

Pepinemab – Anti-SEMA4D Antibody for Cancer Immunotherapy



**KEYNOTE-B84 Study
in HNSCC**

June 10, 2022

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 Head and Neck cancer, 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, the 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 the Company’s 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 most recent year end Annual Report on Form 10-K and subsequent filings with the SEC.

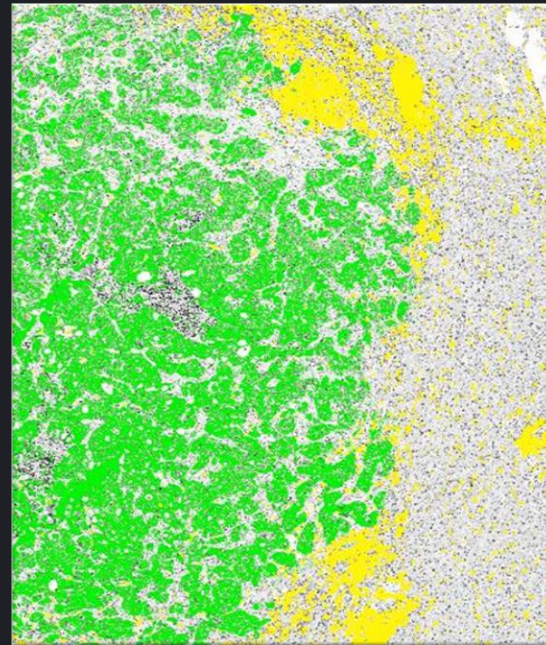


WHY DOES IMMUNE RESPONSE FAIL IN TUMORS?

Immune Exclusion

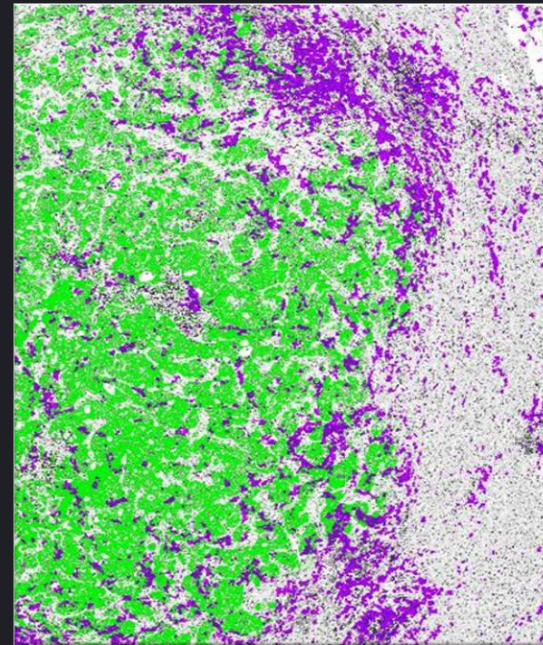
Activated T-cells and dendritic cells can't penetrate tumor

Sema4D is expressed at tumor margin



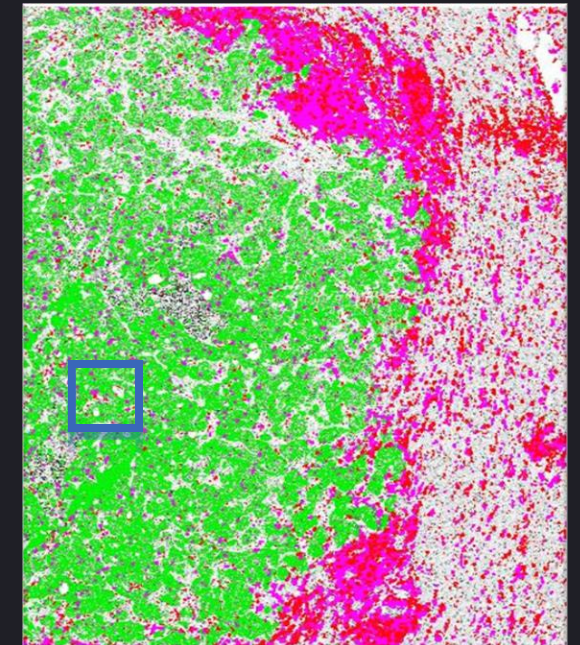
● Tumor ● SEMA4D

Sema4D binds PLXN receptors on DCs and restricts penetration



● Tumor ● Dendritic Cells (CD11c)

T-cells are excluded from tumor



● CD8+ ● CD4+ T Cells

Pro-inflammatory cells are excluded from 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.

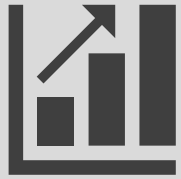
Dendritic Cells express receptors for SEMA4D and are heavily excluded at the invasive edge.

