Pepinemab – Anti-SEMA4D Antibody for Neurodegenerative Disease and Cancer Immunotherapy

VACCINEX

Unique Targets
Novel Mechanisms
New Medicines

Corporate Presentation

November, 2021

VCNX

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. Such statements include, but are not limited to, statements about the Company's plans, expectations and objectives with respect to the results and timing of clinical trials of pepinemab in various indications, the use and potential benefits of pepinemab in Huntington's and Alzheimer's disease and other indications, and other statements identified by words such as "may," "will," "appears," "expect," "planned," "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 the outcome of the Company's 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 the Company's dependence on its lead product candidate pepinemab, the ability to leverage its ActivMAb® platform, the impact of the COVID-19 pandemic, and other matters that could affect its development plans or the commercial potential of its product candidates. Except as required by law, the Company assumes 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 the Company's periodic reports filed with the Securities and Exchange Commission ("SEC") and the other risks and uncertainties described in the Company's Form 10-K for year end December 31, 2020 and subsequent filings with the SEC.

PIPELINE

Research/Preclinical	Phase 1	Phase 2	Phase 3

Pepinemab Antibody Platform (anti-Semaphorin 4D Mab)

Neurology

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

Pepinemab in Alzheimer's Disease — SIGNAL-AD

Oncology

Pepinemab COMBO with avelumab in NSCLC — **Complete** — **CLASSICAL – Lung**

Pepinemab COMBO with pembrolizumab in first-line HNSCC — **KEYNOTE B84**

ActivMAb® Antibody Platform

Drug Discovery, Complex Membrane Protein Receptors

All studies Sponsored by:

VACCINEX

Additional Funding &/or Support by:

alzheimer's association — Alzheimer's Drug Discovery Foundation

Merck KGaA, Darmstadt

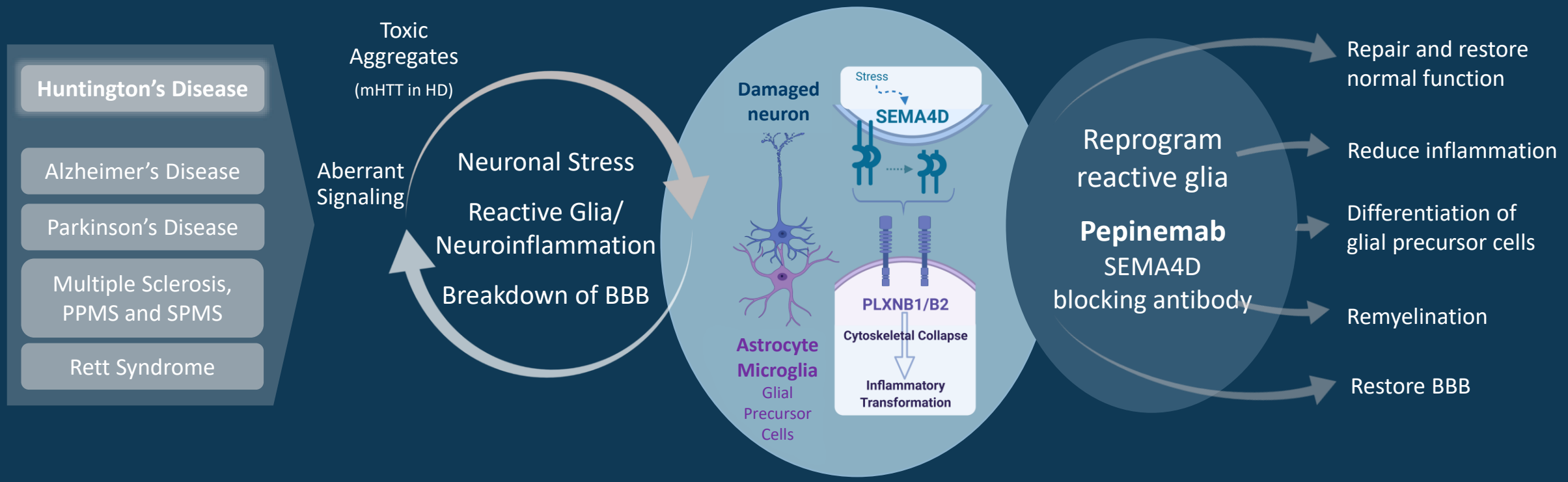
MERCK

Merck, MSD

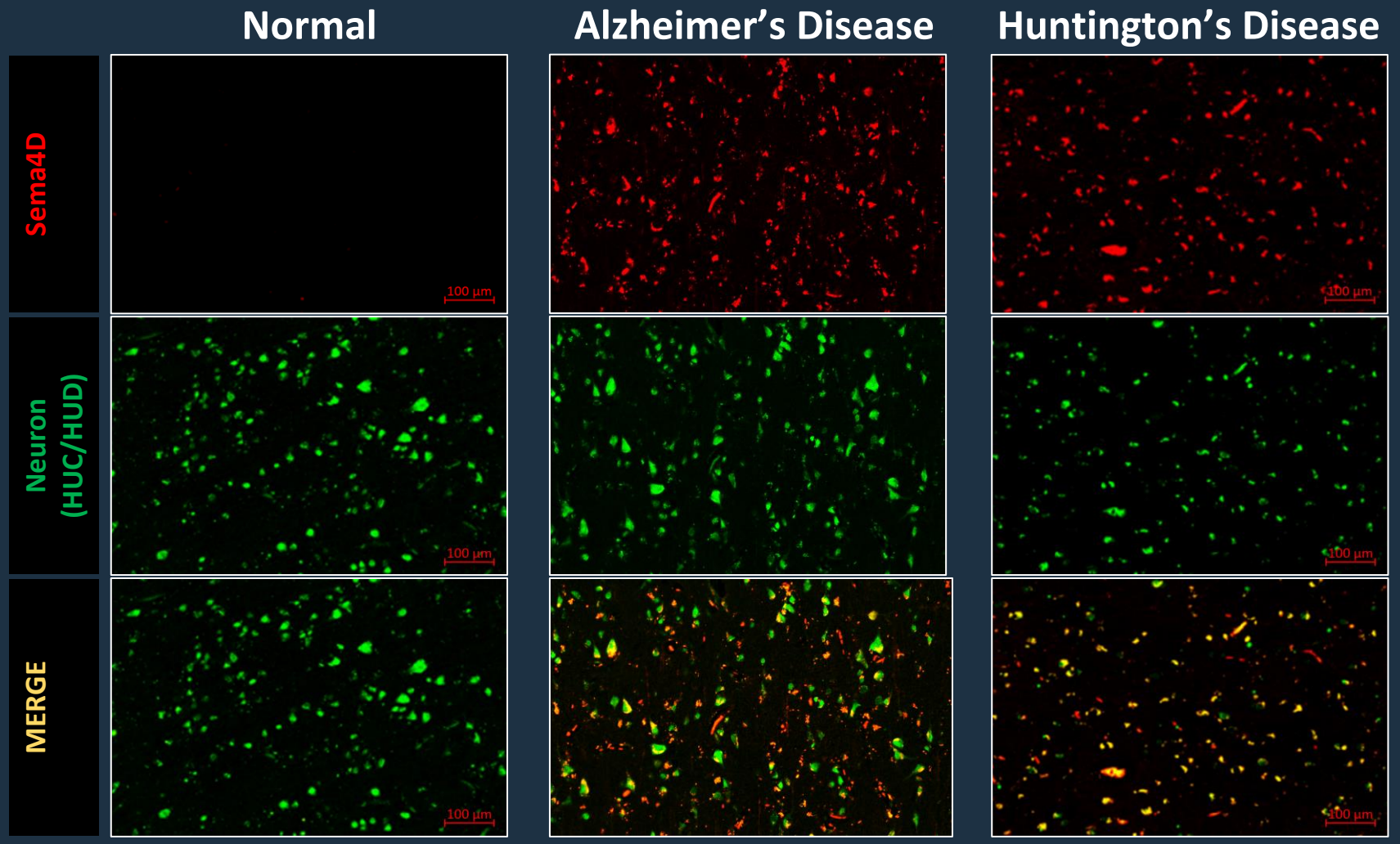
Pepinemab Antibody for treatment of Neurodegenerative Disease

■ Unique Targets ■ Novel Mechanisms ■ New Medicines

PEPINEMAB REPROGRAMS UNDERLYING PATHOLOGY IN CNS DISEASE



SEMA4D is upregulated in neurons during underlying disease progression



Human autopsy sections of frontal lobe

HUNTINGTON'S DISEASE

Genetic Disease

HD is caused by dominant mutation in a single gene.

Unmet need

No approved treatments to alter the course of Huntington's Disease.

~40,000 individuals with manifest disease in US
>150,000 more are at risk of having inherited the HD mutation

