Nasdaq: SAVA

CASSAVA sciences

Remi Barbier - President & CEO

Corporate Overview

June 2020

Forward-Looking Statements & Safe Harbor

This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. To identify such forward-looking statements, in some cases we use terms such as "predicts, "believes," "potential," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "should" or other words that will convey risk or uncertainty of future events or outcomes. Forward-looking statements include risks and uncertainties, including, but not limited to, expected cash use in future periods; current or future plans, if any, to raise capital via equity financings; statements regarding the status of our clinical tests, expected pace of patient enrollment in our open-label study of PTI-125; expected announcements in 2nd half 2020 regarding on-going assessments of clinical data for our Phase 2b study of PTI-125; interim or top-line test results, which are not necessarily indicative of final test results; the interpretation of test results, including potential health benefits, if any, of changes in levels of biomarkers of disease; variability in levels of biomarkers of disease; plans to have CSF samples from all Phase 2b study participants re-analyzed; the potential for a reassessment of Phase 2b study results; the planned analysis of lymphocyte, plasma and cognition data; and the measured effects of PTI-125 on cognition, if any; comments and commentaries made by our employees; the timing of validation studies with SavaDx; and potential benefits, if any, of the Company's product candidates for Alzheimer's disease.

Such statements are based largely on our current expectations and projections about future events. Such statements speak only as of the date of this presentation and are subject to a number of risks, uncertainties and assumptions, including, but not limited to, those risks relating to the ability to conduct or complete clinical studies on expected timelines, to demonstrate the specificity, safety, efficacy or potential health benefits of our product candidates, the severity and duration of health care precautions given the international outbreak of an infectious disease and including those described in the section entitled "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2019 and future reports to be filed with the SEC.

In light of these risks, uncertainties and assumptions, forward-looking statements and events discussed in this presentation are inherently uncertain and may not occur. Actual results could differ quickly, materially and adversely from those anticipated or implied in the forward-looking statements. Accordingly, you should never rely upon forward-looking statements as predictions of future events.

This presentation also may contain statistical data based on independent industry publications or other publicly available information. We have not independently verified the accuracy or completeness of the data contained in these industry publications and other publicly available information. Accordingly, we make no representations as to the accuracy or completeness of that data. You are cautioned not to give undue weight to such data.

We do not undertake any obligation to update this corporate presentation or any forward-looking statements included therein, except as required by law.

The content of this presentation is solely our responsibility and does not necessarily represent the official views of the National Institutes of Health (NIH).

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We are developing novel approaches to detect and to treat Alzheimer's disease.

Cassava (Austin, Tx) is a biotechnology company whose innovations address Alzheimer's disease, the largest potential drug market in the world, where diagnostic methods are currently limited, treatment options are inadequate and the ability to slow disease progression is non-existent.

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Meet the Team

Remi Barbier - Chairman, President & CEO

EXELIXIS® XOMA ARQULE®

Nadav Friedmann, PhD, MD - CMO, Board member

Eight FDA drug approvals prior to Cassava Sciences.

Johnson & Johnson Daiichi-Sankyo Abbott

Lindsay H. Burns, PhD - SVP Neuroscience

Abgenix élan UNIVERSITY OF CAMBRIDGE

Eric Schoen - Chief Financial Officer

VERMILLION® PricewaterhouseCoopers

Michael Zamloot - SVP Technical Operations

Four FDA drug approvals prior to Cassava Sciences.

Boehringer Ingelheim Ciba-Geigy

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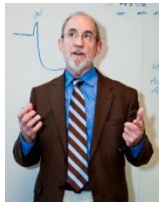
Board of Directors

Sanford Robertson

- Founder, Partner - Francisco Partners
- Formerly, Founder & Chairman - Robertson, Stephens & Company

Robert Gussin, PhD.

- Formerly, Chief Scientific Officer and Corporate Vice President, Science and Technology - J&J



Patrick Scannon, MD, PhD

- Formerly, Founder & CSO/CMO - XOMA Corporation

Michael O'Donnell

- Partner, Morrison & Foerster LLP

Rethinking Alzheimer's disease

20+ years ago

Amyloid-clearing hypothesis

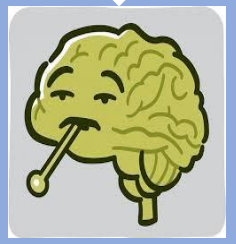
Goal is to prevent, lower or clear out, amyloid from the brain.

10+ years

Target neurodegeneration

Goal is to prevent loss of neurons, often by inhibiting breakdown enzymes in the brain.

5+ years



Target neuroinflammation

Goal is to regulate brain inflammation that may contribute to disease pathology.

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Target both neurodegeneration and neuroinflammation.

GOAL IS TO SLOW THE RATE OF DISEASE PROGRESSION.

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Pipeline Overview

Product Candidate	Description	Target Indication	Development Status
PTI-125	Proprietary, oral, small molecule drug.	Treatment for Alzheimer's disease.	Phase 2a Study – Positive results announced 2019 Phase 2b Study – Top-line results announced May 2020, additional data & analysis expected Q3 2020 Open-label Study – Patient enrollment is on-going
SavaDx	Antibody-based diagnostic system.	Detection of Alzheimer's disease with a simple blood test.	Analytical Development/Clinical Testing

Cassava Sciences owns worldwide rights to its pipeline, without royalty or milestone obligations.

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PTI-125 – A Novel Drug for Alzheimer's disease

- **PTI-125 is Cassava's proprietary, oral, small molecule drug candidate to treat Alzheimer's disease and other dementias.**
  - Program benefits from long-term scientific & financial support from the National Institutes of Health (NIH).