Human metastatic colorectal tumor, in collaboration with Emory University (NCT03373188)

UNIQUE MECHANISM

Pepinemab:

1



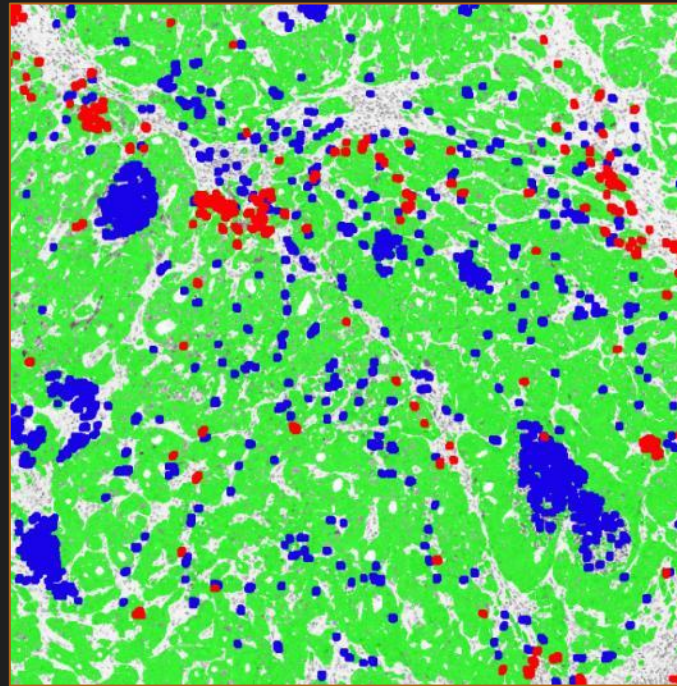
↑ cytotoxic T cells

2



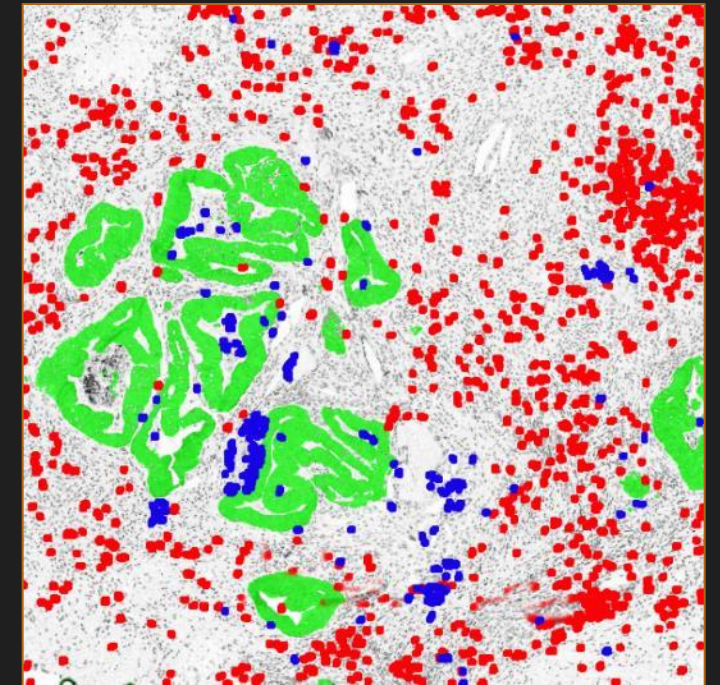
↓ inhibitory suppressor cells

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

Human metastatic colorectal tumor, in collaboration with Winship Cancer Institute, Emory University integrated biomarker study (NCT03373188), Wu et al. Ann Surg Oncol. 2021

RATIONALE FOR TREATMENT OF HNSCC

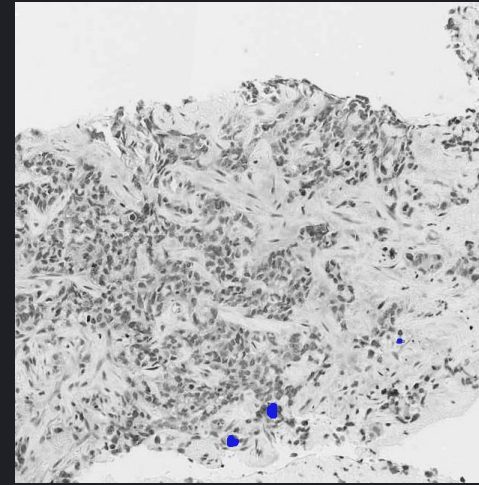
Head and Neck cancer (HNSCC)

- Data suggest that 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

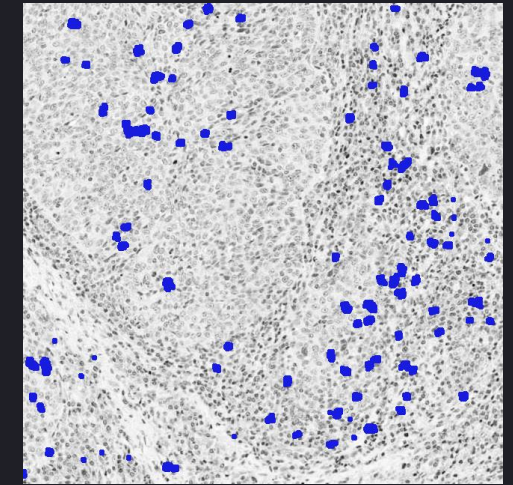


Hypothesis: Inhibiting MDSC with pepinemab may enhance response to pembrolizumab in HNSCC