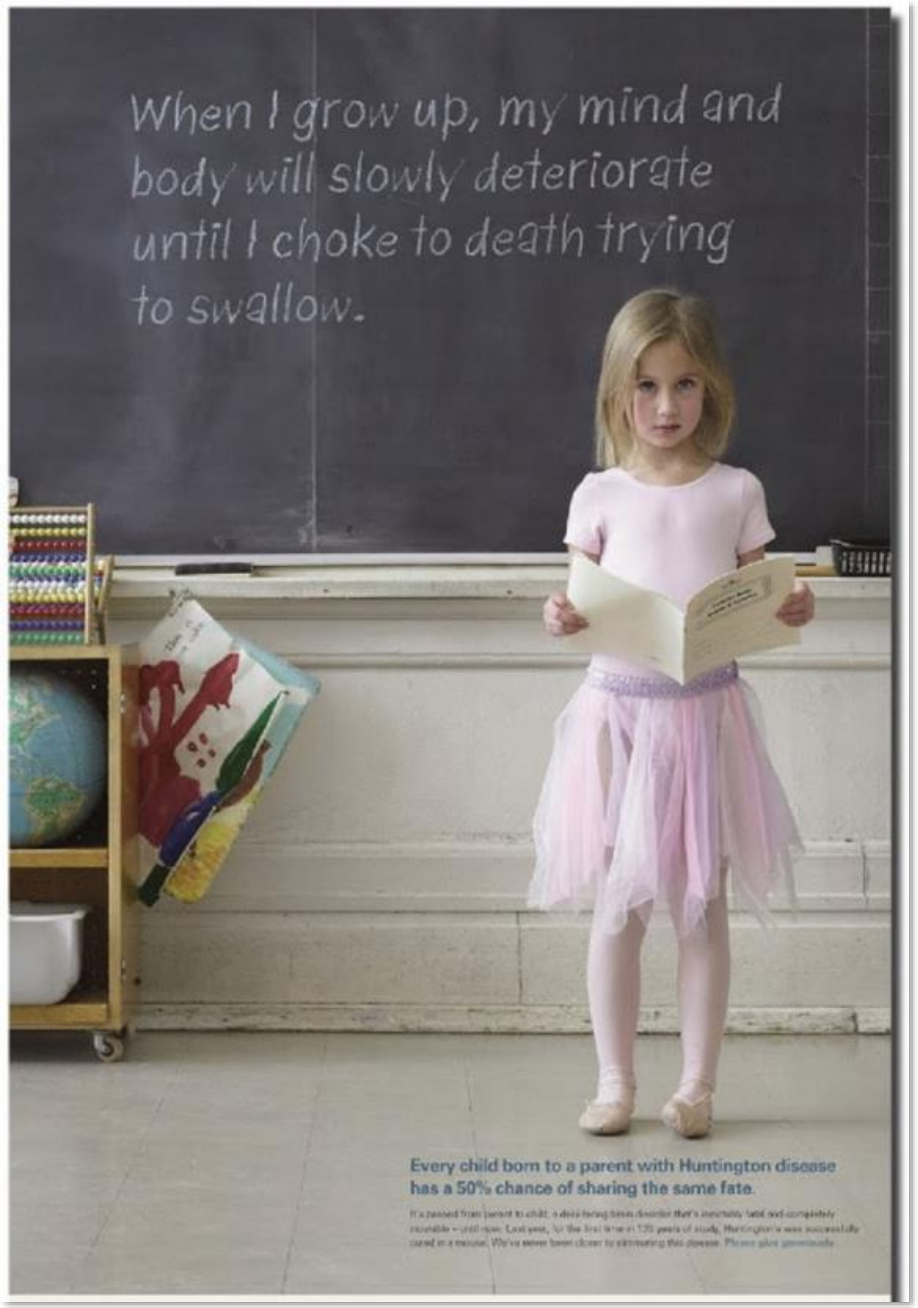
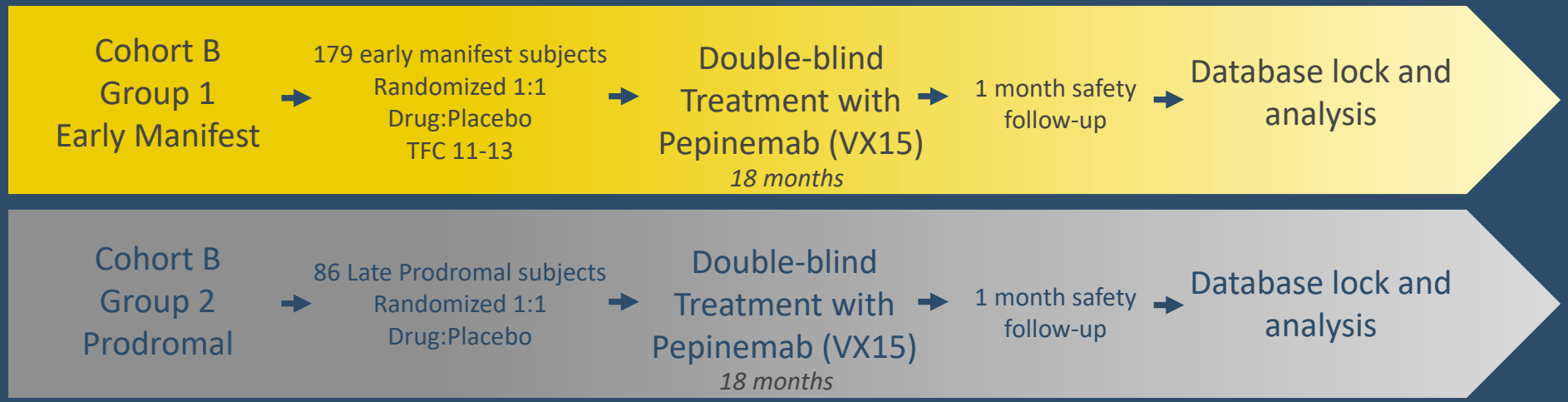


Photo credit: Huntington Society of Canada

SIGNAL: RANDOMIZED PLACEBO-CONTROLLED TRIAL IN SUBJECTS WITH EARLY HD



Key Study Objectives

Safety and tolerability

Co-primary endpoints: HD-CAB and Clinical global impression of change (CGIC)

Secondary and Exploratory including Brain imaging measures

Abbreviated Safety and Baseline Characteristics

mITT population

Pepinemab (PEPI) SEMA4D blocking antibody is well tolerated

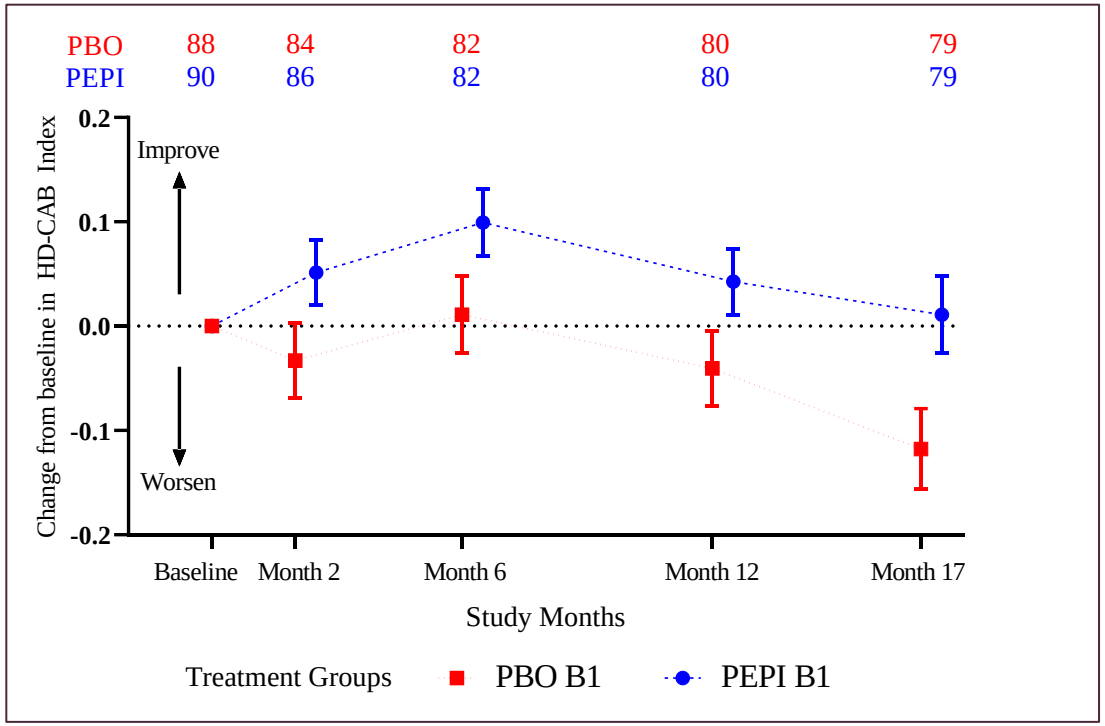
Early Manifest Cohort B1	Placebo (n=88)	Pepinemab (n=91)
Discontinued Treatment Early	10	13
Had any SAE (*)	8	4
Had any Grade 3+ AE (*)	14	17
CAG repeat length	44.1	43.5
CAP score**	470	466
UHDRS-DCL at screening DCL-4, Unequivocal HD (>99% confident)	88 (100%)	91 (100%)
UHDRS-TFC at screening, n (%)		
11 12 13	33 (38%) 18 (20%) 37 (42%)	29 (32%) 37 (41%) 24 (27%)
MoCA score, mean (SE)	26.02 (2.04)	26.14 (2.30)
MoCA <26 subgroup	23.97 (0.94)	23.78 (1.07)
MoCA ≥26 subgroup	27.44 (1.21)	27.72 (1.34)

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

COGNITIVE ASSESSMENT BATTERY (HD-CAB)

Early Manifest HD: Intent to treat population (mITT)

HD-CAB Composite Index of 6 Cognitive Assessments



HD-CAB Composite Index: Pre-specified Exploratory

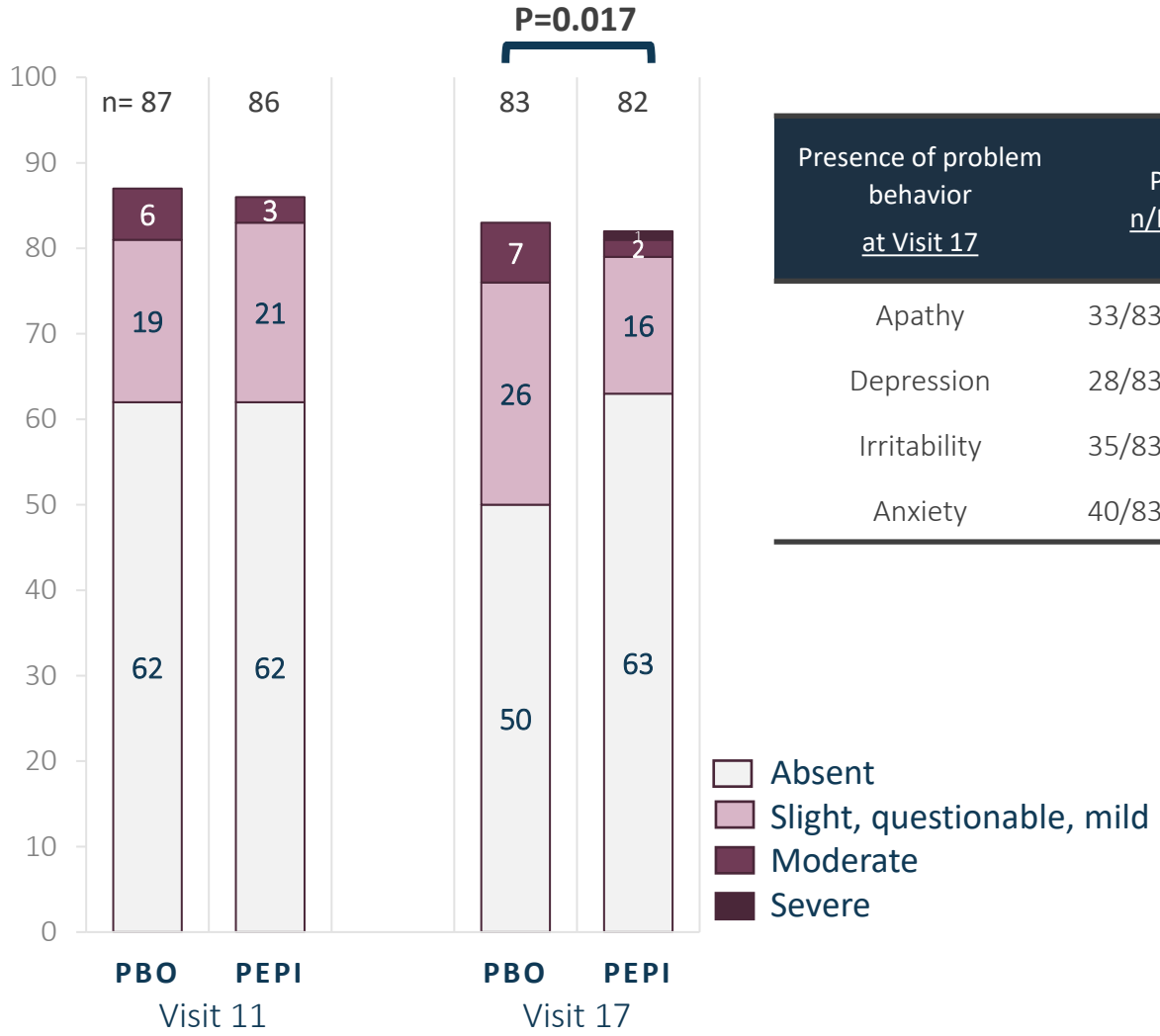
LS Mean Difference Estimate (95% CI)	One-sided p-value	Favors PEPI	Critical value
0.13 (0.03, 0.23)	**0.007**	**Yes**	**Yes [0.025]**

