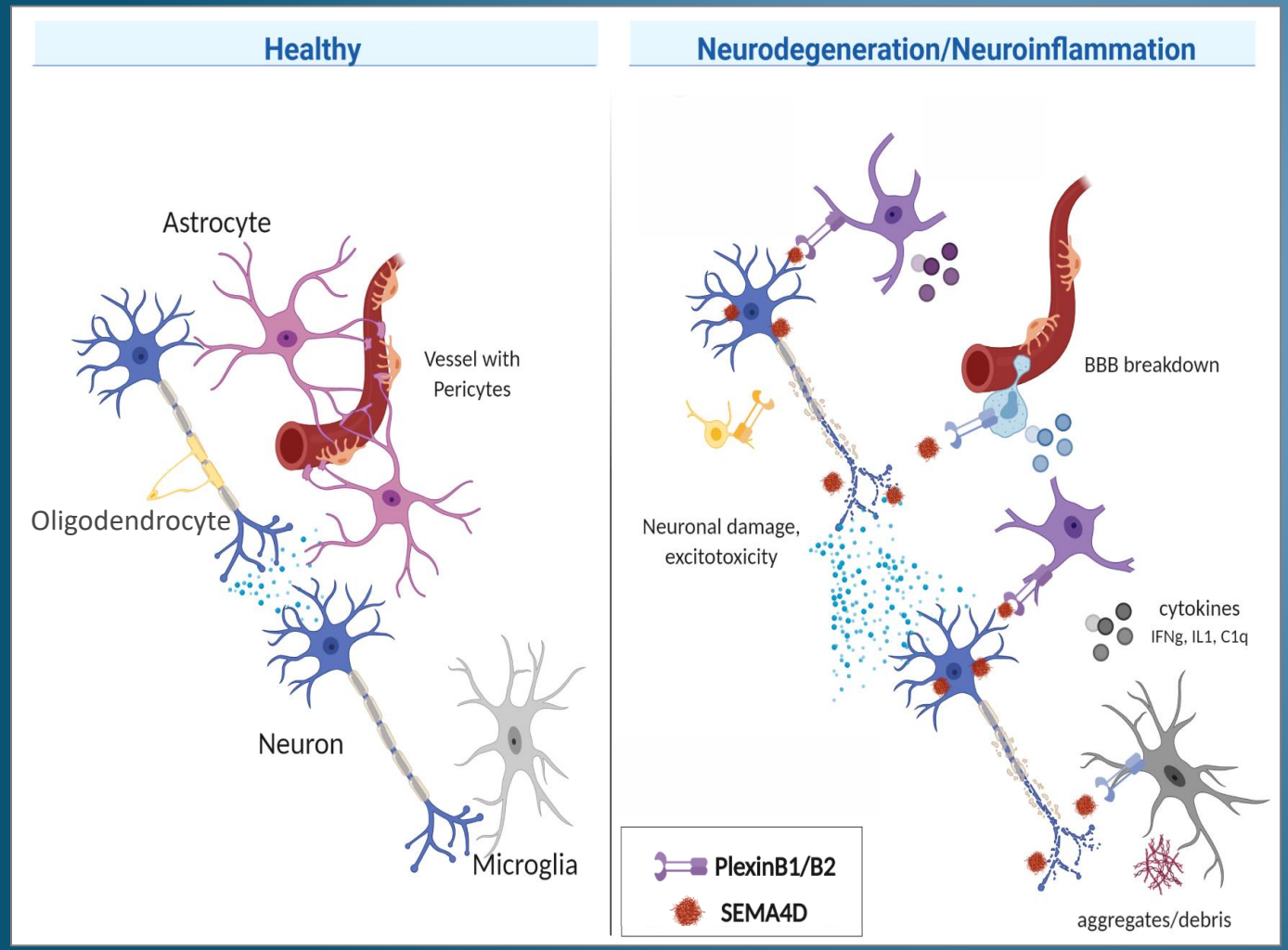


Photo credit: Huntington Society of Canada

Glial cells respond to damage in the brain



Brain cells respond to damage induced by the mutant Huntingtin Protein

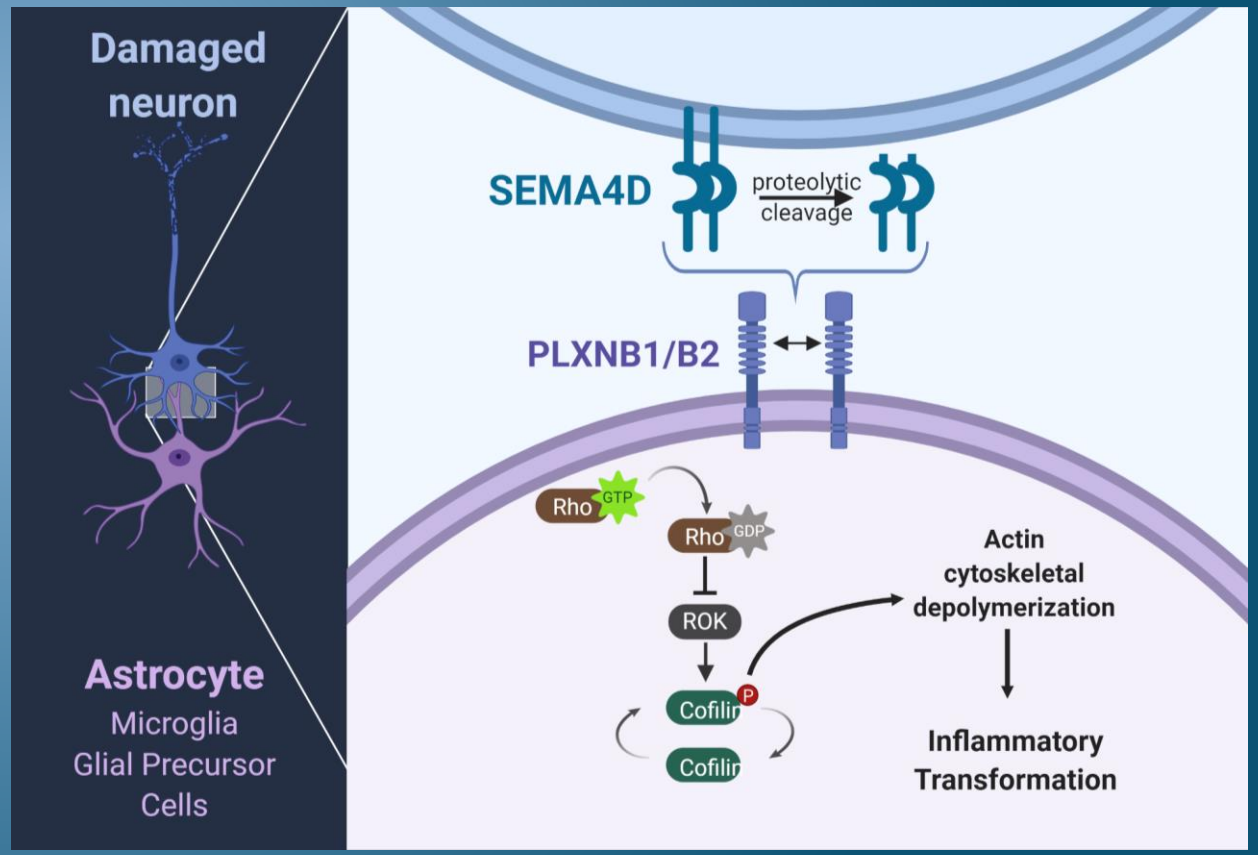
Semaphorin4D: Mechanism of Action

SEMA4D upregulated in stressed neurons signals through PLXNB1 and PLXNB2 receptors on astrocytes to trigger dissociation of polymerized F-actin and collapse of cell's cytoskeleton