● Myeloid Derived Suppressor Cells (MDSC)

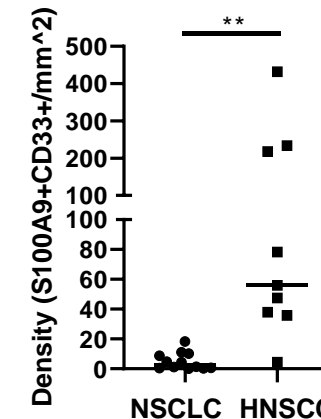


NSCLC



HNSCC

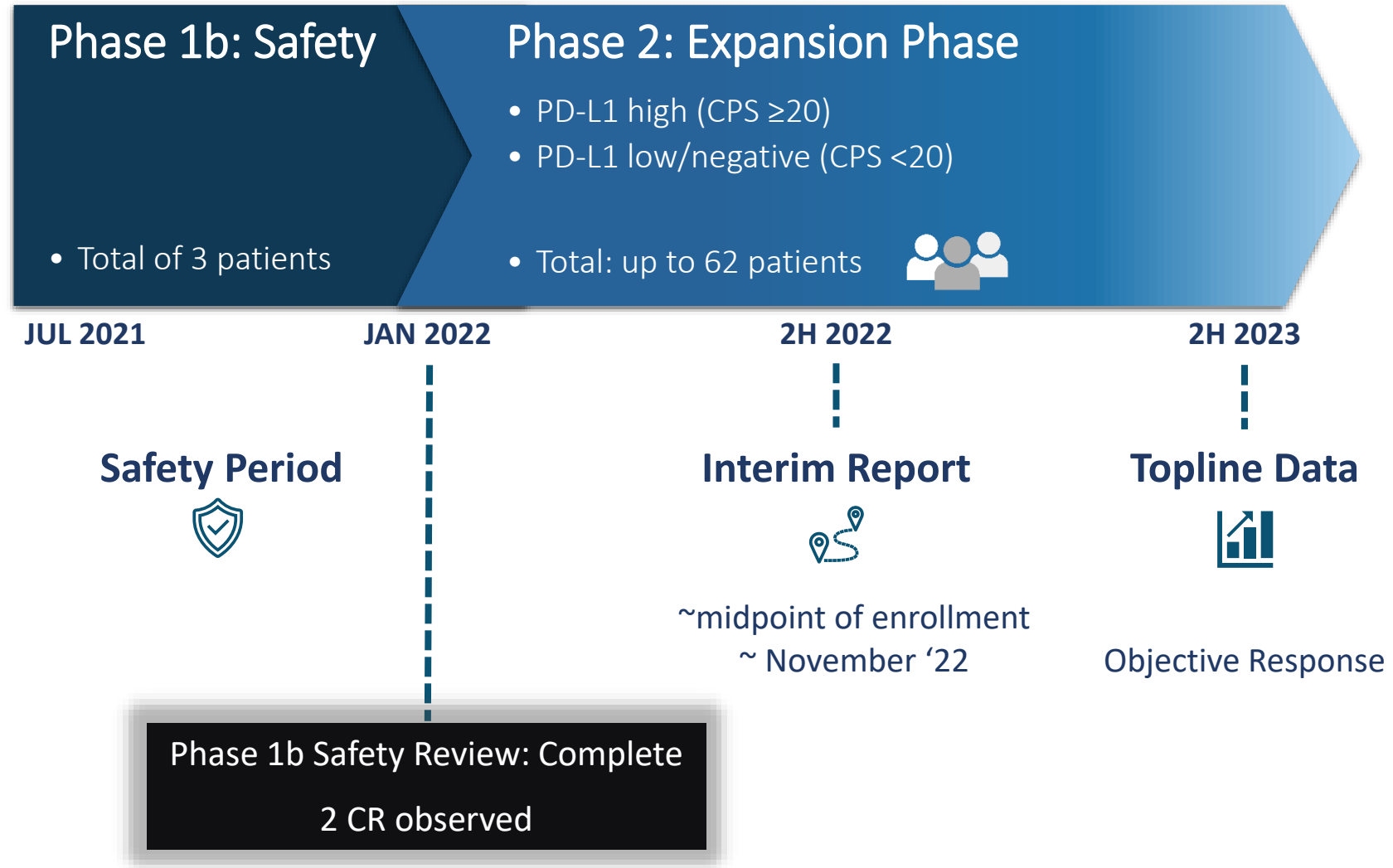
MDSC Density
NSCLC vs HNSCC



KEYNOTE B84 HEAD AND NECK CANCER TRIAL

- All patients receive standard of care Keytruda®, plus pepinemab for first-line treatment
- Ph1b Safety: COMPLETE
 - Appeared to be well tolerated
 - RP2D: 20mg/kg pepi and 200mg pembro, Q3W
- Ph2 Expansion: Accruing
- 17 of 18 sites in USA now actively enrolling
- Open-label, continuous monitoring