Prespecified Co-Primary: Two-item HD Cognitive Assessment

LS Mean Difference Estimate (95% CI)	One-sided p-value	Favors PEPI	Critical value
OTS: -1.98 (-4.00, 0.05)	**0.028**	**Yes**	**Yes [0.025]**
PTAP: 1.43 (-0.37, 3.23)	**0.060**		

PEPINEMAB-RELATED IMPROVEMENT IN PBA-s APATHY SEVERITY SCORE

Several HD studies suggest that among behavioral measures apathy severity correlates best with disease progression and correlates with cognition



Presence of problem behavior at Visit 17	PBO n/N (%)	PEPI n/N (%)	One-Sided p-value (+ Favors PEPI)
Apathy	33/83 (39.76)	19/82 (23.17)	**0.017 (+)**
Depression	28/83 (33.73)	16/82 (19.51)	0.030 (+)
Irritability	35/83 (42.17)	32/82 (39.02)	0.41 (+)
Anxiety	40/83 (48.19)	40/82 (48.78)	0.60 (-)

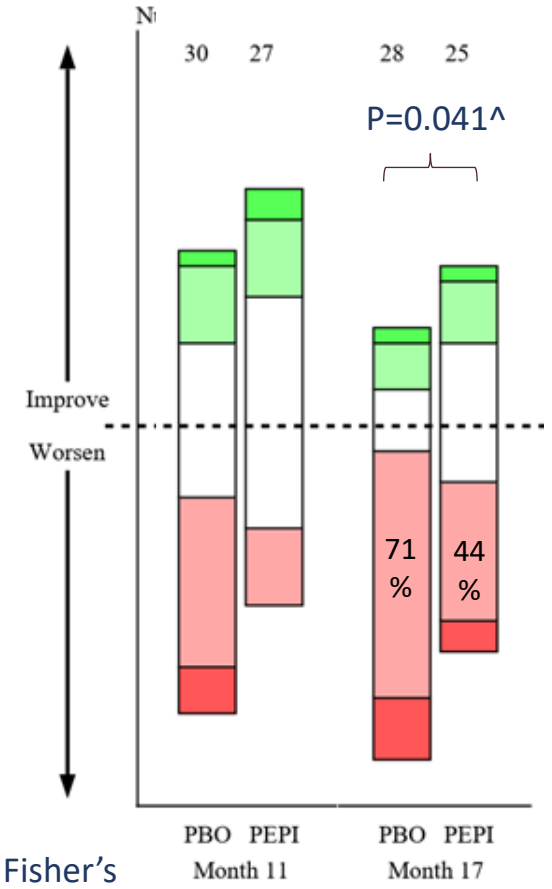
CO-PRIMARY 2: CGIC

Post-hoc Subgroup Analysis, Early Manifest HD

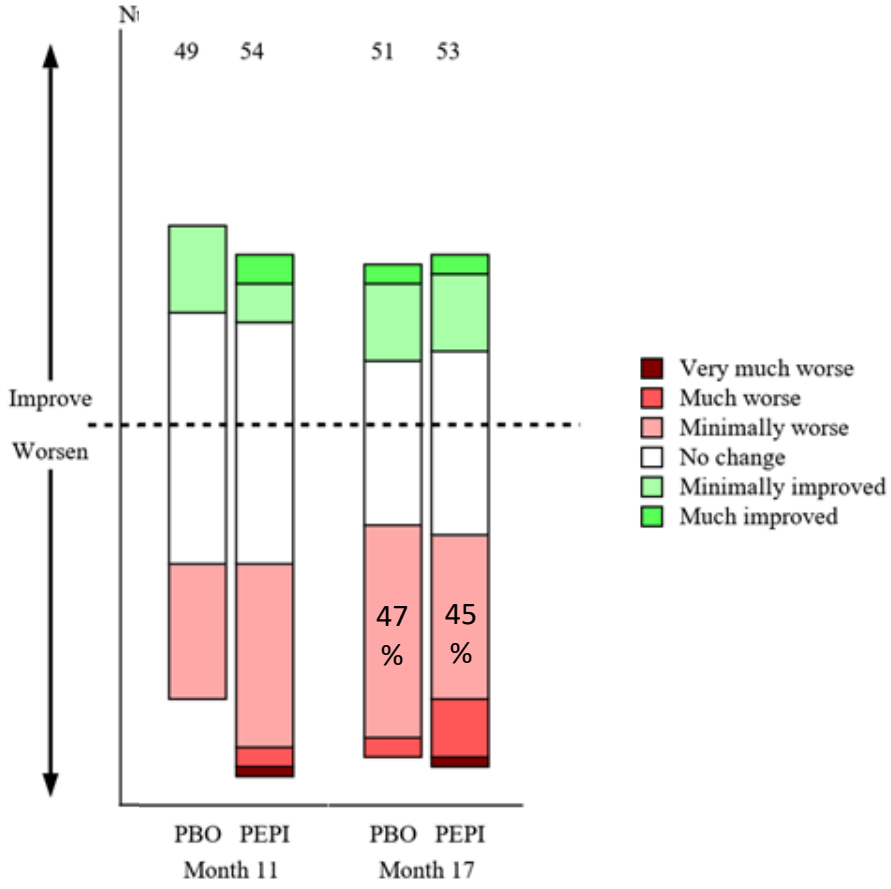
No significant treatment effect in the total early manifest HD population

A treatment effect was, however, evident in subjects with somewhat more advanced disease (TFC 11).

CGIC – Subjects with Baseline UHDRS TFC 11



CGIC – Subjects with Baseline UHDRS TFC 12 and 13

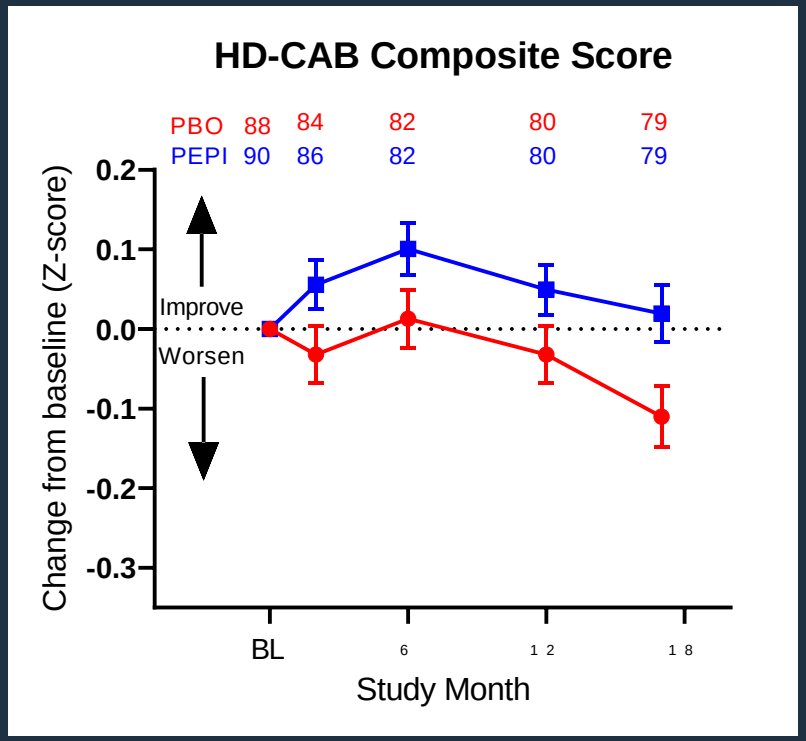


^nominal one-sided p-value, Fisher's exact test for worsening score

HD-CAB STRATIFIED BY BASELINE MoCA

(Montreal Cognitive Assessment, Post-hoc Subgroup Analysis)