- **PTI-125 reduces both neurodegeneration and neuroinflammation by binding to a single target.**

- **Cassava is conducting a comprehensive Phase 2 clinical testing program of PTI-125 in Alzheimer's disease, in collaboration with clinical/scientific advisors.**

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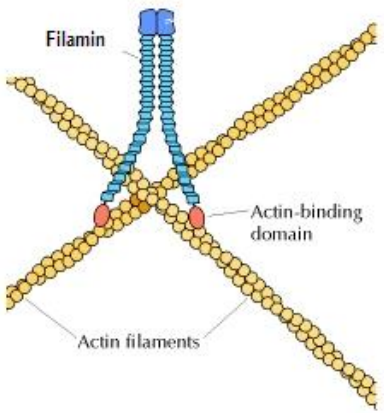
The Target of PTI-125 is *Altered* Filamin A (FLNA)

FLNA is an intracellular scaffolding protein anchored in the cell membrane.

FLNA interacts with > 90 proteins, influencing many signaling pathways.



The Alzheimer's brain carries an *ALTERED* conformation of FLNA.

Altered FLNA is critical to amyloid beta's toxicity.

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PTI-125 Mechanism of Action

- **Altered FLNA enables $A\beta_{42}$ signaling via two different receptors:**
  - α7-nicotinic acetylcholine receptor (α7nAChR) → hyperphosphorylates tau
  - Toll-like receptor 4 (TLR4) → releases inflammatory cytokines

- **PTI-125 binds to the *altered* form of FLNA, restores its proper shape/function, suppresses $A\beta_{42}$ signaling via α7nAChR and TLR4.**
  - Through a single target, PTI-125 reduces both neurodegeneration and neuroinflammation

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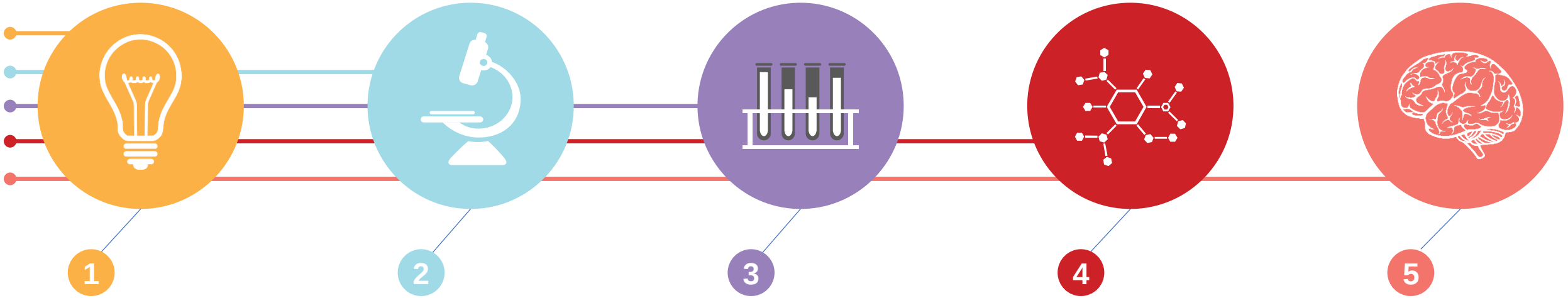
10-Year Development Program



<2008
Basic research around neurobiology of Filamin A (FLNA).

2009
Discovery that altered FLNA associates with α7nAChR when Aβ signals.

2010
Screening/testing of compounds that bind altered FLNA and block α7nAChR/Aβ interaction.

2011
PTI-125 binds altered FLNA with high affinity, blocks α7nAChR/Aβ interactions. Preclinical testing of PTI-125.

2017 - present
Clinical testing of PTI-125. Positive results reported in Alzheimer's patients.

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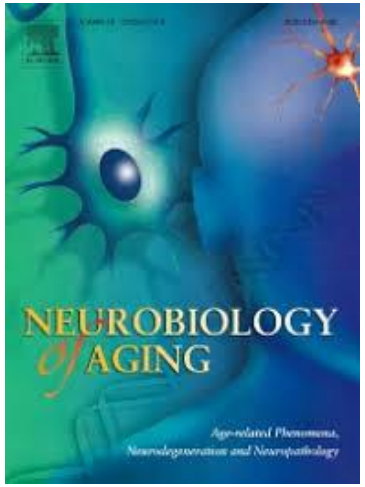
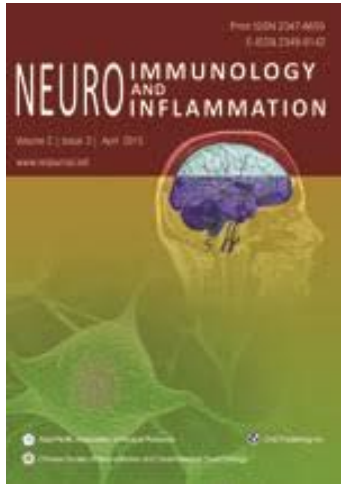
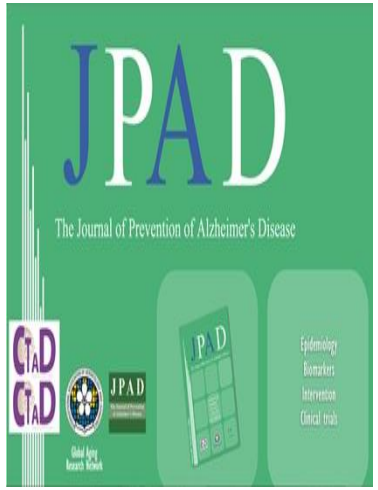
Science is Peer-reviewed

The underlying science for PTI-125 has been subject to the scrutiny of many experts in the field……







….including NIH, which has awarded our science programs >$10 million in research grant awards.