KEYNOTE B84: pepinemab + Keytruda® for first-line treatment of recurrent or metastatic head and neck cancer



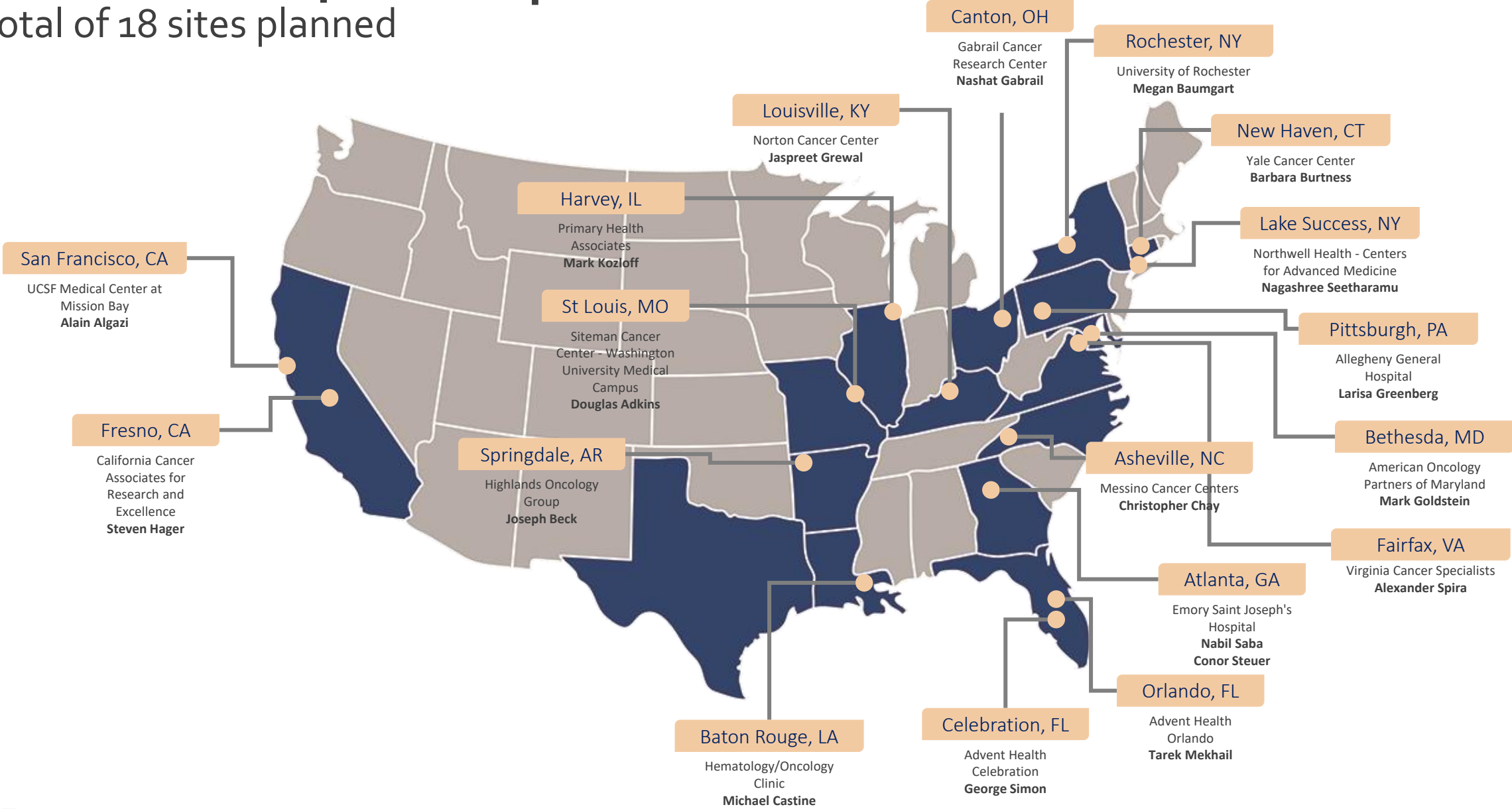
KEYNOTE-B84:

Case studies to illustrate differences in positive response profiles

	Biopsy	Scans			Biomarkers	Adverse Events
	week 5	week 9	week 15	week 21		
Case Study # 1: CR (confirmed) <i>Oropharyngeal cancer</i> <i>Target lesions: metastases to lung</i> <i>(Left 11mm, Right 15mm)</i>	NO malignancy	19% decrease, SD	100% decrease, CR	Confirmed, CR Now 42 Weeks	PD-L1 CPS<20 HPV negative	<i>none of notable severity</i>
Case Study # 2: CR (confirmed) <i>Larynx cancer with direct invasion into thyroid and neck</i> <i>Target lesions: neck mass (37mm)</i>	NO malignancy	100% decrease, CR	Confirmed, CR	Continued CR Now 27 Weeks	PD-L1 CPS<1 HPV negative	<i>Grade 1 rash</i>
Case Study # 4: PR (unconfirmed) <i>Oropharyngeal cancer</i> <i>Target lesions: metastases to lung</i> <i>(Left 24 mm, Right 23 mm)</i>	Not available	6% decrease, SD	72% decrease, PR	Anticipated July '22	PD-L1 CPS≥20 HPV negative	<i>none of notable severity</i>

KEYNOTE B84 Site Map

Total of 18 sites planned



Pepinemab – Anti-SEMA4D Antibody for Huntington's and Alzheimer's Disease

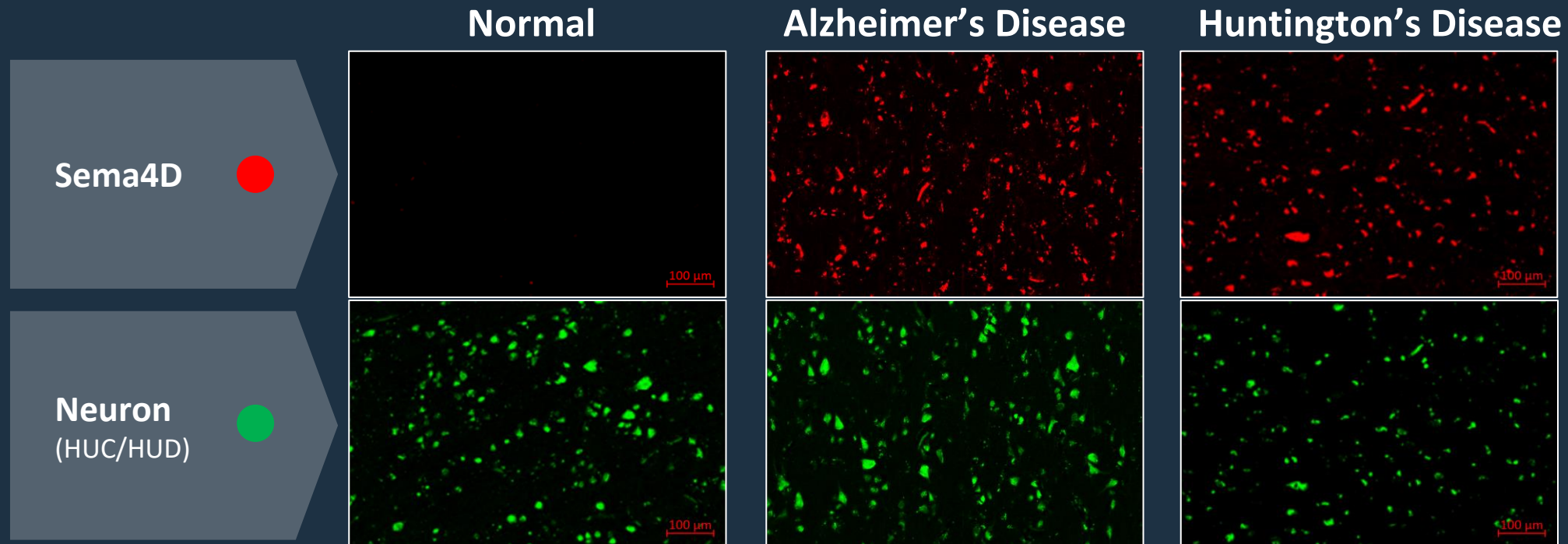


Unique Targets

Novel Mechanisms

New Medicines

SEMA4D IS UPREGULATED IN NEURONS DURING ALZHEIMER'S AND HUNTINGTON'S DISEASE PROGRESSION



Semaphorin 4D is upregulated in neurons of diseased brains and triggers astrocyte reactivity

Elizabeth E Evans, Vikas Mishra, Crystal Mallow, Elaine Gersz, Leslie Balch, Alan Howell, Ernest S. Smith, Terrence L. Fisher, Maurice Zauderer*