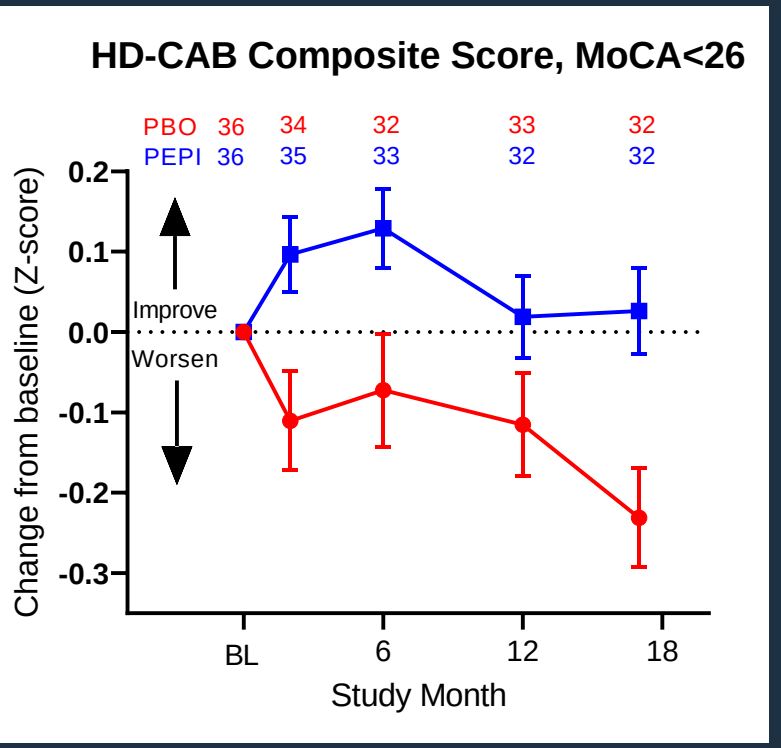
mITT



LS Mean Estimate (SE), month 17

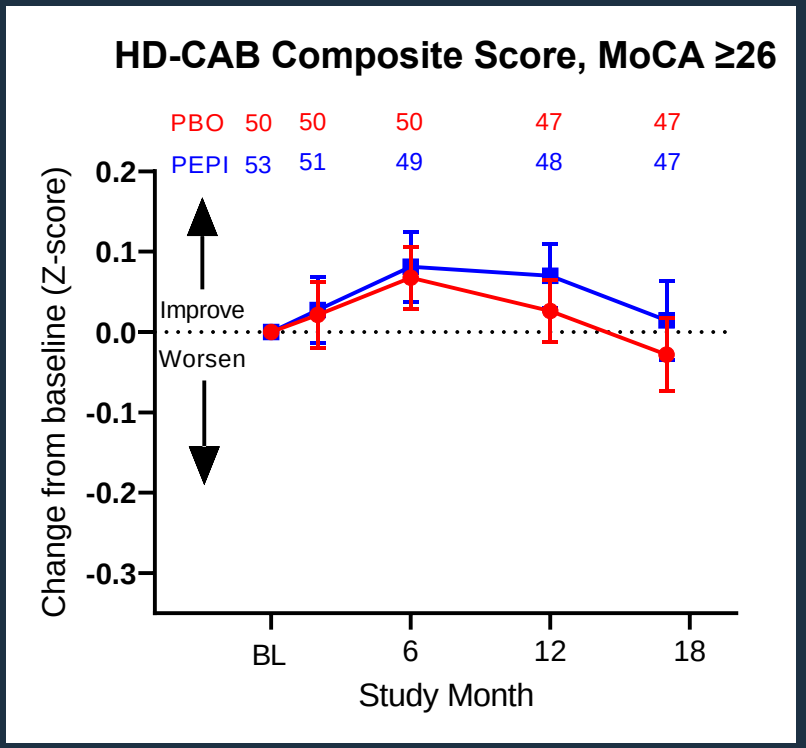
mITT: 0.13 (0.05), **p=0.007**

MoCA < 26



MoCA <26: 0.24 (0.08), **p=0.0025**

MoCA ≥ 26

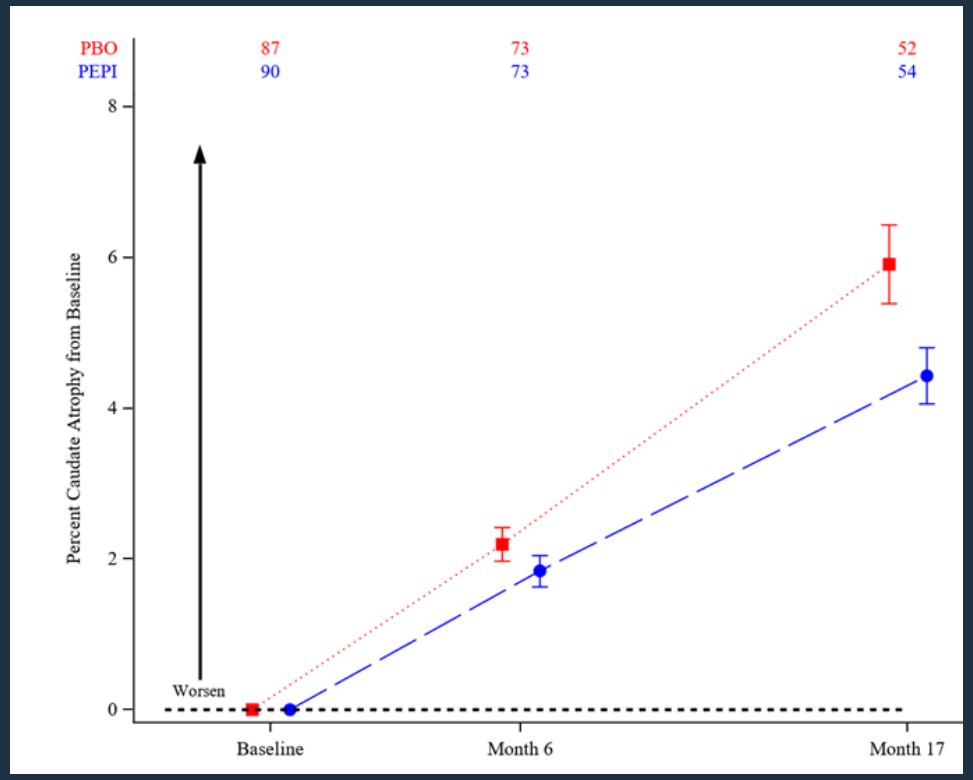


MoCA ≥26: 0.06 (0.06), **p=0.197**

PEPINEMAB REDUCES BRAIN ATROPHY

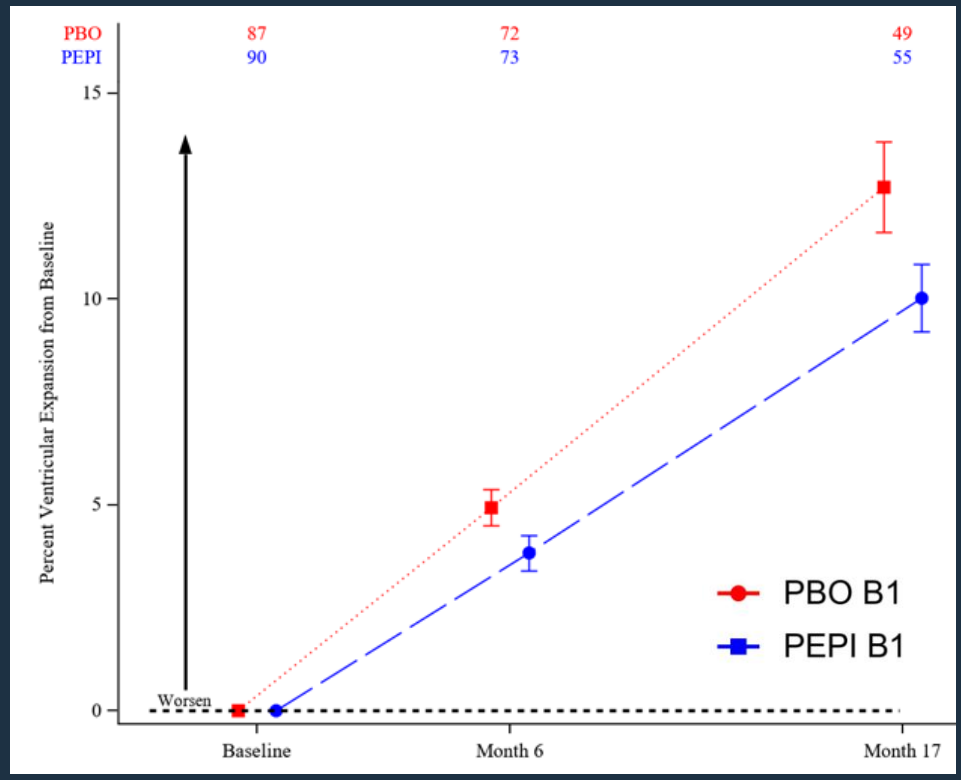
Volumetric MRI– Boundary Shift Integral Analysis
Early Manifest HD

CBSI (caudate atrophy)



LS Mean Difference Estimate (95% CI):
CBSI: -1.54 (-2.79, -0.29);
p = 0.017

VBSI (ventricular expansion)