National Institutes of Health

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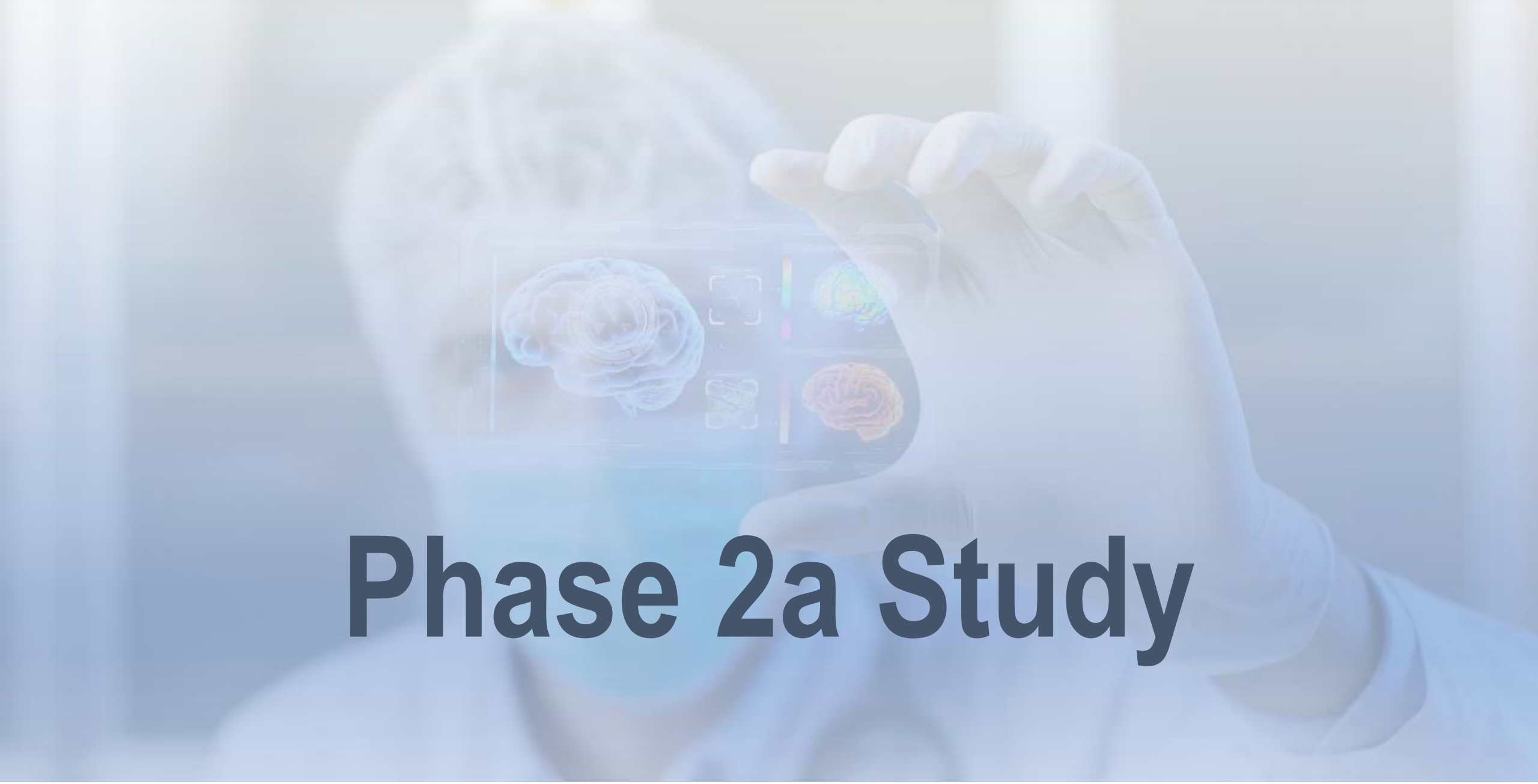

Phase 2a Study

Phase 2a Study Design

- **Objective:** Safety, PK and biomarkers under an IND filed by Cassava Sciences
- **Study Design:** First-in-patient, open-label treatment at 5 study sites in the US
- **Patients:** Mild-to-moderate Alzheimer's, MMSE ≥ 16 ≤ 24, age 50-85
- **Key Inclusion:** Cerebrospinal fluid (CSF) ratio of total tau/$A\beta_{42}$ ≥ 0.30
- **Enrollment:** 13 patients
- **PTI-125 Dose:** 100 mg oral tablets, twice-daily for 28 continuous days
- **Biomarkers:** CSF samples collected at screening and Day 28
  Blood samples for plasma/lymphocyte markers at Days 1, 14 and 28

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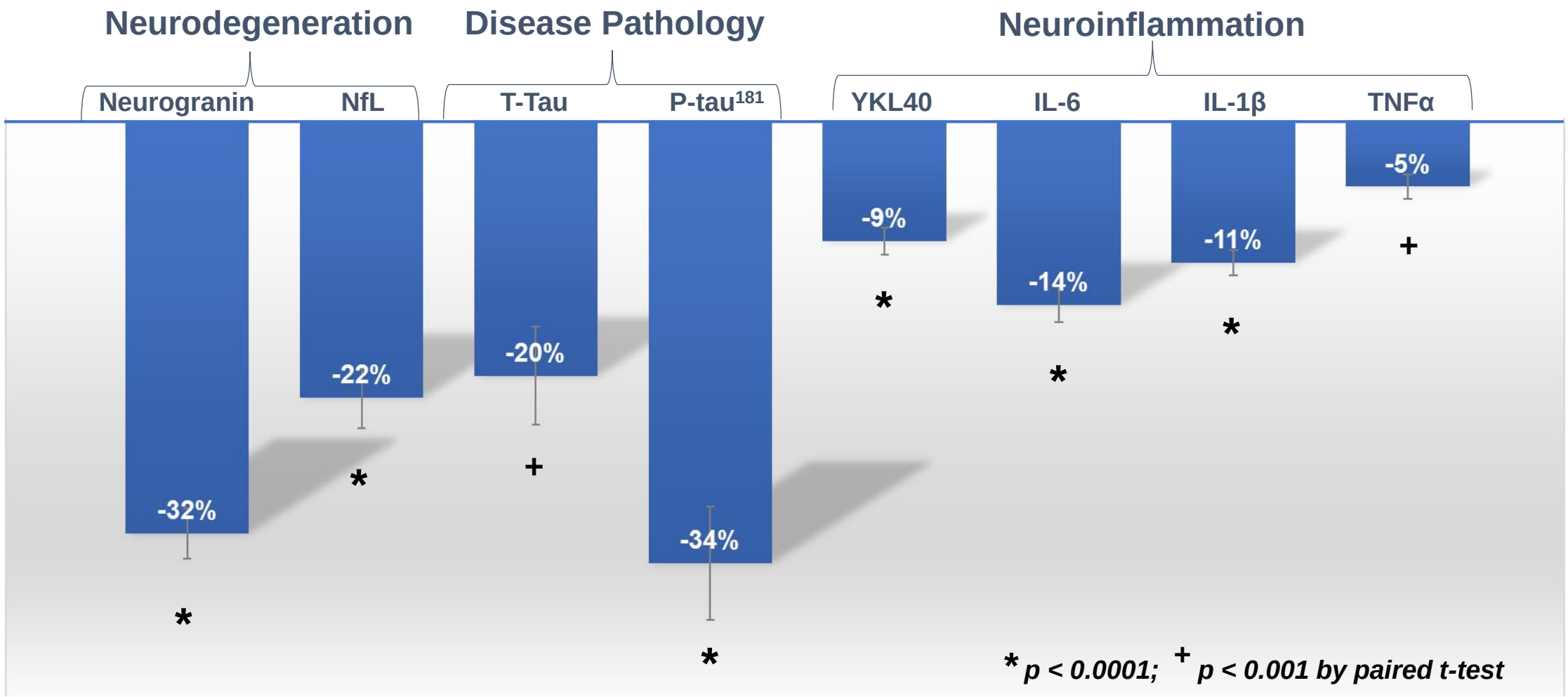
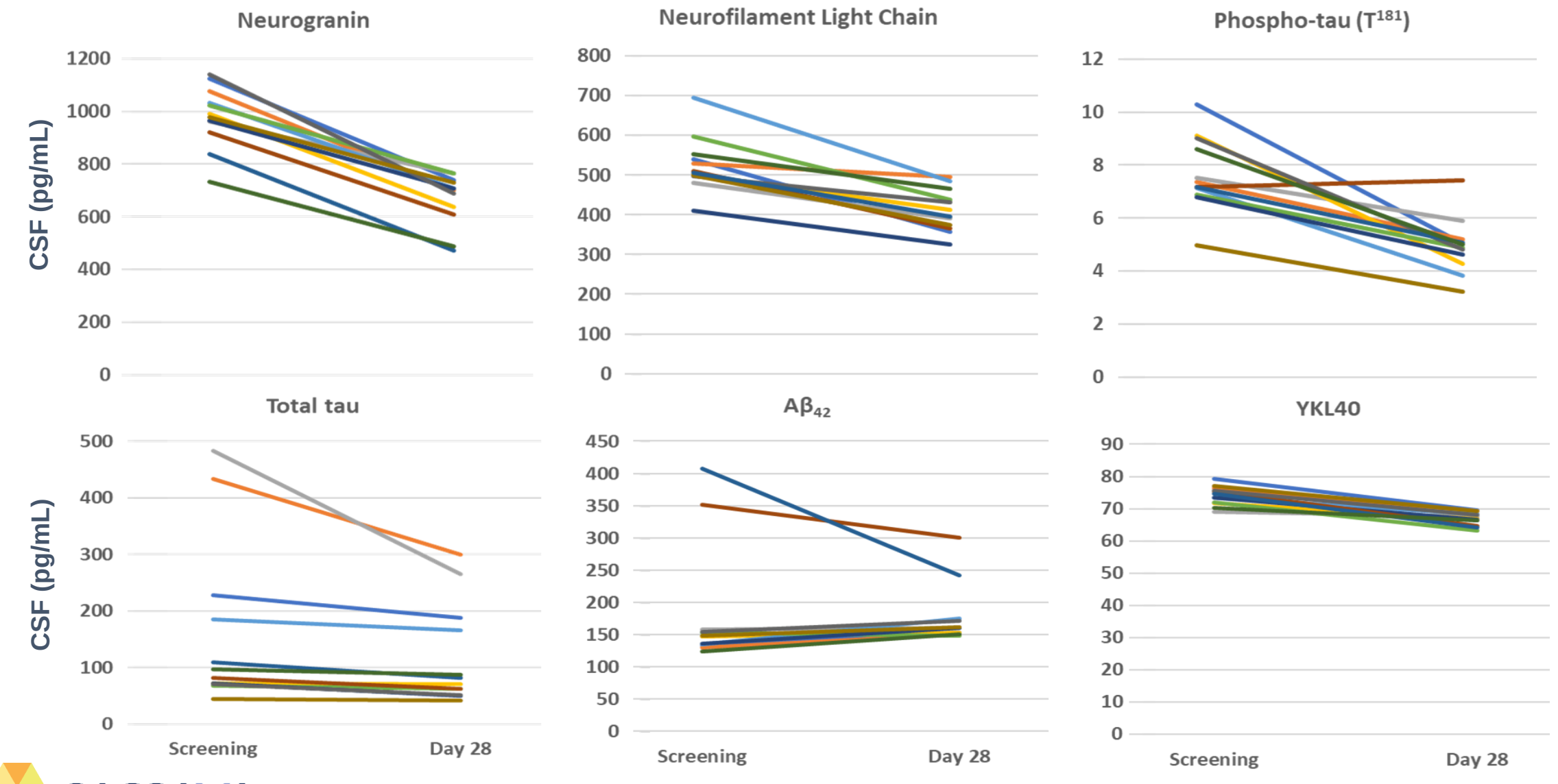
Phase 2a Results - CSF Biomarkers (Baseline to Day 28, sandwich ELISA)