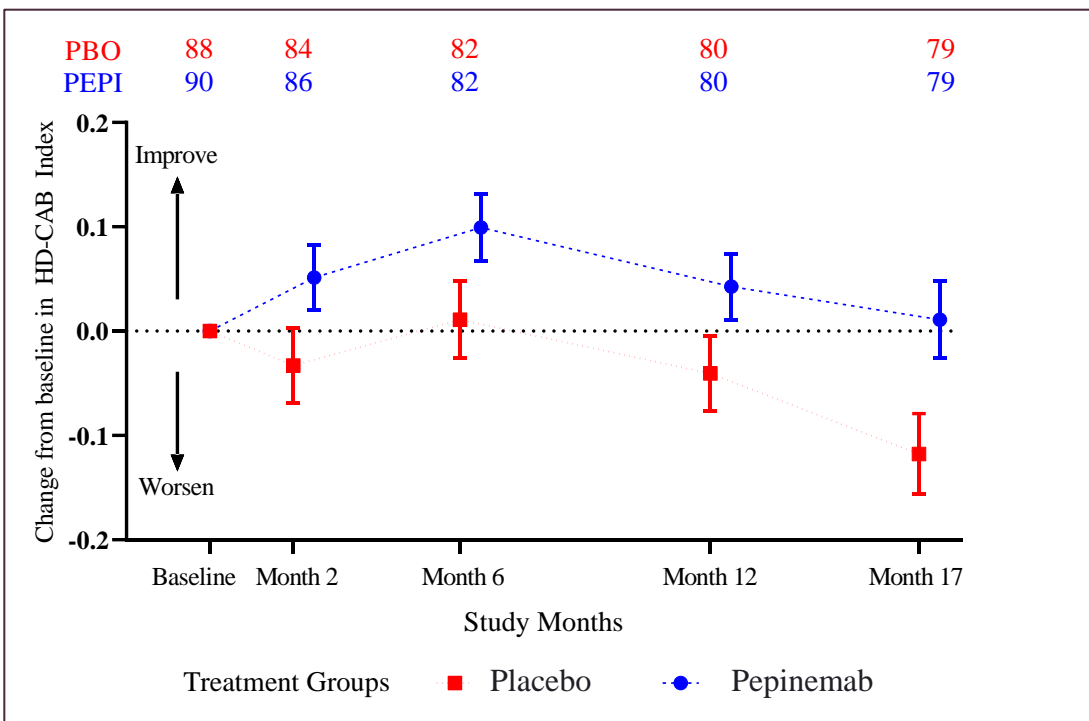
Journal of Neuroinflammation, 2022, *In Press*.

COGNITIVE ASSESSMENT BATTERY (HD-CAB)

Co-Primary and pre-specified Exploratory analysis



HD-CAB Composite Index of 6 Cognitive Assessments



Andrew Feigin et al. *Nature Medicine*, 2022, *In Press*.



Two-item HD Cognitive Assessment: Pre-specified Co-Primary

LS Mean Difference Estimate (95% CI)	One-sided p-value	Favors Pepinemab	Critical value
OTS: -1.98 (-4.00, 0.05)	0.028	Yes	No [0.025]
PTAP: 1.43 (-0.37, 3.23)	0.060		

HD-CAB Composite Index: Pre-specified Exploratory

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

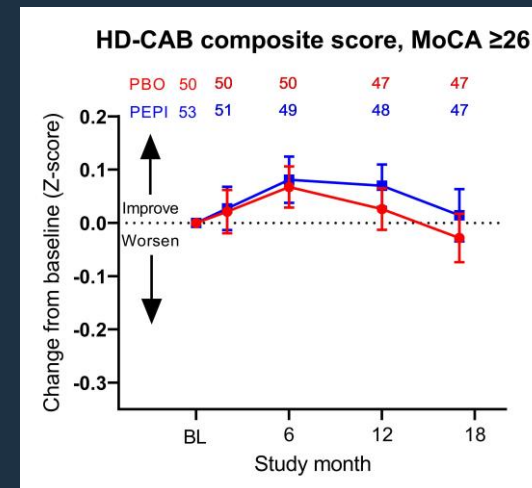
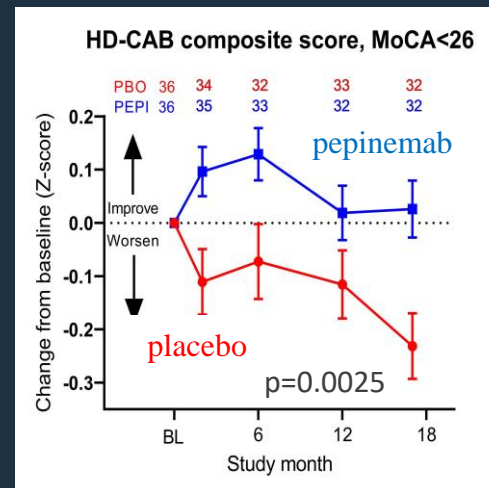
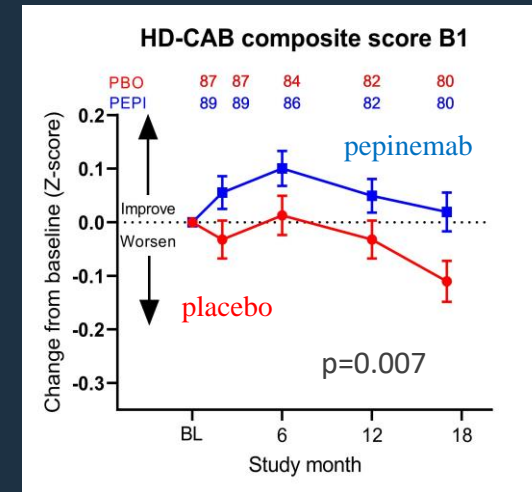
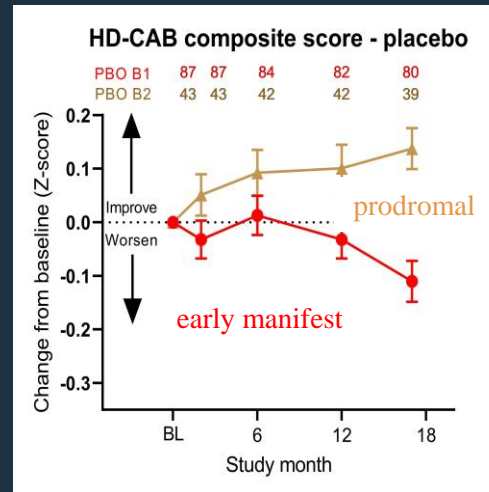
COGNITIVE ASSESSMENT BATTERY (HD-CAB)