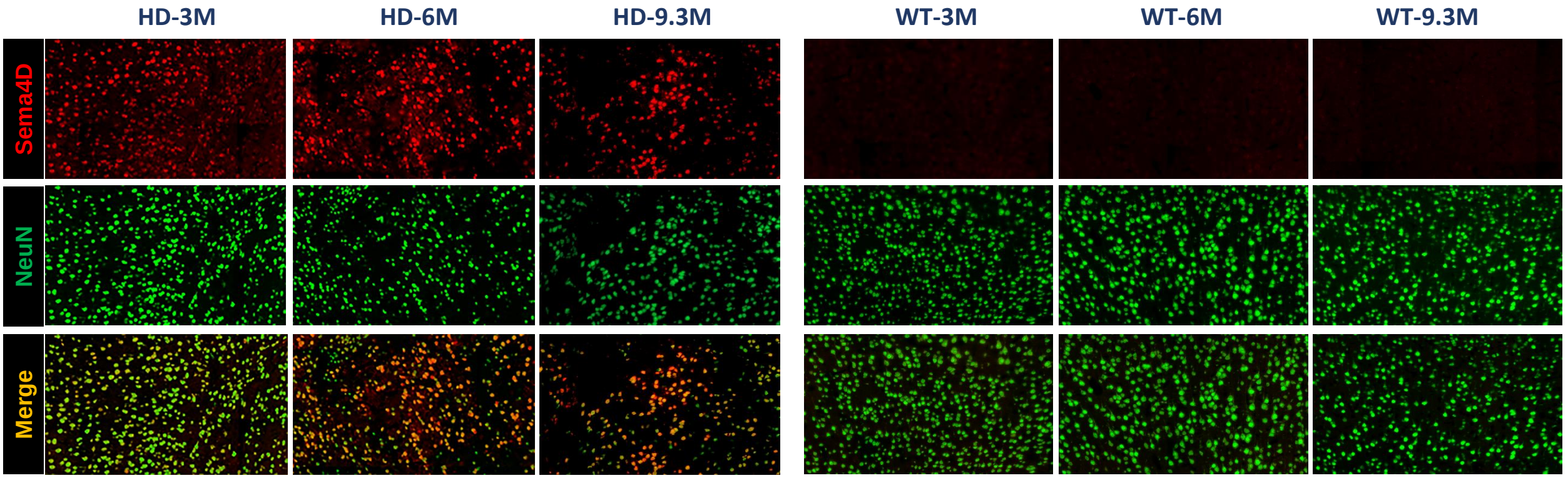
The cell cytoskeleton regulates process extensions which enable direct cell to cell interactions

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 it's signaling activity. This preserves normal astrocyte morphology and function and averts inflammatory transformation



SEMA4D is progressively upregulated in NeuN+ neurons of HD mice



SEMA4D expression is upregulated in Q175 HD transgenic mice as disease progresses, compared to low expression in wild type (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.

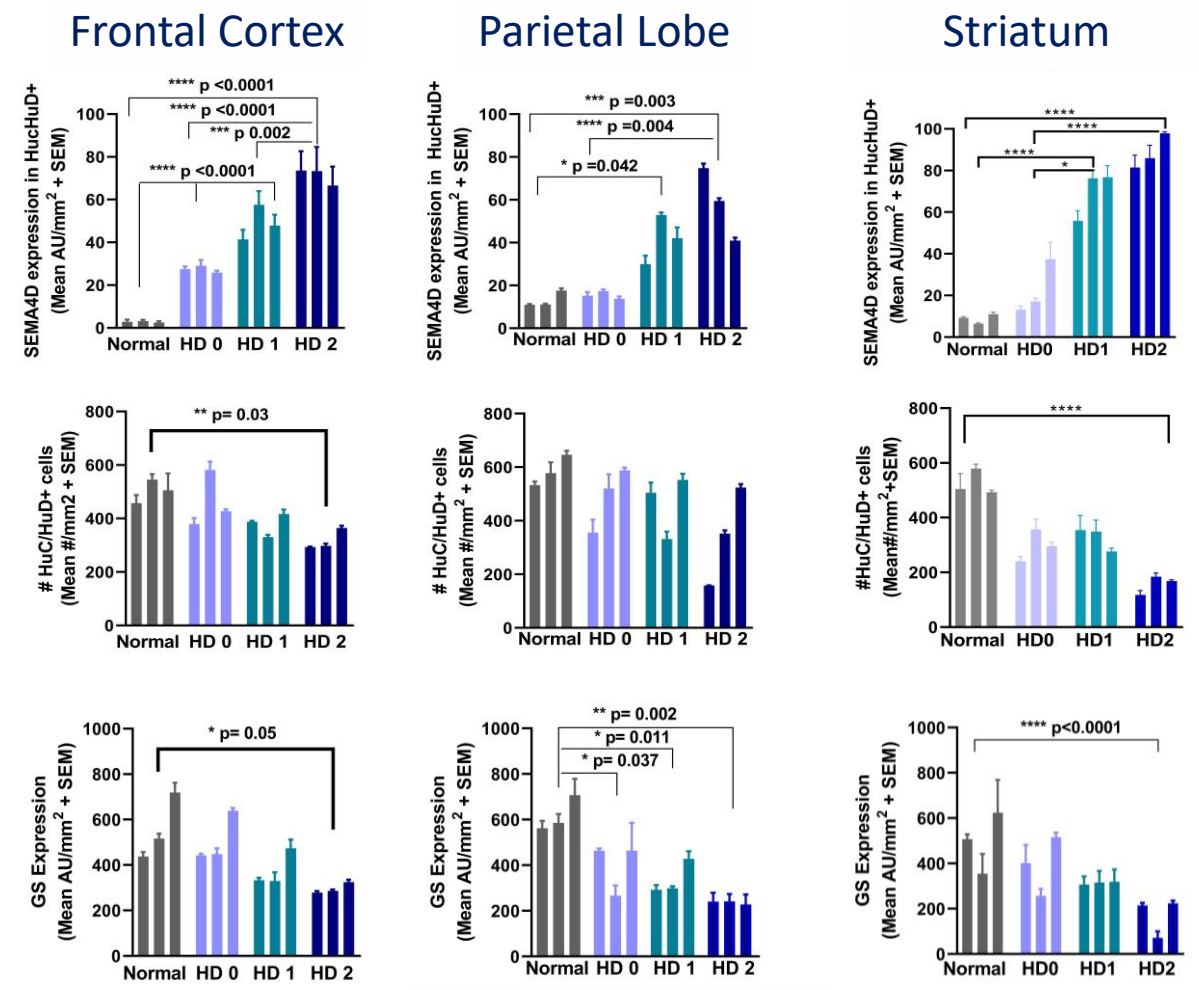
NeuN/Sema staining of retrosplenial cortex region of Q175 knock-in mouse model of HD and age-matched wild type (WT) littermate controls. Representative images are shown from analysis of 3 mice/time-point. M = months of age.

SEMA4D expression correlates with neuronal loss and astrocyte activation during HD progression

SEMA4D expression is increased

Neuronal survival is reduced

Glutamine Synthetase, a marker of normal astrocyte function, is progressively reduced

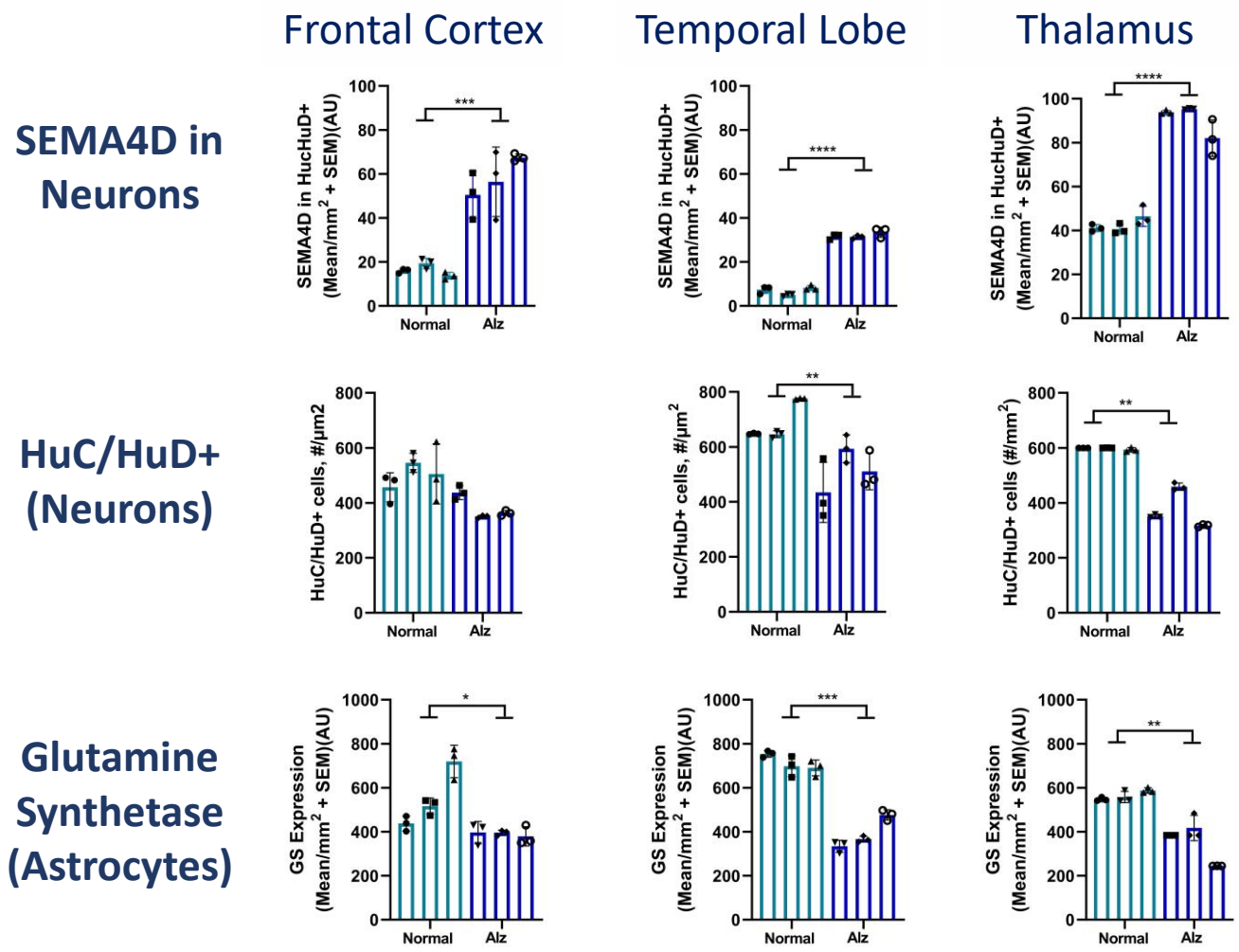


SEMA4D expression correlates with neuronal loss and astrocyte activation in Alzheimer's Disease

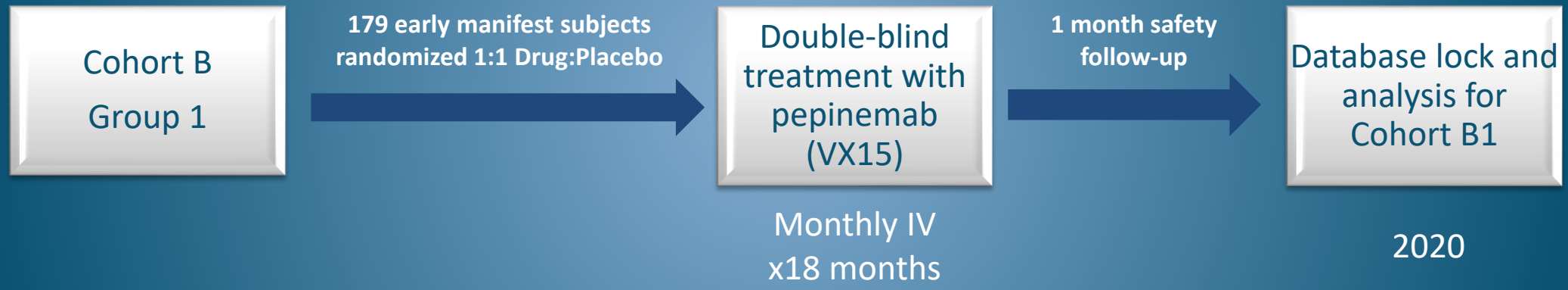
SEMA4D expression is increased

Neuronal survival is reduced

Glutamine Synthetase, a marker of normal astrocyte function, is progressively reduced



Clinical Trial Design – Group B1, Early Manifest HD



Study Objectives

- Safety and tolerability
- Clinical global impression of change (CGIC) and Cognitive Function measures
- Brain imaging measures

Abbreviated Baseline Characteristics and Safety – Cohort B1, ITT population

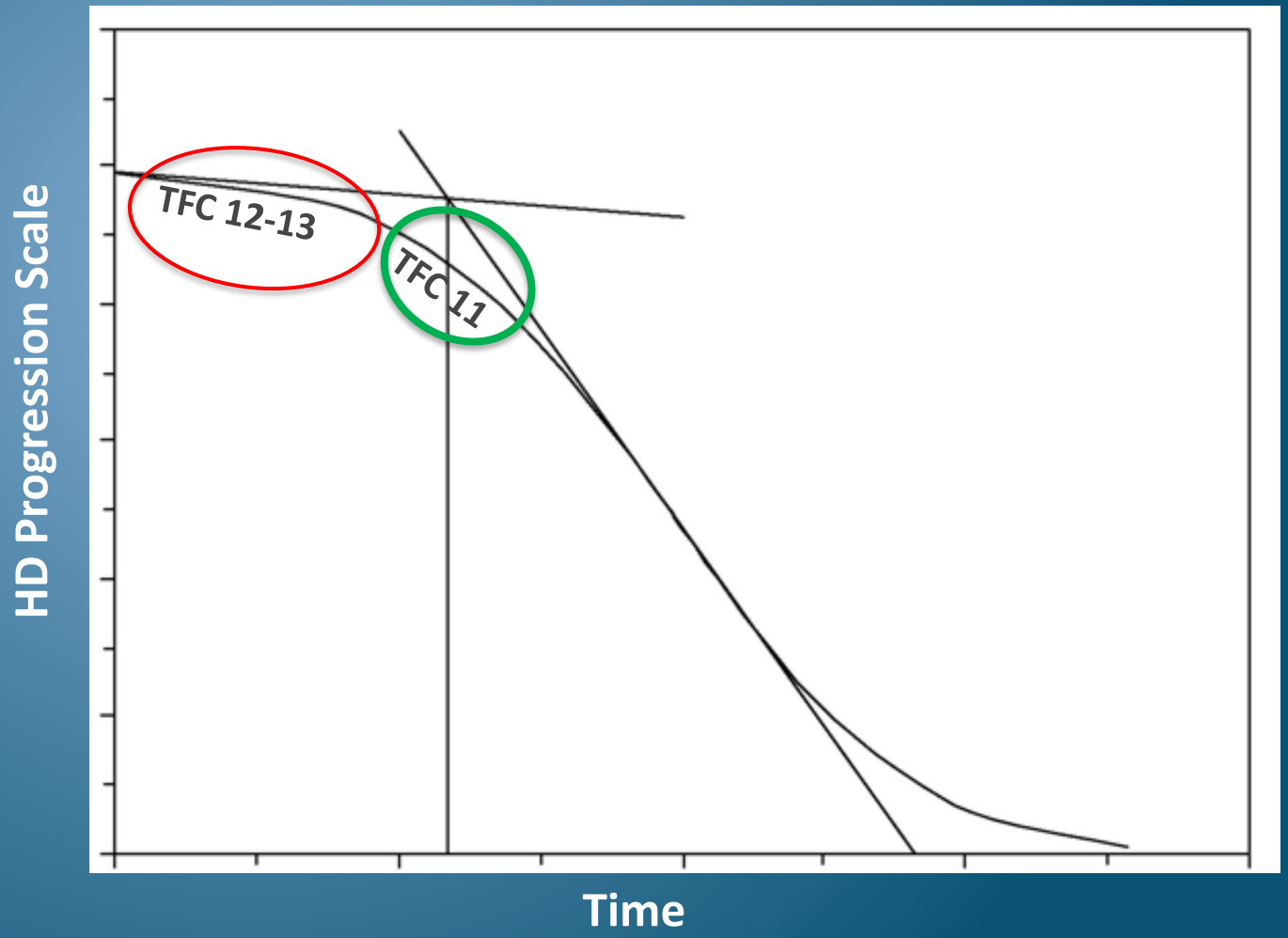
Pepinemab (PEPI) SEMA4D blocking antibody is well tolerated.

	Cohort B1 (N=179)	
	PBO (N=88) Placebo	**PEPI (N=91) Pepinemab**
Discontinued Treatment Early	**10**	**13**
Had Any SAE (*)	**8**	**4**
Had Any Grade 3+ AE (*)	**14**	**17**
CAG repeat length	44.1 (3.8)	43.5 (3.1)
CAP score (**)	470 (96)	466 (85)
UHDRS-DCL at screening, n(%)		
DCL-4, Unequivocal HD (>99% confident)	88 (100%)	91 (100%)

*pre-COVID era; **CAP score = age × (CAG repeat length – 33.66)

Total Functional Capacity (TFC) in HD disease progression

18-month change may be difficult to detect at top of TFC range

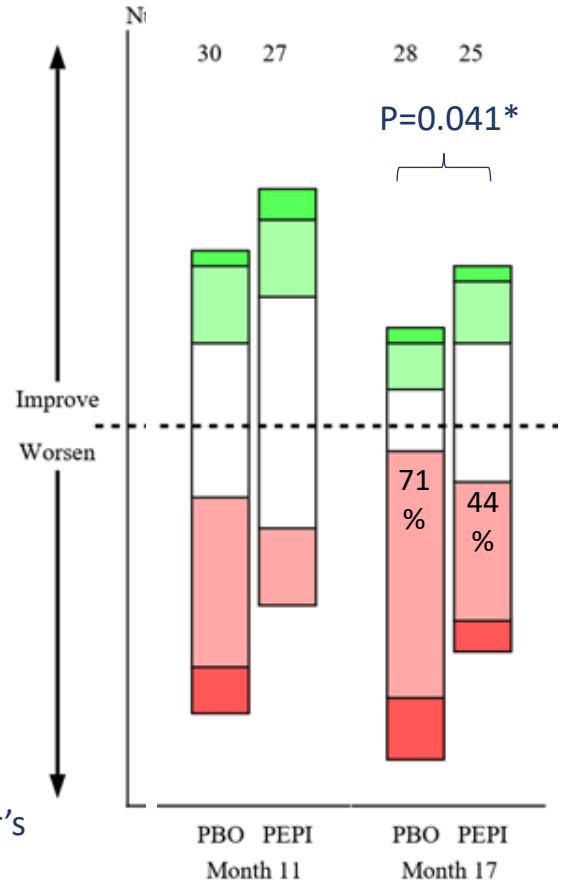


Clinical Global Impression of Change - CGIC Subgroup Analysis– Early Manifest HD

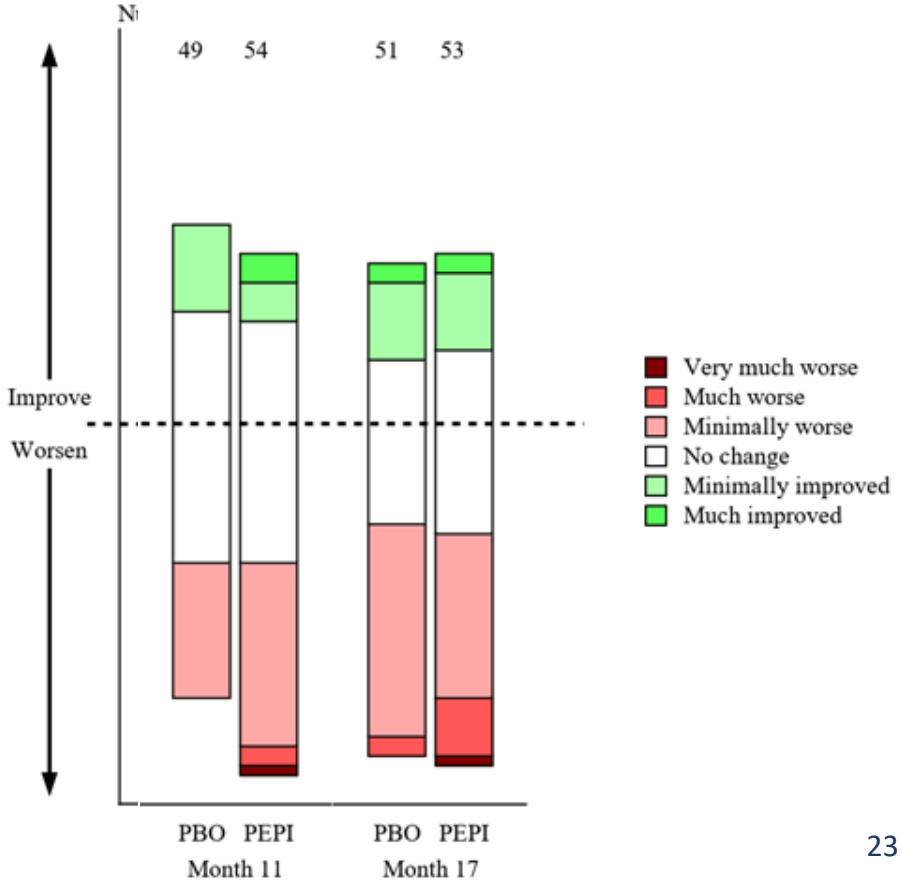
Subjects were less likely to experience decline in CGIC following treatment with pepinemab compared to placebo.

This difference was significant in subjects with more advanced disease (TFC 11).

CGIC – Subjects with Baseline UHDRS TFC 11



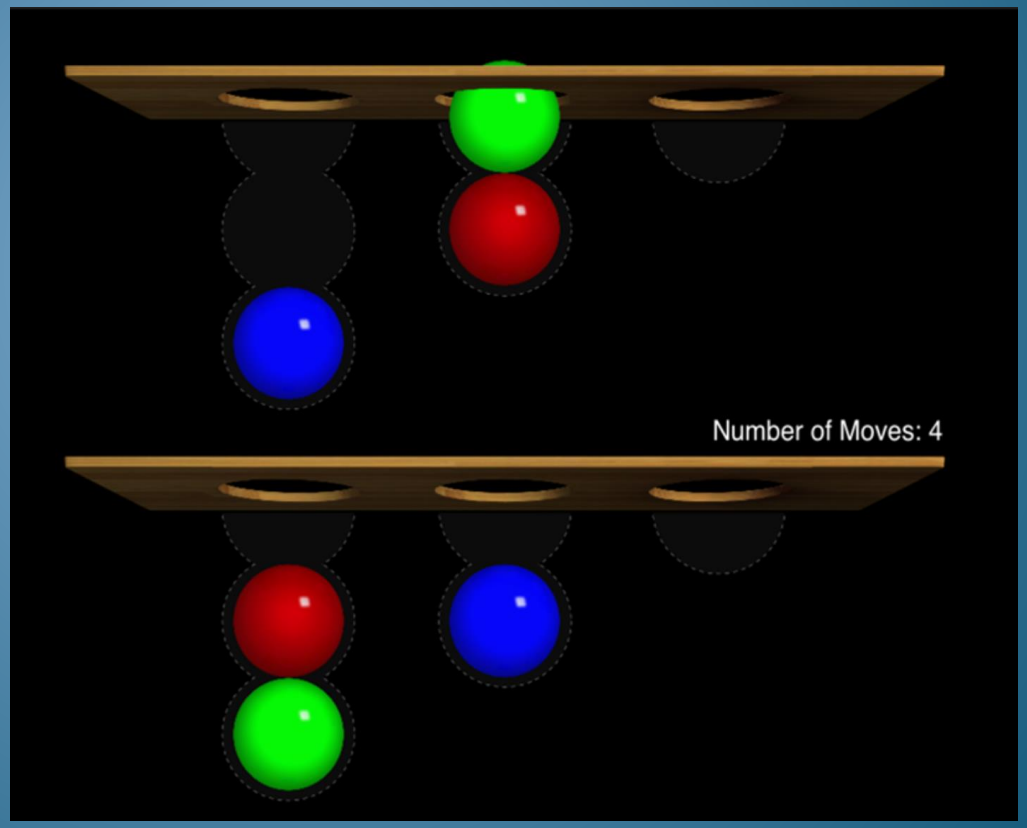
CGIC – Subjects with Baseline UHDRS TFC 12 and 13



*nominal one-sided p-value, Fisher's exact test for worsening score

Cognitive function assessments

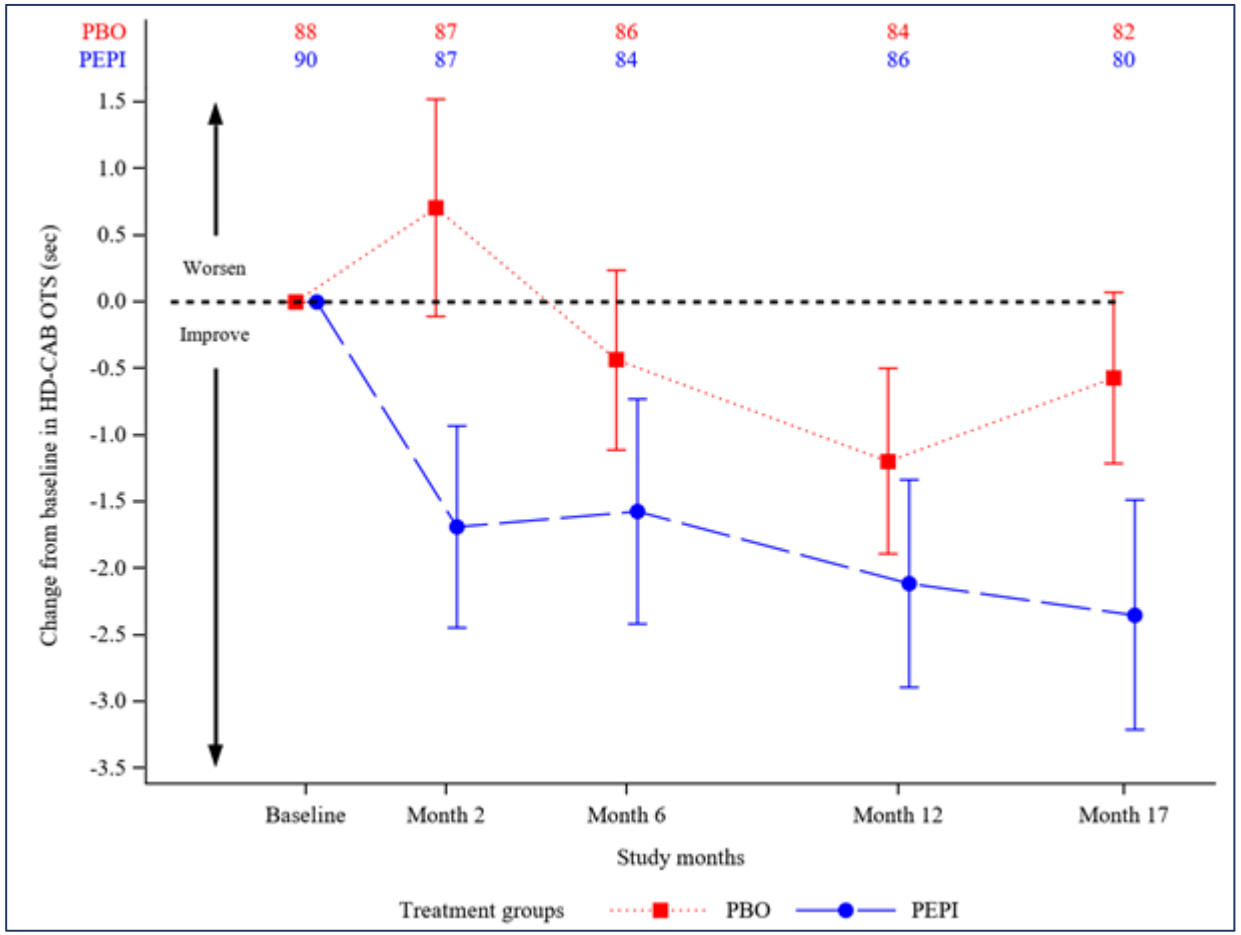
One Touch Stockings is a test of executive function that assesses both spatial planning and the working memory.



Cognitive Assessment Co-Primary 2a: Test of Planning and Memory

One Touch Stockings

Early Manifest HD



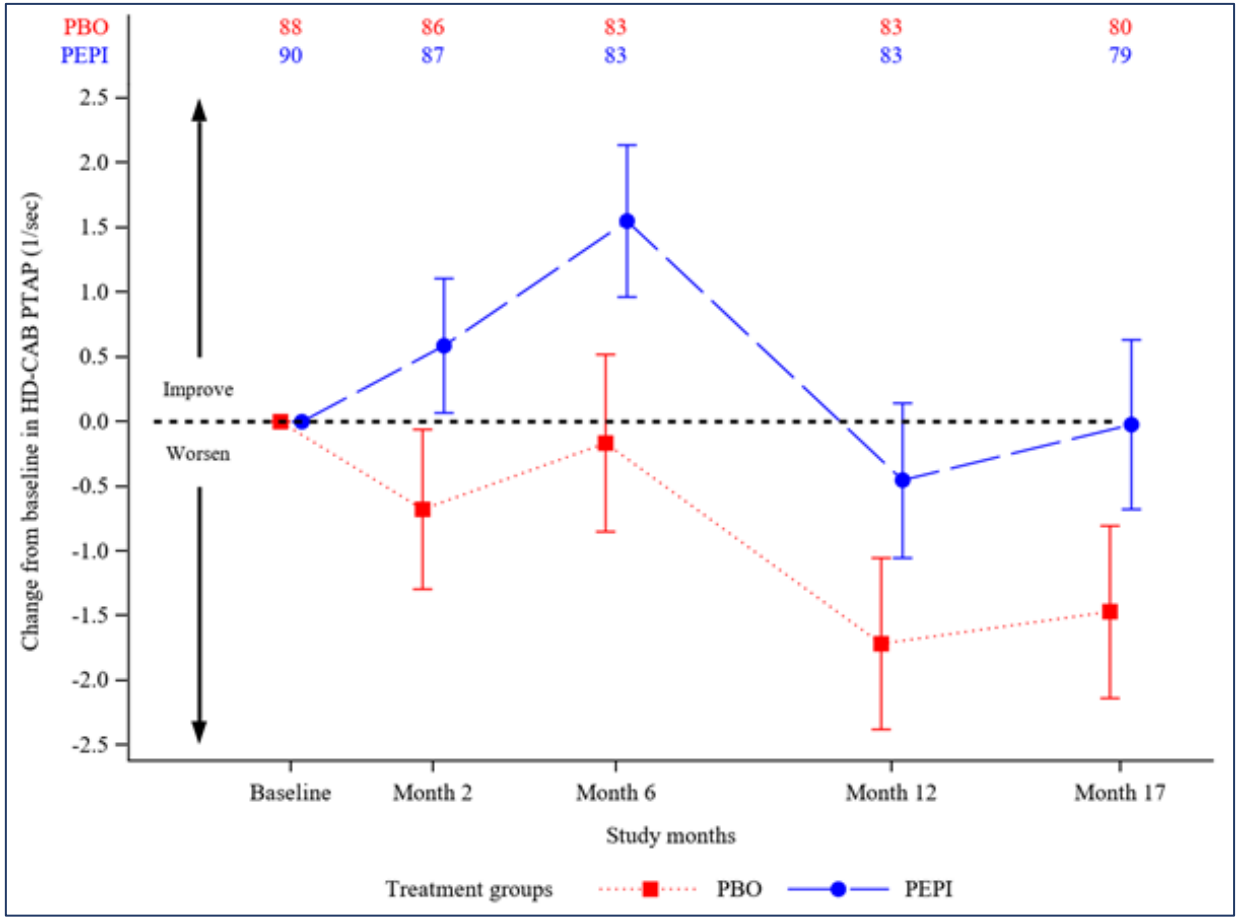
One-sided p-value	Favors PEPI	Success [Critical value]
0.028	Yes	No [0.025] [0.0125]

Difference (PEPI – PBO)
Change from Baseline at Month 17 (95% CI) = -1.98 (-4.00, 0.05)

Cognitive Assessment
Co-Primary 2a: Test of Timing and Processing Speed

Paced Finger Tapping Task

Early Manifest HD



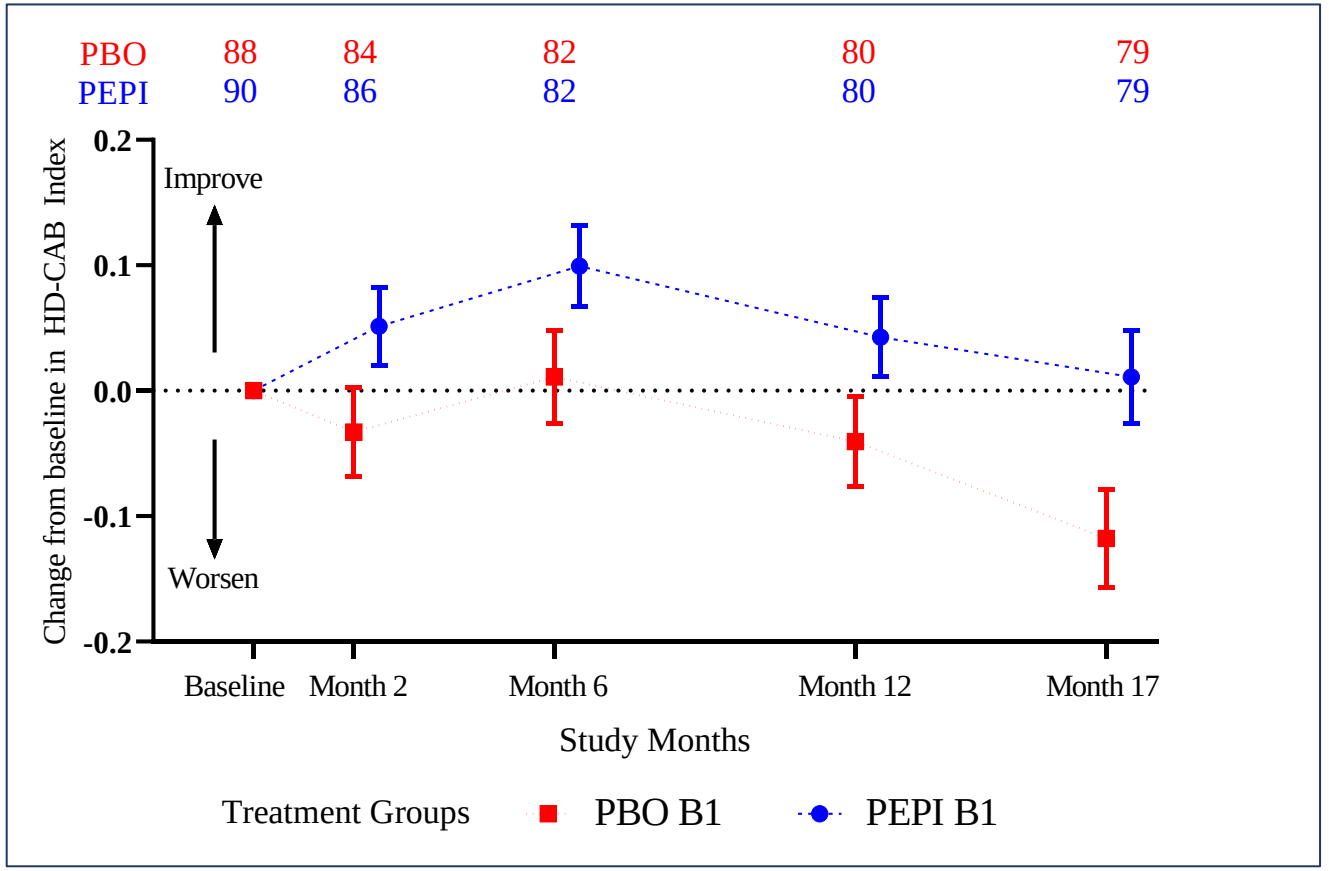
One-sided p-value	Favors PEPI	Success [Critical value]
0.06	Yes	No [0.025] [0.0125]

Difference (PEPI – PBO)
Change from Baseline at Month 17 (95% CI) = 1.43 (-0.37, 3.23)

Cognitive Assessment Battery (HD-CAB)

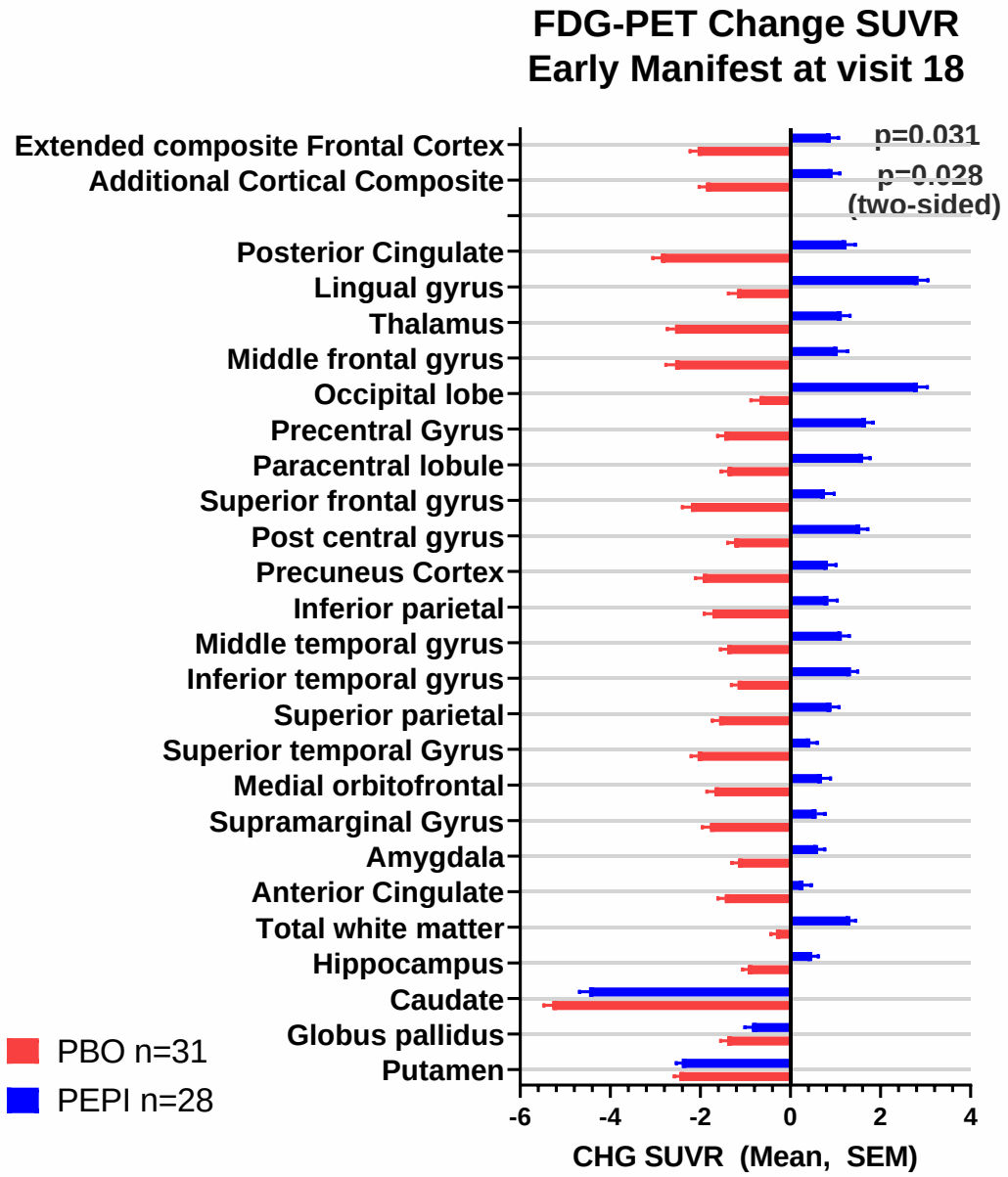
HD-CAB Composite Index of 6 Cognitive Assessments

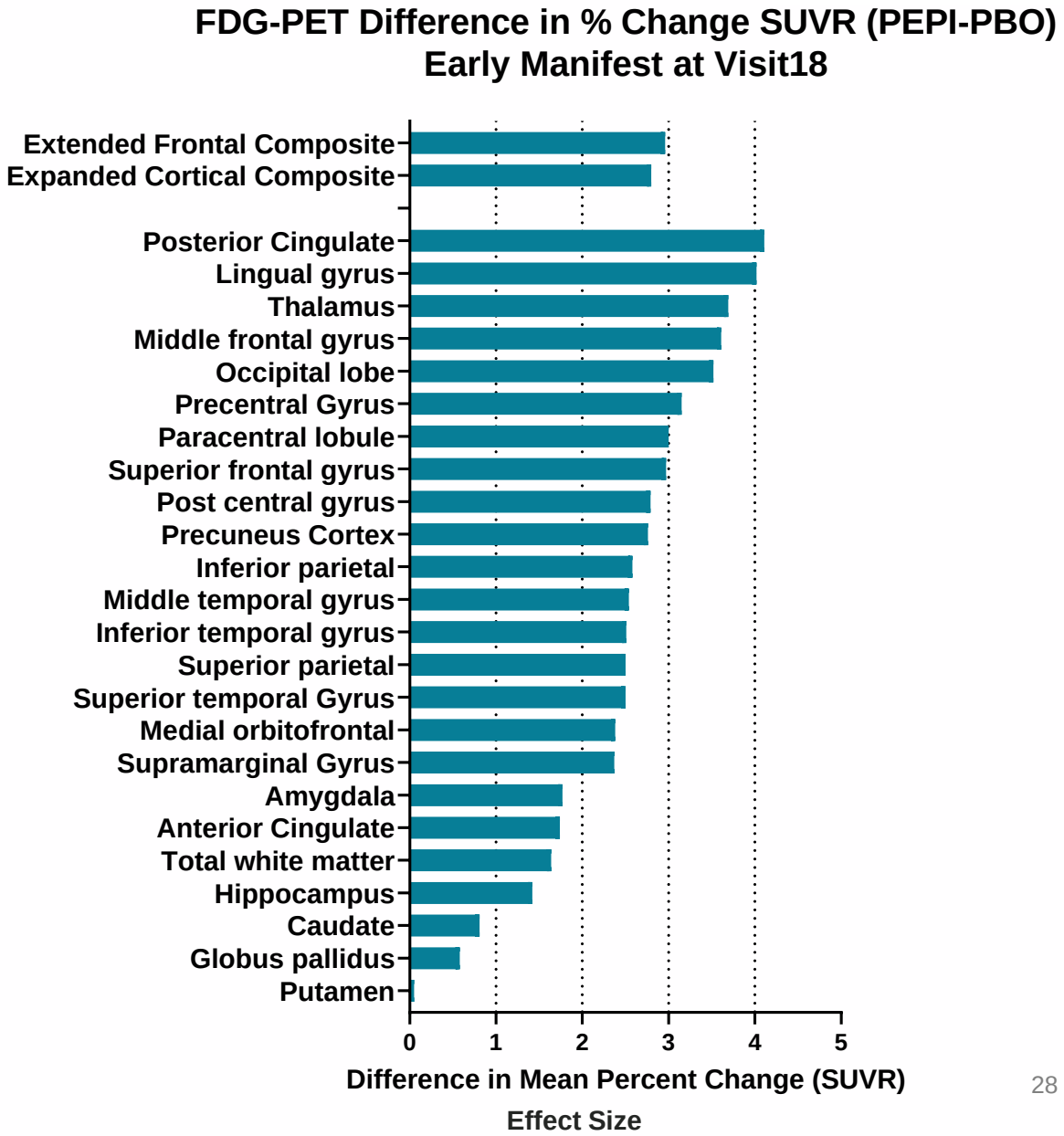
Early manifest HD



One-sided p-value	Favors PEPI	Critical value
0.007	Yes	Yes [0.025]

FDG-PET at 18 Months – Early Manifest: Pepinemab treatment reverses loss of metabolic activity





Anticipated Vaccinex 2021 Milestones

Topline Clinical Data for SIGNAL Cohort B study in Huntington's Disease	September 22, 2020
Clinical Data for Pepinemab in Combination with Avelumab in NSCLC to be published in Clinical Cancer Research	H1 2021
Enrollment of first patient for phase 2 study of Pepinemab in Combination with Keytruda® in front line Head & Neck Cancer – (readout mid-2022)	Q2 2021
Enrollment of first patient in Alzheimer's disease phase 1b/2a study (readout late-2022)	Q2 2021
Publish Clinical Data for SIGNAL study in Huntington's Disease	2021

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	International
Granted / allowed	26	11
Pending	15	13

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, Inc. (Nasdaq: VCNX) is a publicly traded clinical-stage biotechnology company engaged in the discovery and development of targeted biotherapeutics to treat serious diseases with unmet medical needs, including neurodegenerative diseases, cancer and autoimmune disorders.

VCNX (NASDAQ)	
Shares outstanding (fully diluted)	24.9M
Headquarters	Rochester, NY
Employees	39
IPO (proceeds $40M)	August 2018
Subsequent PIPE and ATM (proceeds $32M)	2019/2020
Analysts	Oppenheimer (L. Gershell), BTIG (T. Shrader)