Phase 2a Results: Individual Patient Responses



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Phase 2a Study Conclusions

- **A first-in-patient study with PTI-125, a new drug candidate, demonstrated:**
  - Evidence of target engagement and mechanism of action in Alzheimer's patients
  - Significant improvements in biomarkers of disease
  - Clear correlation between levels of certain biomarkers
  - Clinical validation for FLNA as a target for drug development
  - No drug related safety issues

- **The beneficial drug effects observed in study Phase 2a are consistent with the PTI-125's preclinical data and mechanism of action.**

- **Full study results published in *Journal of Prevention of Alzheimer's Disease* (JPAD, Feb 2020).**

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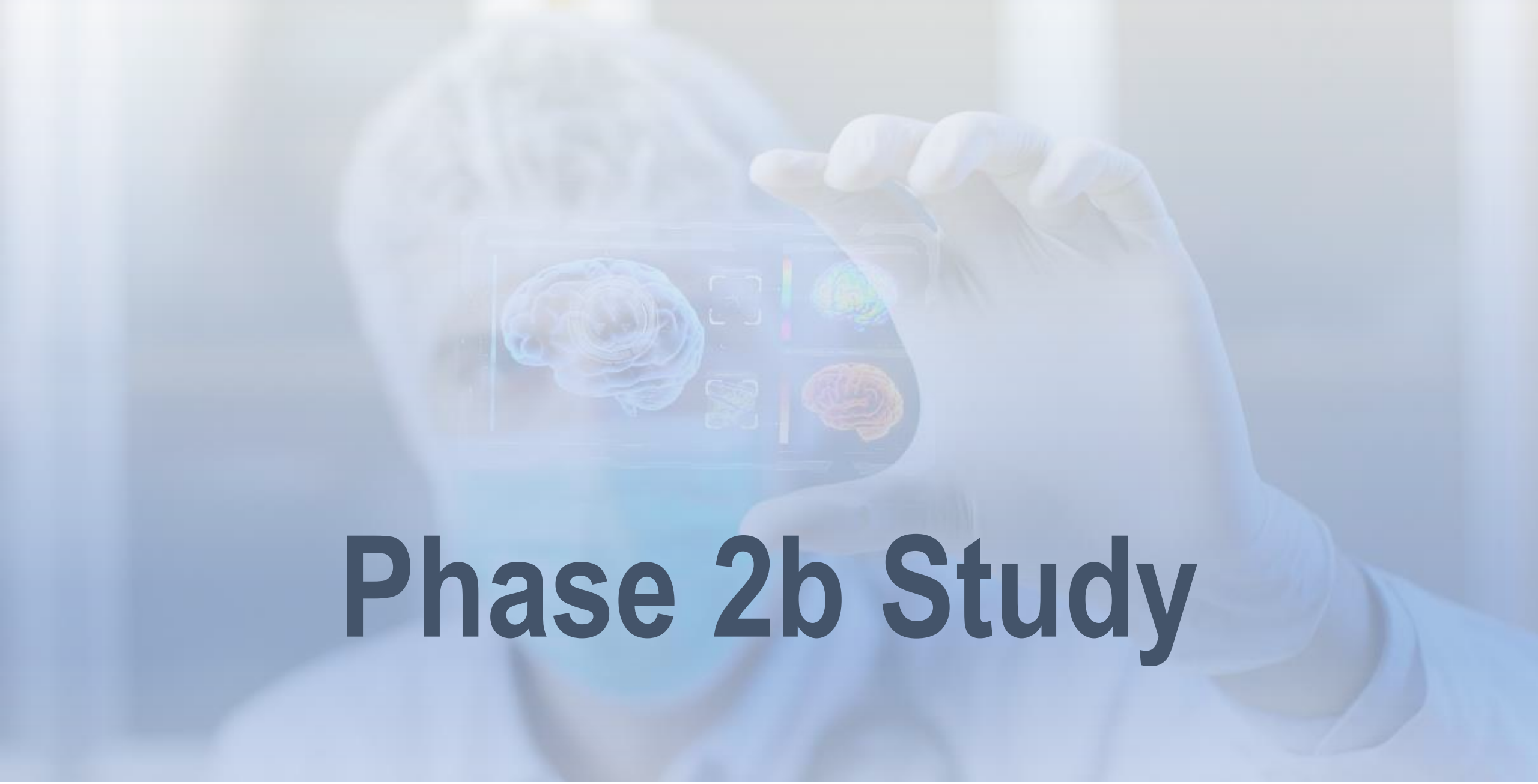

Phase 2b Study

Phase 2b Study

Phase 2b is a confirmatory study of the effects of PTI-125 in patients with Alzheimer's disease.

	Phase 2a	Phase 2b
Status:	Completed	Completed
Design:	Open-label	Blinded, randomized, placebo-controlled
PTI-125 Dose:	100 mg b.i.d.	50 & 100 mg b.i.d.
Treatment Period:	28 days	28 days
# Patients:	13	64
Alzheimer's Stage:	Mild-to-moderate	Mild-to-moderate
MMSE Score:	16-24	16-26
Primary Endpoint:	Biomarkers (CSF/plasma)	Biomarkers (CSF/plasma)
Cognition Endpoint:	No	Yes

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Phase 2b Study Design

- **Objective:** Safety and biomarkers under an IND filed with FDA
- **Study Design:** Randomized, placebo-controlled, U.S. multi-site study
- **Patients:** Mild-to-moderate Alzheimer's, MMSE ≥ 16 ≤ 26, age 50-85
- **Key Inclusion:** Cerebrospinal fluid (CSF) ratio of total tau/$A\beta_{42}$ ≥ 0.30
- **Enrollment:** 64 patients
- **Three Arms:** Placebo, 50mg or 100mg oral tablets, twice-daily for 28 continuous days
- **Biomarkers:** CSF samples collected at screening and Day 28
  Blood samples for plasma/lymphocyte markers at Days 1, 14 and 28
- **Cognition Assay:** Cambridge Neuropsychological Test Automated Battery (*CANTAB*)

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Top-line Phase 2b Study Results

- **As reported in May 2020, study Phase 2b did not achieve its pre-specified primary outcome, defined as a drug effect on CSF levels of tau protein and other biomarker assessments.**
  - PTI-125 significantly (p<0.035) reduced CSF levels of IL1-beta, a secondary outcome.
  - Effects of PTI-125 on cognition remains under evaluation & analysis.

- **Unexpectedly, placebo-treated patients showed significant swings (in both directions) in levels of certain CSF biomarkers of disease over 28 days.**
  - For example, placebo-treated patients recorded changes in levels of CSF tau and p-tau ranging from -54% to +34% and -49% to +253%, respectively, from baseline to Day 28.

- **Unexpectedly, placebo-treated patients showed no clear correlation between levels of certain biomarkers of disease.**

High variability in levels of biomarkers in the control group may drive a reassessment of study results.

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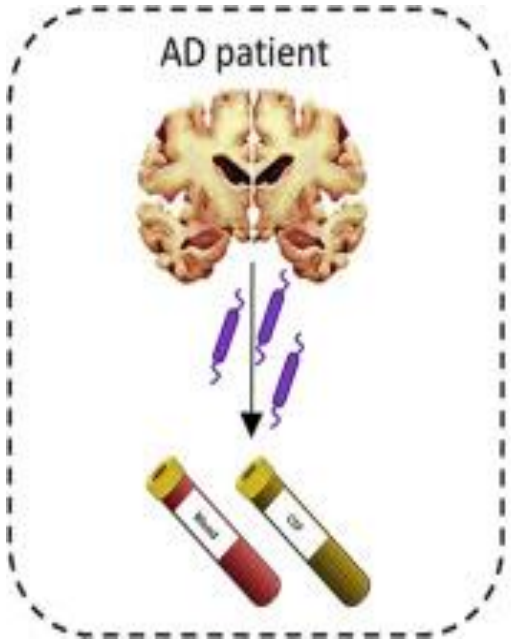
Measuring CSF Biomarkers

Outside labs used a different type of enzyme linked immunosorbent assay (ELISA) to detect and quantify CSF biomarkers in our two Phase 2 studies.



The Phase 2b study:

- Used an automated Digital ELISA[1] technique on a high-throughput machine with detection limits in the femtomolar range, i.e. highly sensitive to small assay volumes.

The Phase 2a study:

- Used a manual Sandwich ELISA[2] technique with detection limits in the picomolar range, i.e. less sensitive to small assay volumes.

Generally, a trade-off: more sensitivity = more variability
less sensitivity = less variability

Footnotes

1 - Amplifies a digital fluorescent signal that corresponds to analyte concentration.

2 - Quantifies analyte concentrations "sandwiched" between two antibodies, i.e. the capture antibody and detection antibody.

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Data Variability in Phase 2b Study Results

- **CSF samples in the Phase 2b study were measured on an automated machine (using digital ELISA) that is highly sensitive and generates variable results.**
  - Difference between measurements of the same sample in two different runs may exceed ± 20%.
  - Inaccuracies are amplified by machine miscalibration, improper shut-down, deferred maintenance, etc.
  - Implicitly, a placebo-treated patient, who has no actual change in levels of a biomarker from baseline to 28 days, could record a ± 40% change in a biomarker through use of the automated machine.

- **Another potential source of data variability may include differences in sample storage or handling among clinical sites, or other causes, all of which are difficult to establish or assess.**

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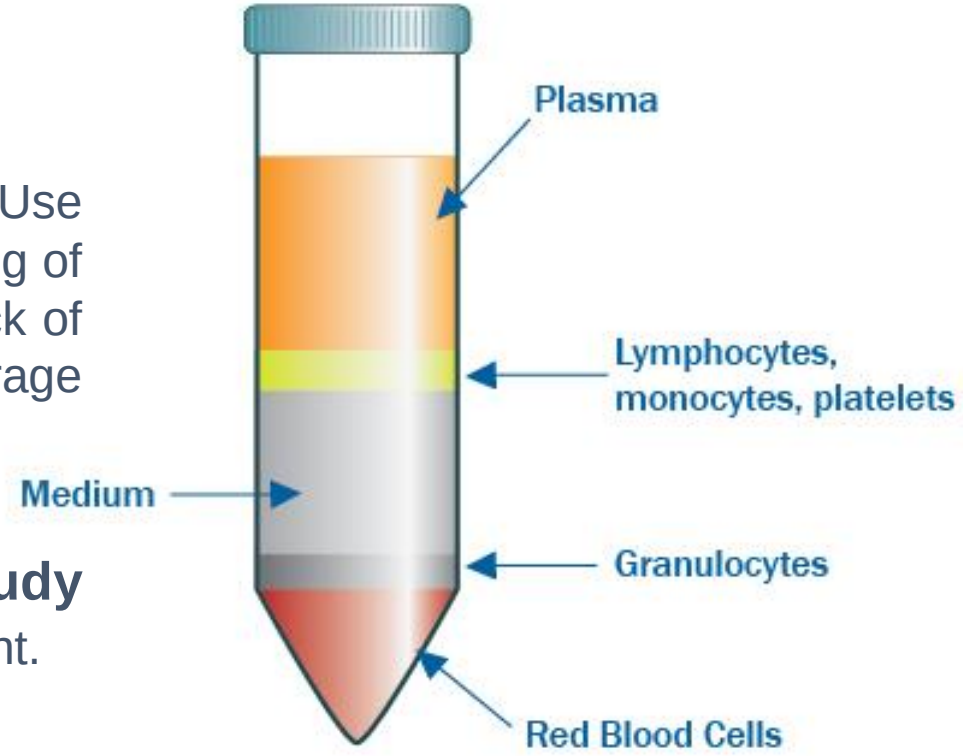
Strategy to Reassess Phase 2b Study Results

In the months ahead, we plan to:

- ✓ **Re-analyze CSF samples from all study participants**….. Use of sandwich ELISA by outside lab may provide better understanding of overall study outcome, *provided*, however, that our remaining stock of CSF samples are not degraded due to differences in sample storage or handling among clinical sites, or other causes.

- ✓ **Analyze lymphocyte and plasma samples from all study participants…..**may provide direct evidence of target engagement.

- ✓ **Evaluate effects of PTI-125 on cognition….**may provide earliest evidence for stabilization, or even reversal, of cognitive decline in patients with Alzheimer's disease.



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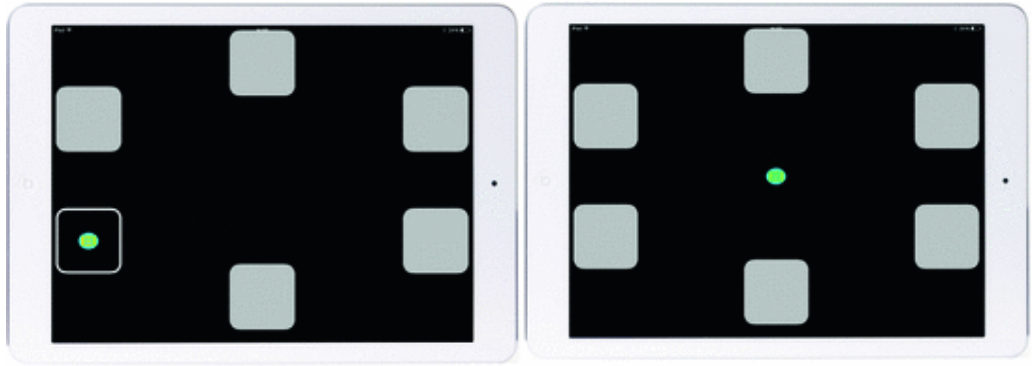
Cognition Endpoint in Phase 2b Study

- **Our Phase 2b study used the Cambridge Neuropsychological Test Automated Battery (*CANTAB*) to evaluate cognition.**



Stage 1: Encoding Stage 2: Retrieval

- **CANTAB's primary endpoint, Paired Associates Learning (PAL), assesses visual memory and new learning skills – independent of language skills, speed or gender.**
  - Patients learn to pair two items in memory – object & location of object
  - Patients are exposed to progressively more difficult levels of testing
  - Outcome measures = number of errors made by participants, so…….

Lower score is better.

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Summary

- High variability in levels of biomarkers in the study control group, and other factors, may drive a reassessment of overall results for Phase 2b.
- In the months ahead, we plan to re-analyze CSF biomarkers from all study participants to better understand the outcome of Phase 2b.
- We are evaluating the effects of PTI-125 on cognition.

We expect to announce top-line results of these analyses approx. Q3 2020.

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On-going Open-label Study

- **In March 2020, we announced the initiation of an open-label study to evaluate PTI-125 in approximately 100 patients with mild-to-moderate Alzheimer's disease.**

- **We continue to see strong interest in this study from patients and physicians.**
  - In May 2020, we announced this study was approximately 20% enrolled.

- **Continues to be substantially funded by a grant award from NIH.**

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SavaDx

SavaDx: Our Investigational Diagnostic for Alzheimer's

- The underlying science for PTI-125 supports the development of a diagnostic technology to detect Alzheimer's disease with a simple blood test, called SavaDx.
- Goal is to detect Alzheimer's disease before the appearance of memory loss.
- SavaDx development plan benefits from long-term scientific & financial support from NIH.

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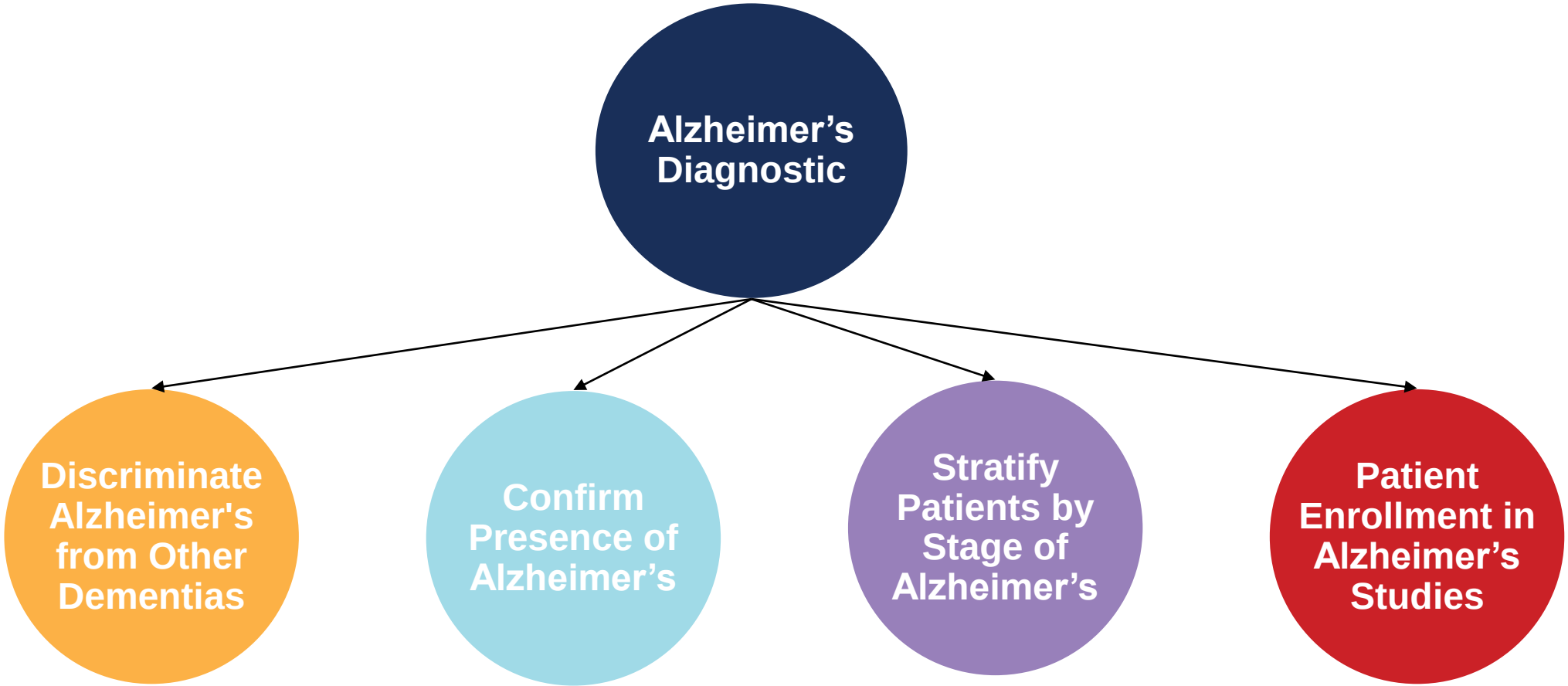
Profound Need for an Alzheimer’s Diagnostic Test

Goal is to identify people destined to develop Alzheimer’s long before symptoms occur and to cease — or at least slow down — brain damage before it is too late.



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SavaDx: Topline Study Results

In blinded studies, SavaDx detected more than 10-fold separation between Alzheimer's patients and age-matched normal controls or young cognitively intact subjects (N~232).

First Clinical Test

N=44
Site A (US)

Positive Result:
>10-fold separation of Alzheimer's patients from normal, healthy controls.

Second Clinical Test

N=88
Site B (US)

Positive Result:
>10-fold separation of Alzheimer's patients from normal, healthy controls.

Third Clinical Test

N=100+
Site C (Europe)

Positive Result:
>10-fold separation of Alzheimer's patients from normal, healthy controls.

Fourth Clinical Test

N=44 Site D (Asia)

Inconclusive result due to failure of commercial antibody.
We are currently developing a proprietary antibody system for use with SavaDx.

In 2020, we expect to initiate a validation/disease specificity study of SavaDx.

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Finance and Milestones

Key Financials

Nasdaq ticker: SAVA	
Shares Outstanding	24.8 million
Warrants Outstanding	1.6 million
Total Outstanding =	***26.4 million***

Unaudited Financials	
Cash Balance at March 31, 2020	≈$25.6 million
Expected Net Cash Use Full-year 2020	≈$ 5 million
No Debt	

Our scientific programs continue to be supported by funding from the National Institutes of Health (NIH): $2.9 million of new NIH research grant awards announced in 2020.

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2020 Anticipated Key Milestones

Product Candidate	Description	Anticipated Milestone
PTI-125	Proprietary, small molecule drug candidate for the treatment of Alzheimer's disease.	❑ Re-analyze CSF biomarkers from study participants to better understand the outcome of Phase 2b in Alzheimer's disease. ❑ Analyze lymphocyte & plasma samples from our Phase 2b study. ❑ Evaluate effects of PTI-125 on cognition in our Phase 2b study. ❑ Continue patient enrollment for an open-label study of PTI-125 in Alzheimer's disease.
SavaDx	Blood-based investigational diagnostic to detect Alzheimer's.	❑ Development of proprietary antibodies and other detection systems. ❑ Initiation of a validation/disease specificity study of SavaDx. ❑ Technical update at a major scientific conference.

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THANK YOU !

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Scientific Advisory Board

Jeff Cummings, MD
Research Professor of the Department of Brain Health, UNLV and Director of the Center for Neurodegeneration and Translational Neuroscience of the Cleveland Clinic Lou Ruvo Center for Brain Health

Trevor William Robbins, CBE FRS FMedSci
Professor of Cognitive Neuroscience and former Head of the Department of Psychology at the University of Cambridge. Past President of the British Neuroscience Association.

Barbara Sahakian, FBA, FMedSci
Professor of Clinical Neuropsychology at the Department of Psychiatry and Medical Research Council/Wellcome Trust Behavioral and Clinical Neuroscience Institute, University of Cambridge.

Hoau-Yan Wang, PhD
Tenured Medical Professor at CUNY Medical School. Co-lead scientist on discovery & development of PTI-125 and SavaDx.

Steven E. Arnold, M.D.
Translational Neurology Head of the Interdisciplinary Brain Center, Massachusetts General Hospital, Harvard Medical School.

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Appendix: Key Publications

Journal of Prevention of Alzheimer's Disease
2020; DOI: 10.14283
PTI-125 Reduces Biomarkers of Alzheimer's Disease In Patients:
http://link.springer.com/article/10.14283/jpad.2020.6

Neuroimmunology and Neuroinflammation
2017;4:263-71:
Altered filamin A enables amyloid beta induced tau hyperphosphorylation and neuroinflammation in Alzheimer's disease:
http://nnjournal.net/article/view/2313

Neurobiology of Aging
(Volume 55) July 2017, Pages 99—114)
PTI-125 binds and reverses an altered conformation of filamin A to reduce Alzheimer's disease pathogenesis:
http://www.neurobiologyofaging.org/article/S0197-4580(17)30087-8/

Alzheimer's & Dementia
Volume 8, Issue 4, Supplement, 1 July 2012, Pages p259-p260
PTI-125 reduces amyloid-related Alzheimer's pathogenesis by targeting filamin A:
https://www.sciencedirect.com/science/article/pii/S1552526012008242

Journal of Neuroscience
18 July 2012, 32 (29) 9773-9784
Reducing amyloid-related Alzheimer's disease pathogenesis by a small molecule targeting filamin A
http://www.jneurosci.org/content/32/29/9773.short

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