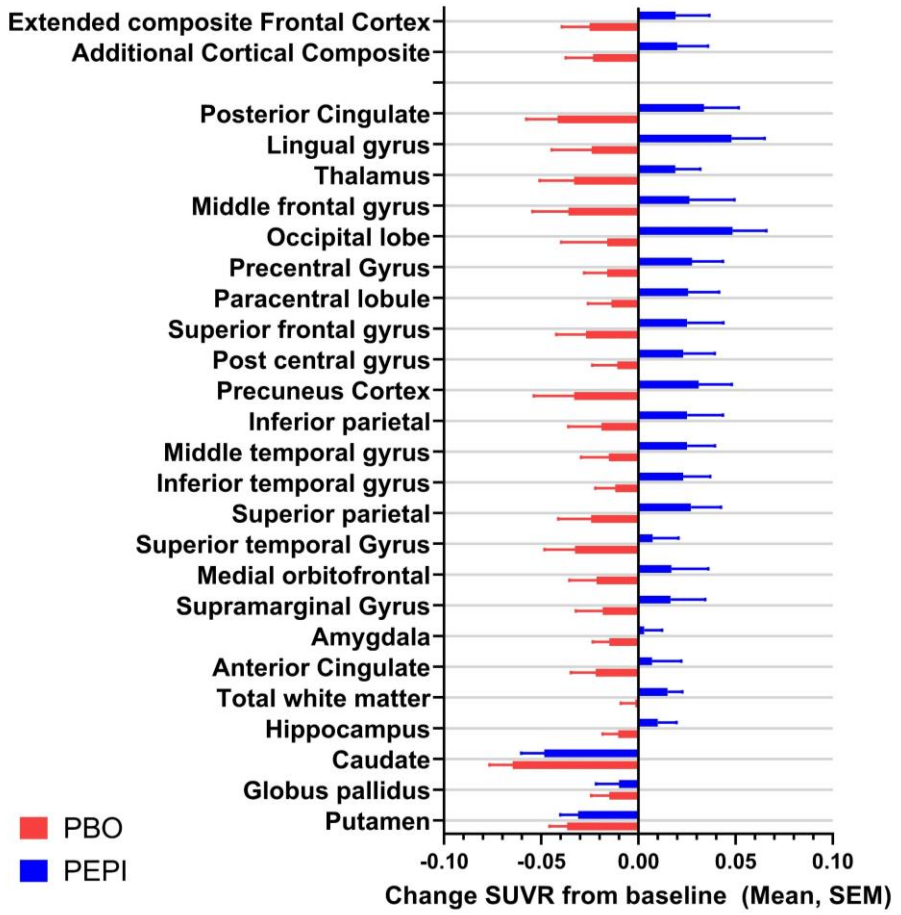
VBSI:-2.47 (-5.04, 0.10);
p = 0.060

FDG-PET CORRELATES WITH COGNITIVE FUNCTION

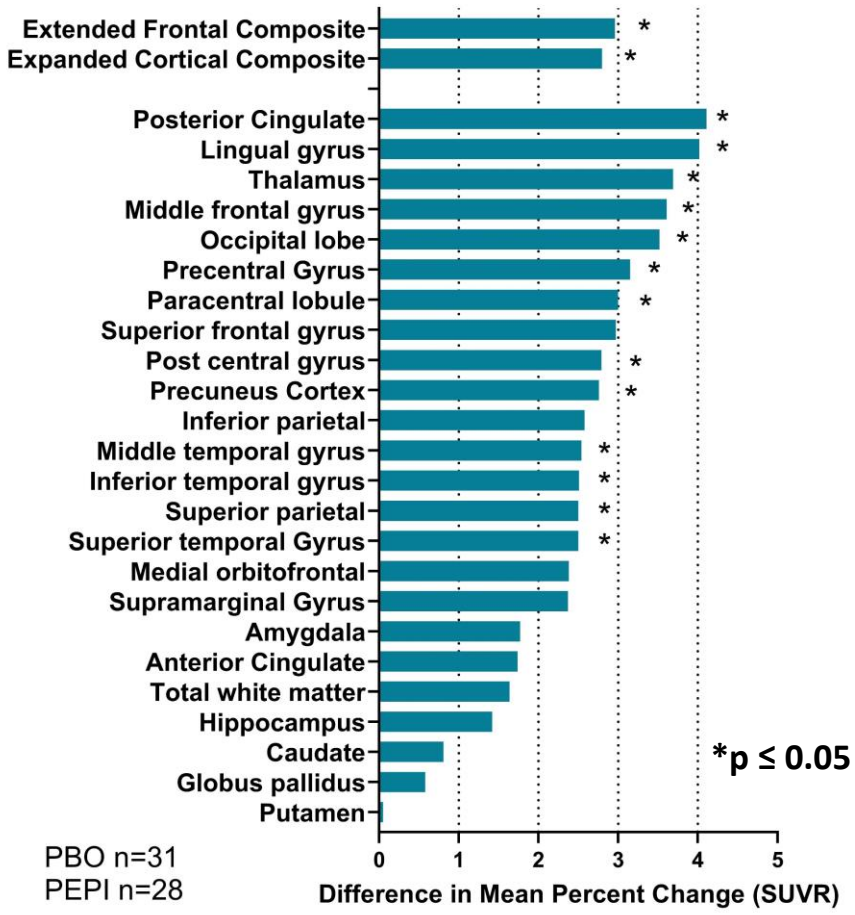
Early Manifest HD

Pepinemab treatment reverses loss of metabolic activity

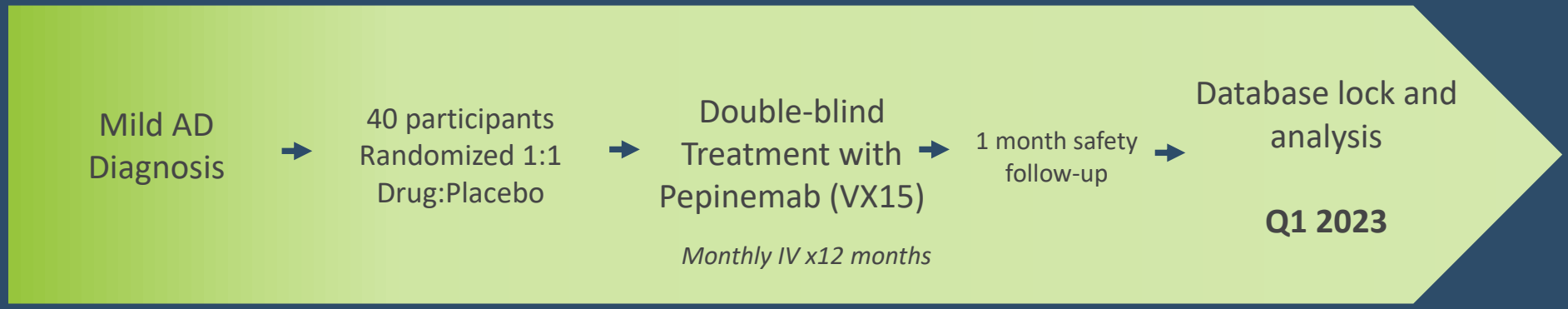
FDG-PET Change SUVR
Early Manifest at Visit 18



FDG-PET Difference in % Change SUVR (PEPI-PBO)
Early Manifest at Visit 18



CLINICAL TRIAL DESIGN: Alzheimer's Disease



Key Study Objectives

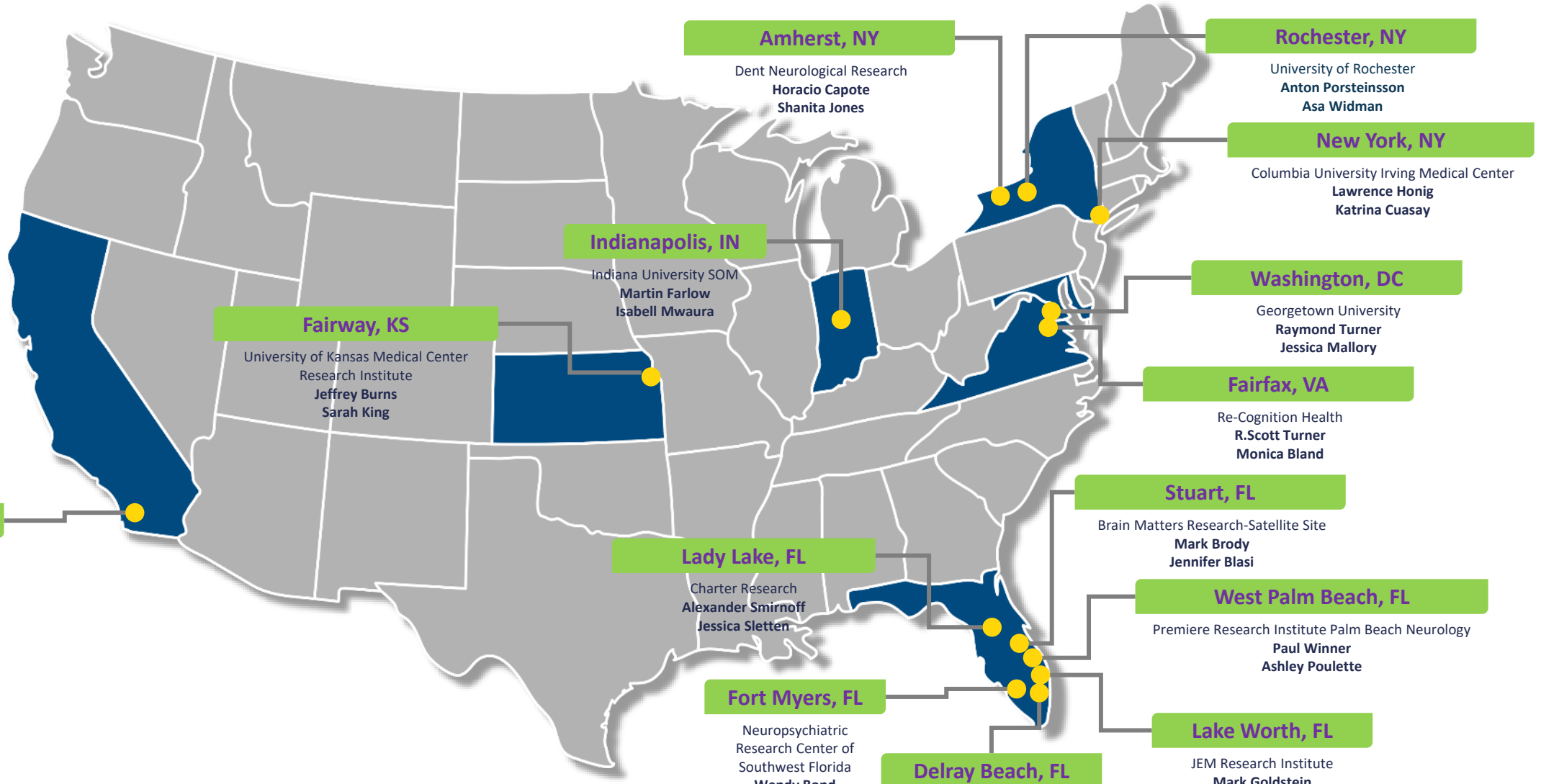
Safety and tolerability

Cognitive Function measures, CDR-SB, ADAS-Cog13

Brain imaging measures, FDG-PET

Funded by:
Alzheimer's Association and
Alzheimer's Drug Discovery Foundation

Signal-AD Site Map



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Jeffrey Burns
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Wendy Bond

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JEM Research Institute
Mark Goldstein
Valerie Nevins

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Brain Matters Research
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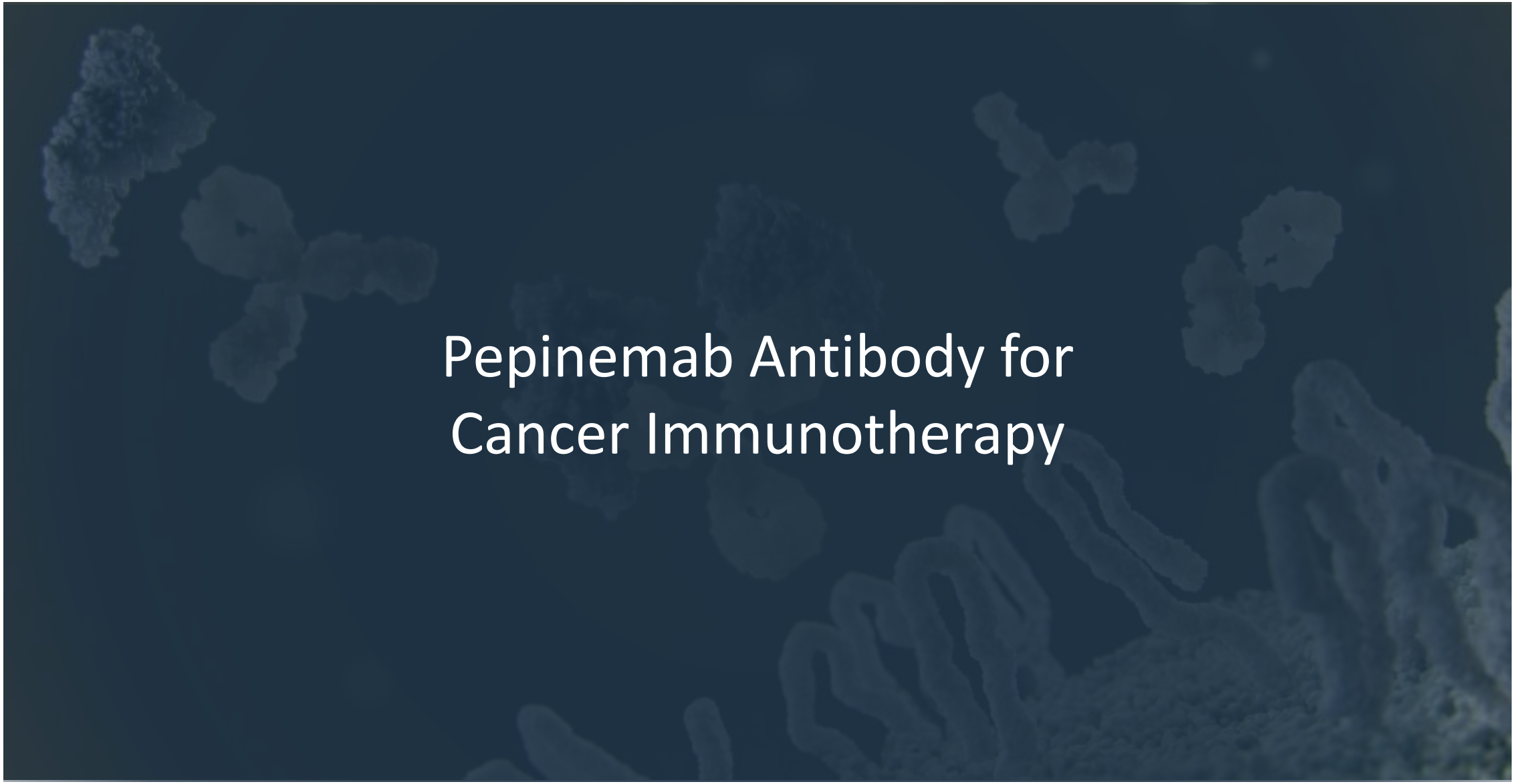


Pepinemab Antibody for Cancer Immunotherapy

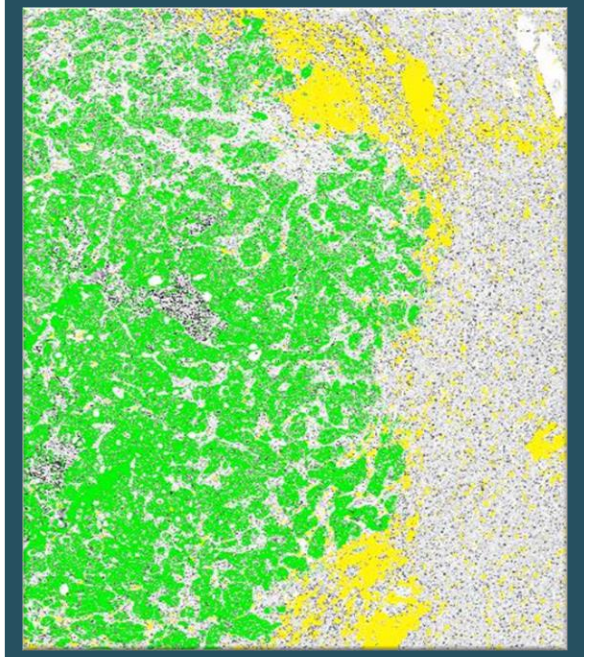
■ Unique Targets ■ Novel Mechanisms ■ New Medicines

WHY DOES IMMUNE RESPONSE FAIL IN TUMORS?

Immune Exclusion

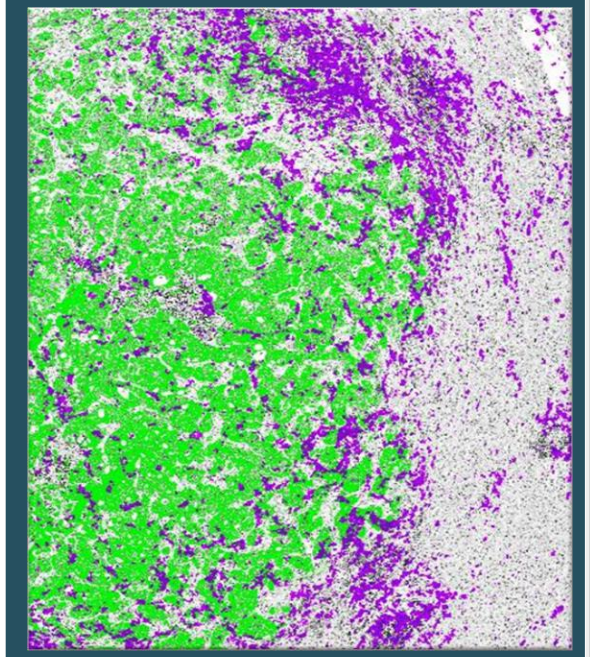
Activated T-cells and dendritic cells can't penetrate tumor

Sema4D is expressed at tumor margin



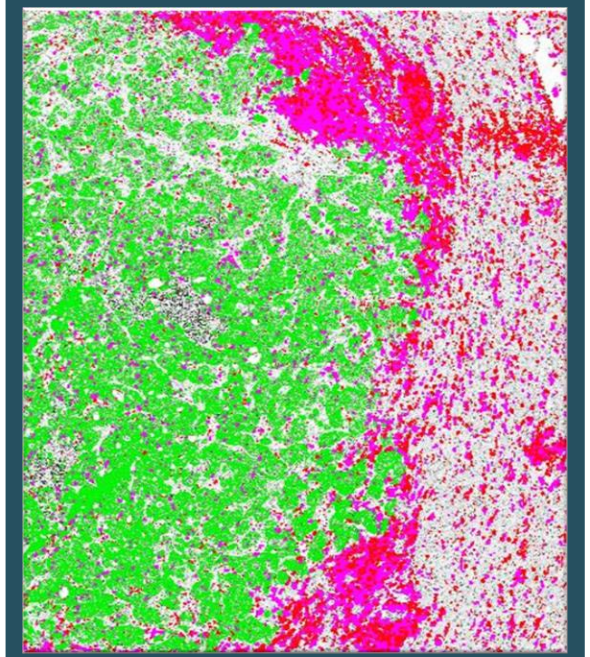
Tumor SEMA4D

Sema4D binds PLXN receptors on DCs and restricts penetration



Tumor Dendritic Cells (CD11c)

T-cells are excluded from tumor



Tumor CD8+ CD4+ T Cells

Pro-inflammatory cells are excluded from the metastatic CRC tumor and build up at the invasive edge

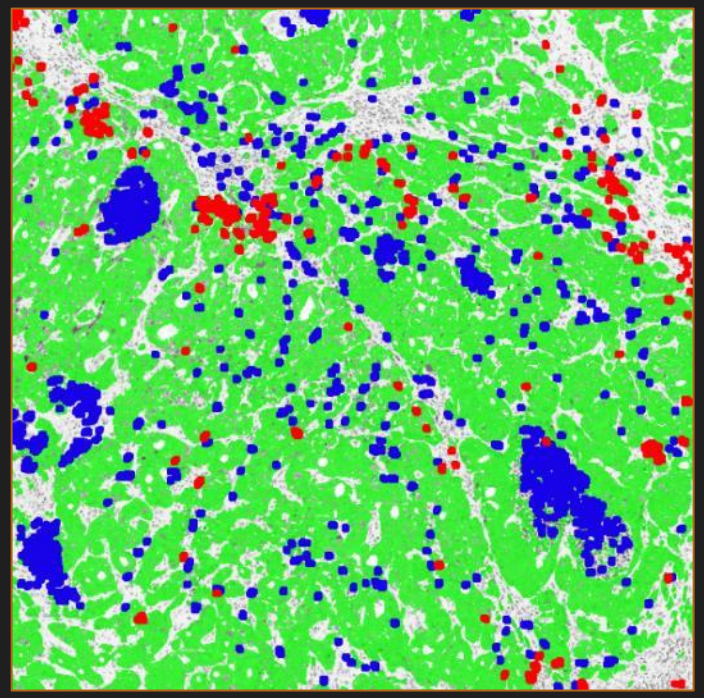
CD8 T cells align with Sema4D at the invasive edge of the tumor. Most of these excluded T-cells express Sema4D. Dendritic Cells express receptors for SEMA4D and are heavily excluded at the invasive edge.

Pepinemab Impact on Tumor Micro-Environment (TME)

Pepinemab:

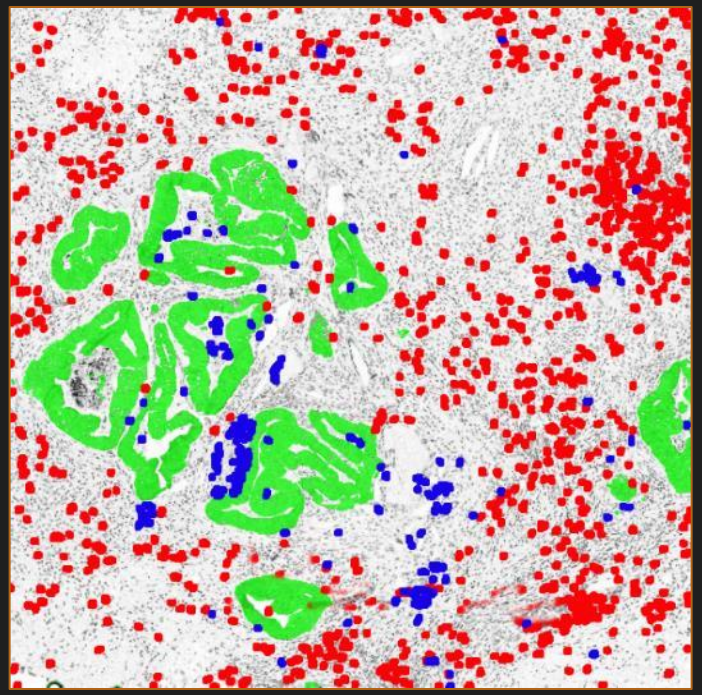
1. ↑ cytotoxic T cells
2. ↓ inhibitory suppressor cells

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



Myeloid Derived Suppressor Cells (MDSC)

Pepinemab
High CD8+ T cells
Low tumor content and MDSC



Tumor CD8+ T cells

Biopsies from patients with metastatic MSS Colorectal Cancer

In collaboration with Winship Cancer Institute, Emory University – integrated biomarker study (NCT03373188), Wu et al. Ann Surg Oncol. 2021

Unique Mechanism
complements other immunotherapies

Pepinemab
Facilitates T-cell infiltration
Reduces immune suppression

Immune Checkpoint Inhibitors
Sustain T-cell activity

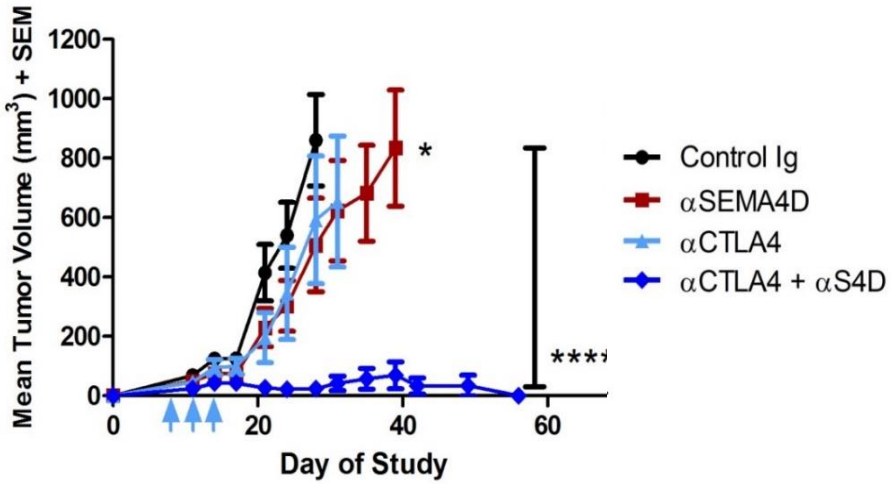
Combination therapy to overcome multiple immune resistance mechanisms

Research Article | Cancer Immunology Research

Antibody Blockade of Semaphorin 4D Promotes Immune Infiltration into Tumor and Enhances Response to Other Immunomodulatory Therapies

Elizabeth E. Evans, Alan S. Jonason Jr, Holm Bussler, Sebold Torno, Janaki Veeraraghavan, Christine Reilly, Michael A. Doherty, Jennifer Seils, Laurie A. Winter, Crystal Mallow, Renee Kirk, Alan Howell, Susan Giralico, Maria Scrivens, Katya Klimatcheva, Terrence L. Fisher, William J. Bowers, Mark Paris, Ernest S. Smith, and Maurice Zauderer

Combination therapy: Preclinical Data



Pepinemab complements other immune-activating therapies:

anti-PD1/L1, anti-CTLA-4, anti-LAG3, anti-TGF-β, DC vaccine, etc

VACCINEX

Clinical POC

Phase 1b/2 CLASSICAL-Lung

July 1, 2021 | Volume 27 | Number 13

CLINICAL CANCER RESEARCH

HIGHLIGHTS

Selected Articles from This Issue

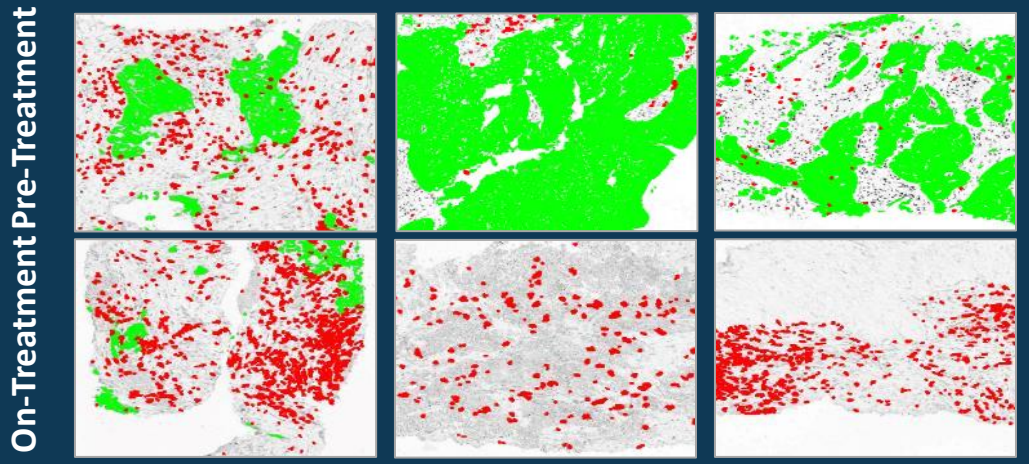
A Phase Ib/2 Study of Pepinemab in Combination with Avelumab in Advanced Non–Small Cell Lung Cancer AC

Michael Rahman Shafique[1], Terrence Lee Fisher[2], Elizabeth E. Evans[2], John E. Leonard[2], Desa Rae Electa Pastore[2], Crystal L. Mallow[2], Ernest Smith[2], Vikas Mishra[2], Andreas Schröder[3], Kevin M. Chin[4], Joseph Thaddeus Beck[5], Megan Ann Baumgart[6], Ramaswamy Govindan[7], Nashat Y. Gabrail[8], Alexander I. Spira[9], Nagashree Seetharamu[10], Yanyan Lou[11], Aaron Scott Mansfield[12], Rachel E. Sanborn[13], Jonathan W. Goldman[14], and Maurice Zauderer[2]

Sponsored by: VACCINEX

Co-funded by: MERCK

1. **Well tolerated.** Pepinemab does not increase immune-related toxicities of partner drug, but does increase penetration of cytotoxic T cells.
2. **Unmet Need: PD-L1 low/negative tumors**
   - Reported single agent anti-PDx: **ORR ~10-15%**
   - Combination with pepinemab: **ORR 25-33%**
3. **Unmet Need: Antitumor activity in immune checkpoint resistant/refractory tumors**



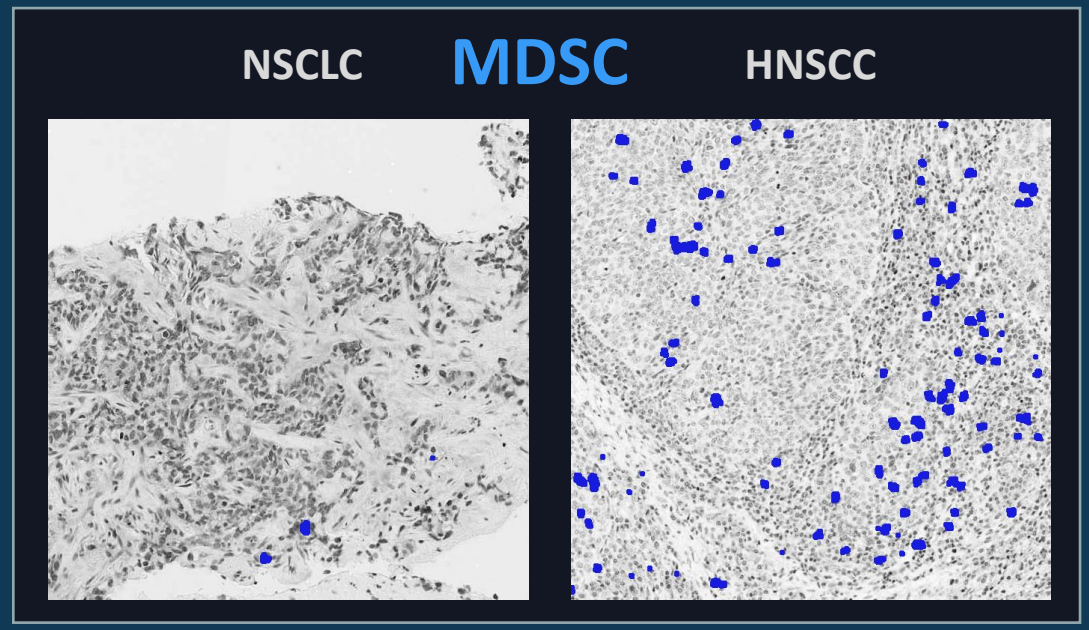
Lessons Learned

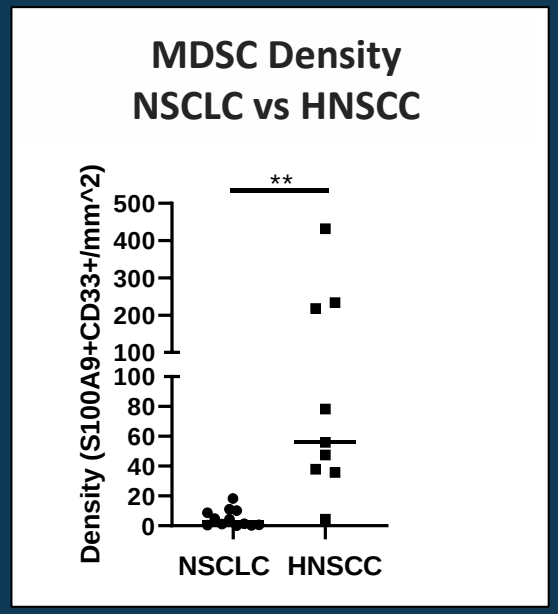
Next Steps - HNSCC

Head and Neck cancer (HNSCC)

- SEMA4D is strongly expressed in HNSCC & induces high levels of myeloid derived suppressor cells (MDSC)
- Relatively low (17-19%) response rate to immune checkpoint therapy in HNSCC

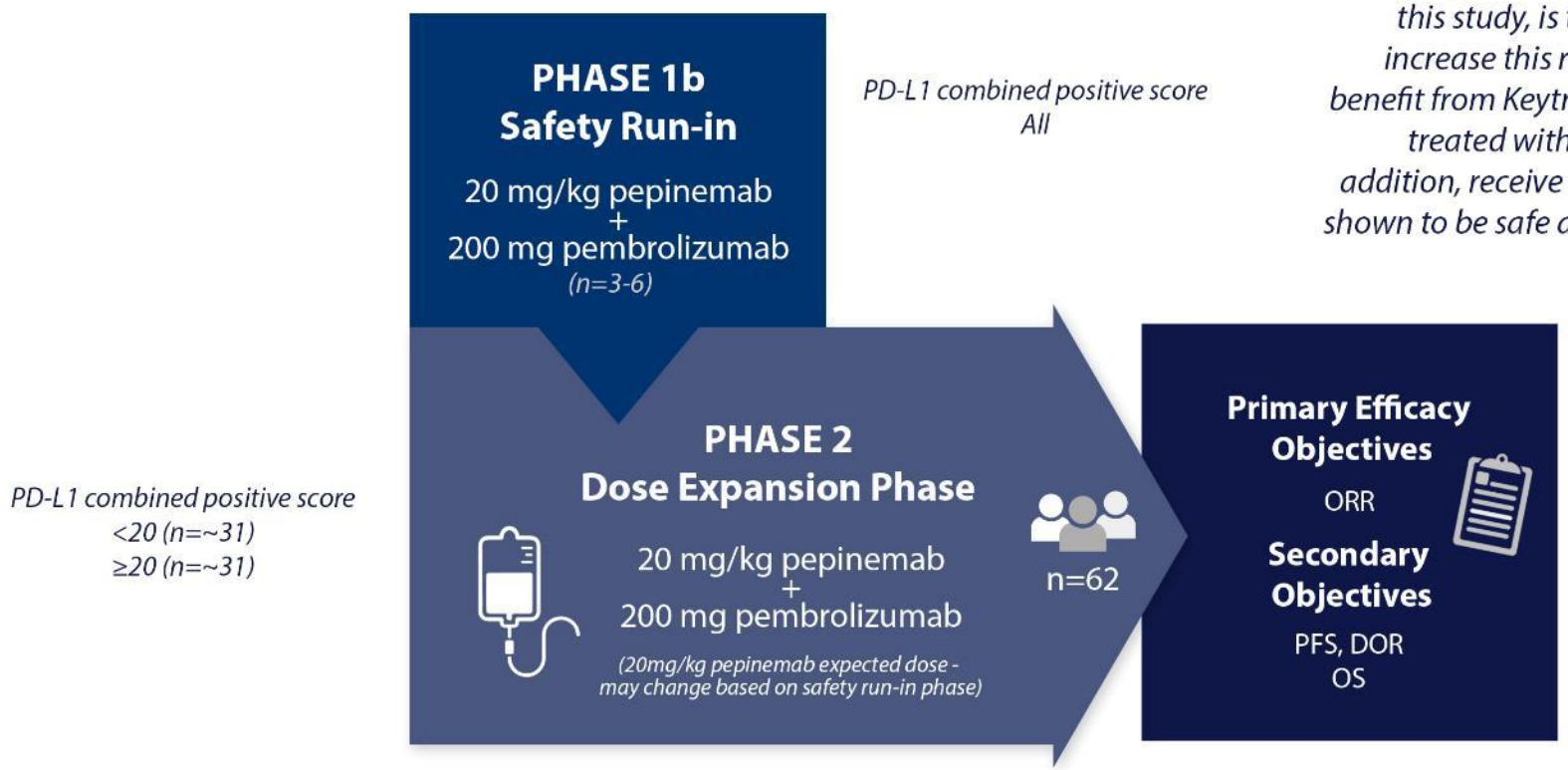
Hypothesis: Inhibiting MDSC with pepinemab will enhance response to pembrolizumab in HNSCC





CLINICAL TRIAL DESIGN: Keynote B84

Enrollment initiated,
total of 18 planned sites
Data anticipated H2-2022



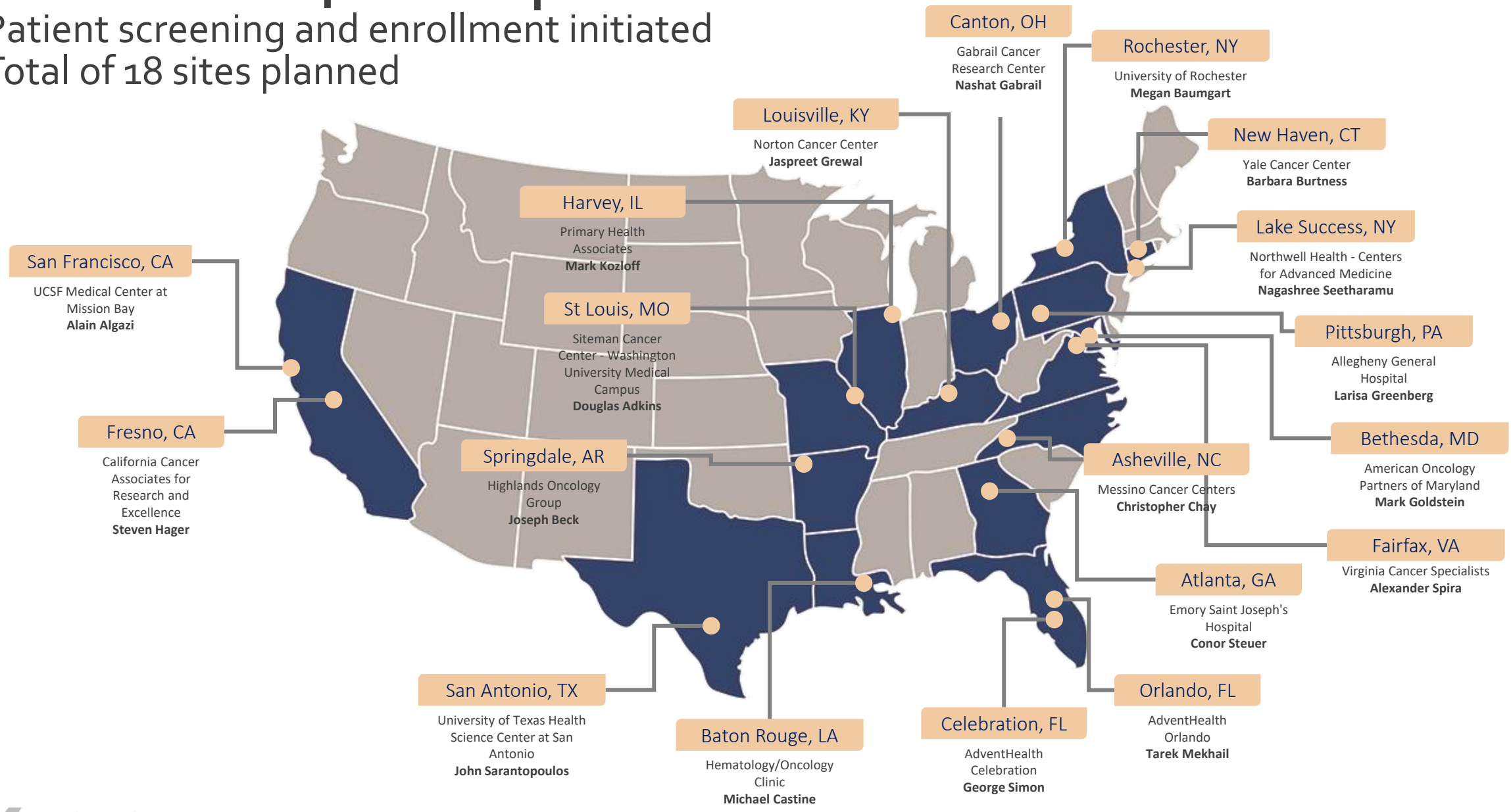
A major goal of current head and neck cancer research, and this study, is to identify a combination therapy that can increase this relatively small percentage of patients who benefit from Keytruda alone. All patients in our study will be treated with the standard dose of Keytruda and will, in addition, receive treatment with pepinemab, that had been shown to be safe and tolerable to date in many clinical trials.

Sponsor: VACCINEX

This study is conducted in collaboration with Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA

KEYNOTE B84 Site Map

Patient screening and enrollment initiated
Total of 18 sites planned



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 cancer and neurodegenerative diseases.

INCORPORATED
2001

HEADQUARTERS
Rochester, NY

EMPLOYEES
39

IPO NASDAQ VCNX
August 2018

FEBUARY 2021 CAPITAL RAISE
$32 M

CASH BALANCE*
$13.8 M

SHARES OUTSTANDING*
$30.8 M

ANALYSTS
BTIG (T.Shrader)

*as of 30SEP2021

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Vaccinex Scientific Advisors - Neurology

Eric Siemers, MD	President ofSiemersIntegration LLC. Distinguished medical fellow for Eli Lilly and Company's Alzheimer's Disease Global Development Team, founded and headed the Indiana University Movement Disorder Clinic. Served on the Board of Directors of the American Society of Experimental Neurotherapeutics, as founding member and Chair of the Alzheimer's Association Research Roundtable, and Steering Committee member for the Alzheimer's Disease Neuroimaging Initiative (ADNI).
Karl D. Kieburtz, MD, MPH	President of ClintrexLLC, providing services regarding research and regulatory strategy for therapeutic development of interventions for brain disorders. Chair of the FDA Peripheral and Central Nervous System Drugs Advisory Committee and sits on the American Academy of Neurology (AAN) Clinical Research Subcommittee, the International Executive Committee of the Movement Disorders Society (MDS), the Board of Directors for the American Society for Experimental NeuroTherapeutics(ASENT), and the Council of the American Neurological Association (ANA),chair of the FDA Peripheraland Central Nervous System Drugs Advisory Committee.
Ira Shoulson, MD	Dr. Shoulsonis a long time leader in Huntington's disease research. From 2011 to July 2018, Dr Shoulsonwas Professor of Neurology, Pharmacology and Human Science and Director of the Program for Regulatory Science and Medicine (PRSM) at Georgetown University where he was principal investigator of the FDA-Georgetown University Collaborating Center of Excellence in Regulatory Science and Innovation. From 1990 to 2011, Dr Shoulsonwas the Louis C. Lasagna Professor of Experimental Therapeutics and Professor of Neurology, Pharmacology and Medicine at the University of Rochester School of Medicine & Dentistry in Rochester, New York. Dr. Shoulsonis an elected member of the National Academy of Medicine of the National Academy of Sciences.
Ralf Reilmann, MD	Founding Director and C.E.O. of the George-Huntington-Institute, Dept. of Radiology at the University of Muenster and the Dept. of Neurodegeneration and HertieInstitute for Clinical Brain Research at the University of Tuebingen.

Vaccinex Scientific Advisors - HNSCC Clinical Advisory Board

Barbara Burtness, MD	Professor of Medicine (Medical Oncology) at Yale, leader of the Disease Aligned Research Team for the Head and Neck Cancers Program and Co-Leader of the Developmental Therapeutics Research Program at Yale Cancer Center. Chair of ECOG-ACRIN Head and Neck Therapeutics Committee, served on the NCCN and SITC Head and Neck Guidelines Committee, and the NCI Head and Neck Cancer Steering Committee. Co-chair of the NCI Clinical Trials Planning Meeting on TP53-Mutated Head and Neck Cancer and FDA Project 2025 for Head and Neck. Founding Director of the Yale Head and Neck Cancer SPORE and has led numerous clinical trials, including the international phase III trial which led to regulatory approval of immunotherapy in first-line treatment of head and neck cancer.
Robert Haddad, MD	Chief, Division of Head and Neck Oncology. McGraw Chair, Head and Neck Oncology, Dana-Farber Cancer Institute. Professor, Medicine, Harvard Medical School.
Douglas Adkins, MD	Professor, Department of Medicine, Oncology Division, Medical Oncology, Washington University School of Medicine in St. Louis. NCI Head and Neck Steering Committee and Metastatic and Recurrent Head & Neck Cancer Task Force
Nabil Saba, MD	Director of the Head and Neck Cancer Medical Oncology Program at Winship Cancer Institute of Emory University, Professor and Vice Chair for Quality and Safety in the Department of Hematology and Medical Oncology and holds a joint appointment as Professor in the Department of Otolaryngology at Emory University School of Medicine. Chair of the National Cancer Institute's task force for recurrent metastatic head and neck cancer and Chair of the Rare Tumors Task Force of the National Cancer Institute's Head and Neck Cancer Steering Committee. Member of the NRG Oncology and Eastern Cooperative Oncology Group (ECOG) Head and Neck Cancer Core Committees, the ASCO clinical guidelines committee, and the ASCO Head and Neck Guideline Advisory Group.

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.