Exploratory and Post-hoc analysis



- “Learning effect” is lost when HD symptoms become manifest
- Pepinemab treatment restores the ability to benefit from experience (ie, to learn)

Pepinemab antibody blockade of SEMA4D in early Huntington’s Disease: the randomized, placebo-controlled, phase 2 SIGNAL trial
 Andrew Feigin, Elizabeth E. Evans, Terrence L. Fisher, John E. Leonard, Ernest S. Smith, Alisha Reader, Vikas Mishra, Richard Manber, Kimberly A. Walters, Lisa Kowarski, David Oakes, Eric Siemers, Karl D. Kieburtz, Maurice Zauderer*, and the Huntington Study Group SIGNAL investigators
Nature Medicine, 2022, In Press.



ALZHEIMER'S DISEASE

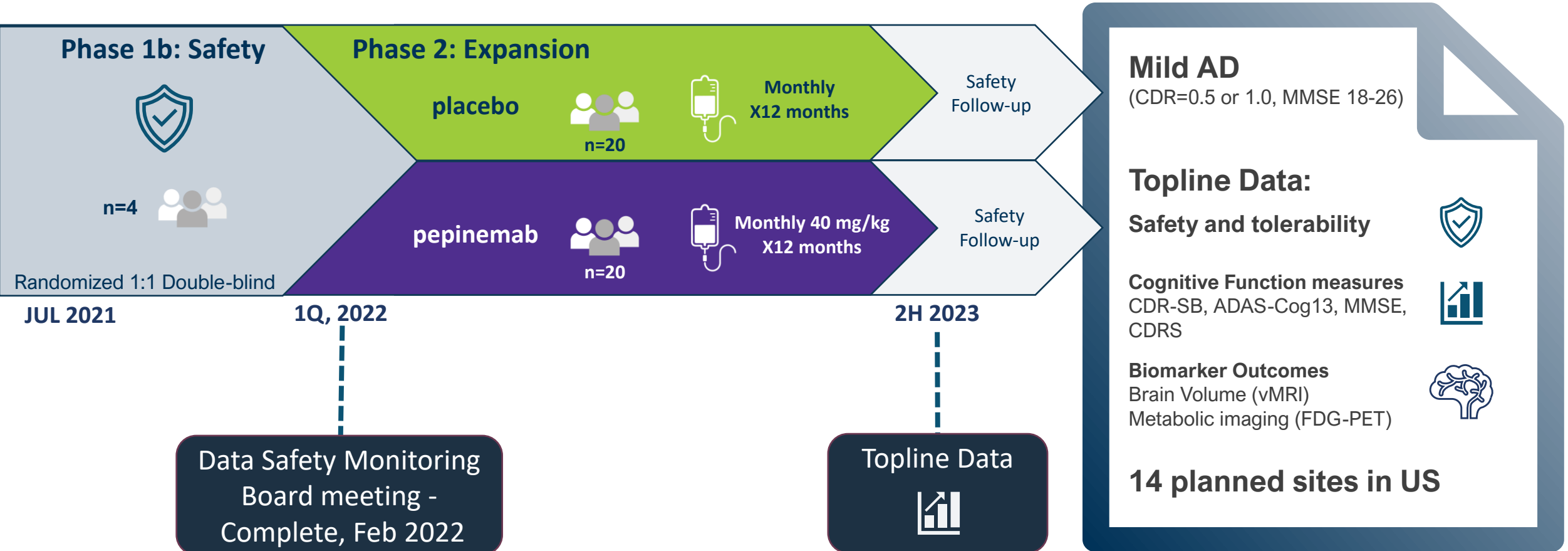
Phase 1b/2 Trial Design



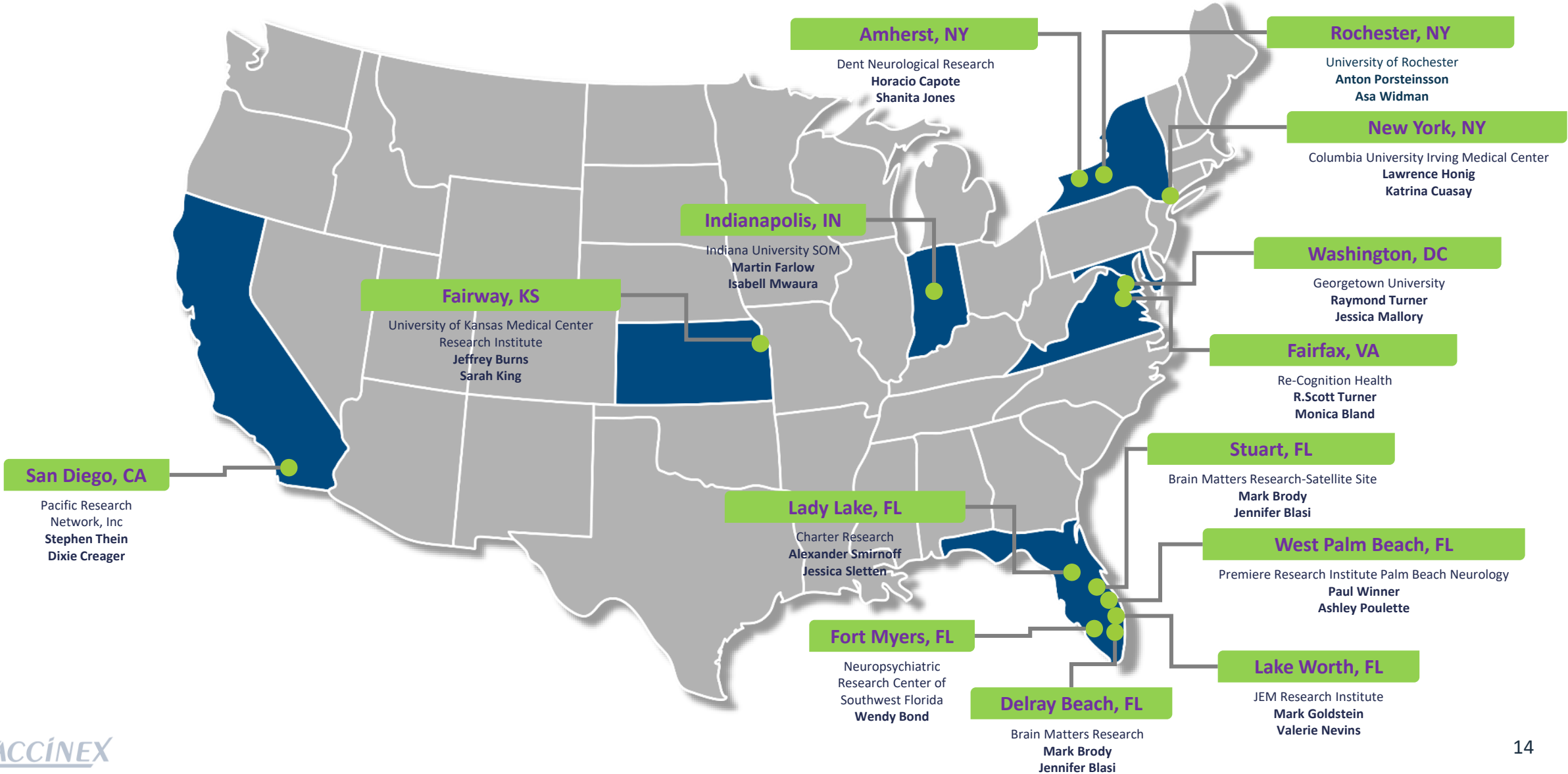
Funding by



Alzheimer's
Drug Discovery
Foundation



Signal-AD Site Map





INCORPORATED
2001



HEADQUARTERS
Rochester, NY



EMPLOYEES
39



IPO NASDAQ VCNX
August 2018



CAPITAL RAISE
FEBRUARY 2021 \$32.0, JANUARY 2022 \$13.2 M



CASH BALANCE*
\$16.8 M



SHARES OUTSTANDING*
42.66 M









ANALYSTS
BTIG (T.Shrader)

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.

*as of 31MAR2022

PIPELINE and MILESTONES



Research/Preclinical	Phase 1	Phase 2	Phase 3	Partner/Funding	Milestone
Pepinemab Antibody Platform (anti-Semaphorin 4D Mab)					
Oncology					
Pepinemab COMBO with Avelumab in Non Small Cell Lung Cancer			CLASSICAL- Lung	 Merck, KGaA Darmstadt	Complete, Published 2021
Pepinemab COMBO with Pembrolizumab in Head and Neck Cancer			KEYNOTE- B84	 Merck, MSD	Ongoing Next data 2H 2022
Neurology					
Pepinemab in Huntington's Disease (Orphan Drug and Fast Track Designations)				  Alzheimer's Drug Discovery Foundation	Complete, Nat. Med in press
Pepinemab in Alzheimer's Disease					Ongoing Data 2H 2023

All Studies Sponsored by:

