CASSAVA sciences

NASDAQ: SAVA

CORPORATE OVERVIEW

June 2019

Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including statement about our prospects for growth, intellectual property protection, market size or growth, competitive position, regulatory agency action, and the anticipated development, timing, data readouts and therapeutic scope and value of our development stage products. You should not place undue reliance on these statements.

These statements involve significant risks and uncertainties. Our results may differ materially from those contained in such statements, including, among others: our inability to protect our intellectual property rights and to have sufficient rights or resources to develop or to commercialize our products; product competition; clinical trials of our products may fail or not be initiated or conducted in a timely manner; our products may show insufficient therapeutic or diagnostic effects or unacceptable safety profiles; adverse decisions or delays by regulatory authorities; existing preclinical and clinical data with respect to our products may not be indicative of future results; and the inability to manufacture successfully our products.

Additional factors that could cause actual results to differ significantly from those projected in our forward-looking statement are discussed in our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and recent Current Reports on Form 8-K. Our forward-looking statements are based on our current beliefs and expectations and speak only as of the date of this presentation.

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

Our Mission is to Detect & Treat Alzheimer's Disease

- **We are developing a clinical-stage, disease-modifying drug treatment for patients with Alzheimer's disease (AD).**
  - PTI-125 is a proprietary oral drug with a novel mechanism of action.
  - PTI-125 stabilizes a critical protein in the brain (*it does not seek to clear amyloid out of the brain).*
  - The target of PTI-125 is an altered conformation of filamin A (FLNA), a scaffolding protein that is critical to beta amyloid's toxicity.
  - We own worldwide rights to our programs in neurodegeneration, without royalty obligation to any third-party.

- **We are also developing a diagnostic to detect Alzheimer's disease with a simple blood test.**

- **We are conducting a Phase 2 clinical program, with scientific & financial support from the National Institutes of Health (NIH).**
  - In 2nd half 2019, we expect to announce results of a Phase 2a study in Alzheimer's disease.
  - Appromixately mid-2019, we expect to initiate a Phase 2b study.

Upcoming Phase 2a Study Results

- In 2nd half 2019, we expect to announce results of a Phase 2a safety study with PTI-125 in patients with Alzheimer's disease.

- Consistent with >10 years of basic research + the drug's mechanism of action + preclinical data + Phase 1 results with PTI-125, in this Phase 2a study we expect evidence of:

    - Safety, tolerability and pharmacokinetics *and*
    - Validated biomarkers of Alzheimer's disease.

Our Scientific Approach is Unique

- **PTI-125, our drug for Alzheimer's, exerts powerful anti-neuroinflammatory effects and restores the function of key receptors in the brain.**
  - In animal models of disease, chronic treatment with PTI-125 abolished IL-6 production and significantly suppressed levels of TNFα and IL-1β (by 86% and 80%, respectively).
  - PTI-125 restores the normal function of three receptors that are pivotal to brain cell survival, cognition and memory.
    - alpha-7 nicotinic acetylcholine receptor (α7nAChR)
    - N-methyl-D-aspartate (NMDA) receptor
    - the brain insulin receptor (IR)
  - In animal models of disease, treatment with PTI-125 resulted in dramatic improvements in brain health, such as improved learning and memory, improved insulin receptor signaling and reduced amyloid and tau deposits.

Summary of Our Drug Program

- **PTI-125 represents a new target for Alzheimer's drug development.**
  - By reversing multiple AD neuro-pathologies, our drug is expected to slow the course of AD.
- **Our drug is designed to stabilize a critical protein in the brain (altered Filamin A).**
  - PTI-125 is *not* dependent on clearing amyloid from the brain.
- **PTI-125 produces multiple beneficial effects by binding to a single target (i.e., FLNA).**
  - Reduced neuroinflammation, tau hyperphosphorylation, insulin resistance in the brain, etc.
- **Strong scientific rationale, peer-reviewed publications and multi-year support from NIH.**
  - The underlying science for our programs in neurodegeneration is published in several prestigious peer-reviewed technical journals, including *Journal of Neuroscience*, *Neurobiology of Aging*, and *Journal of Biological Chemistry*.
- **PTI-125 is a small molecule.**
  - Advantages include well-defined structure; simple & predictable manufacturing; stable; non-immunogenic; and simple oral administration for chronic use in an elderly patient population.

In addition, we believe the underlying science for PTI-125 supports the development of a diagnostic/biomarker to detect Alzheimer's with a simple blood test.

Our Scientific Approach

Filamins are a class of proteins that are evolutionarily conserved.

The biology of the brain is heavily regulated by Filamin A (FLNA).

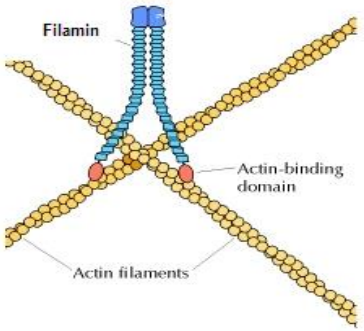
FLNA helps to build, organize, maintain and anchor the brain.

FLNA interacts with at least 90 different proteins in the brain. This indicates FLNA is involved with signaling pathways and cell function, not just cell structure.

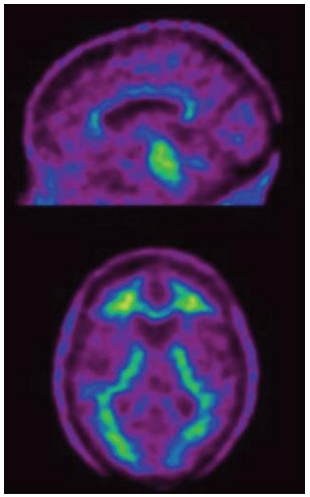
Healthy Filamin = Healthy Brain

Healthy FLNA:

proper cell structure,
proper cell signaling,
proper cell function.



Healthy, Elderly Brain

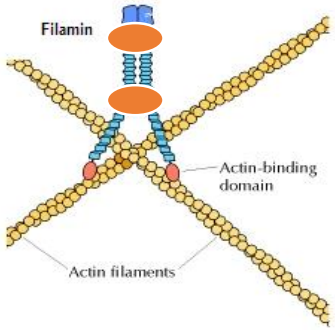


Altered Filamin = Neurotoxicity

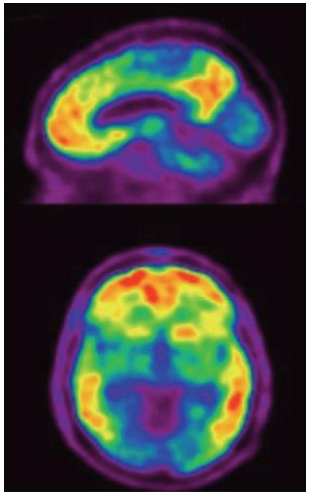
The precise biological events that lead to Alzheimer's are unknown.
However, a large body of scientific evidence shows that an altered conformation of Filamin A enables the massive neuroinflammation/neuropathology observed in the Alzheimer's brain.

Altered FLNA:

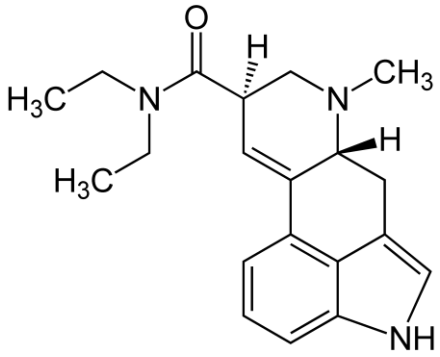
dysfunctional cell signaling,
impaired cell function,
unstable cell structure.



Alzheimer's Brain



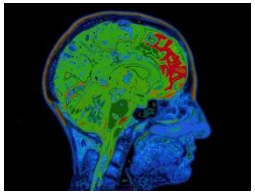
Our Drug Stabilizes Altered FLNA



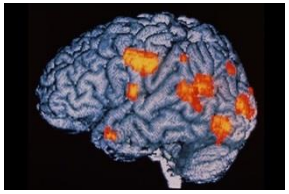
PTI-125 dramatically improves brain health in animal models of disease.

Reduced amyloid and tau deposits

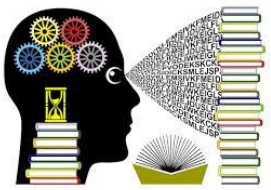
Reduced neuroinflammation



Improved insulin receptor signaling



Improved learning and memory



Summary of Treatment Effects

In animal models of disease, chronic treatment with PTI-125:

- Restores the function of the alpha-7 nicotinic receptor (α7nAChR); the N-methyl-D-aspartate (NMDA) receptor; and the brain insulin receptor (IR);
- Reduces neuronal damage (improves K^+-evoked Ca^{+2} influx);
- Reduces $A\beta_{42}$-induced tau hyper-phosphorylation;
- Reduces $A\beta_{42}$ deposits and neurofibrillary tangles (NFTs);
- Reduces pro-inflammatory cytokine release;
- Reduces α7nAChR – $A\beta_{42}$ complexes;
- Improves synaptic plasticity.

Drug Mechanism Of Action

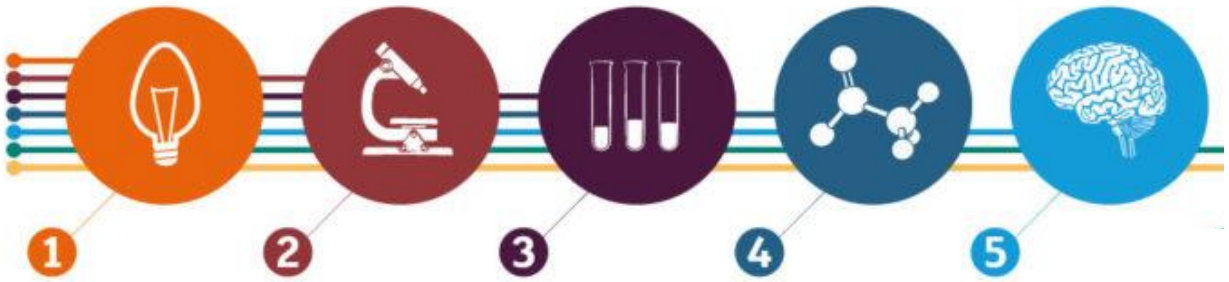
IN BRIEF, VOLUME 11 | SEPTEMBER 2012

Targeting Filamin A Reduces Alzheimer's Signaling

In Alzheimer's disease (AD), toxic amyloid-β_{42} ($A\beta_{42}$) binds to, and aberrantly signals through, the α7-nicotinic acetylcholine receptor (α7nAchR). Using tissue from both mouse models of AD and patients with AD, we show that $A\beta_{42}$ signaling is dependent upon the recruitment of the scaffolding protein filamin A to the α7nAchR. An orally available small molecule that bound to filamin A (PTI-125) reduced abnormal signaling of α7nAChRs, decreased levels of tau phosphorylation and Aβ aggregates, and prevented Aβ-induced inflammatory cytokine release. PTI-125 greatly reduced the affinity of $A\beta_{42}$ for α7nAChRs and could dissociate existing $A\beta_{42}$–α7nAChR complexes.

ORIGINAL RESEARCH PAPER Wang, H.-Y. *et al.* Reducing amyloid related Alzheimer's disease pathogenesis by a small molecule targeting filamin A. *J. Neurosci.* **32**, 9773–9784 (2012)

10-year Drug Discovery Program



<2008
Basic research indicates the opioid receptor antagonists naloxone and naltrexone bind a specific site on FLNA with high affinity.

2009
We then discovered that FLNA associates with a7nAChR when Aβ signals.

2010
We tested many FLNA-binding compounds against this interaction.

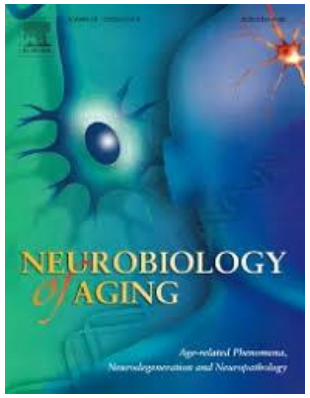
2011
PTI-125 was the most potent inhibitor.

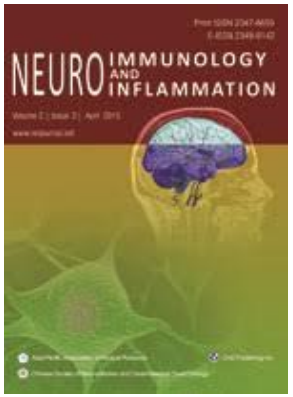
2017 - present
Human testing of PTI-125

PTI-125, a small molecule, was designed in-house and characterized by academic collaborators from City University of New York.

Multiple Peer-reviewed Publications

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





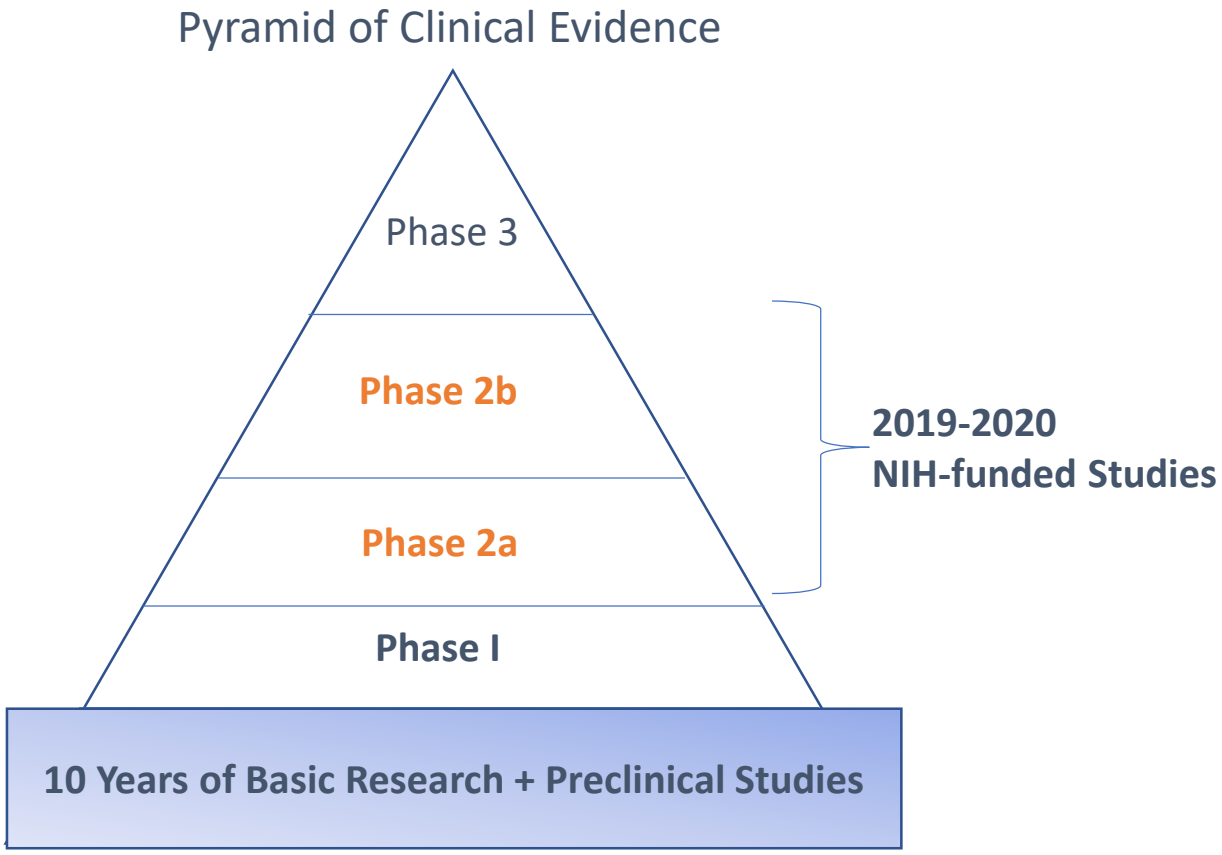
Long-term Scientific & Financial Support From NIH

NIH has awarded our neurodegeneration programs >$10 million in research grants.

Each NIH grant was awarded following an in-depth, confidential, peer-reviewed evaluation of our approach for scientific and technical merit.

Our Clinical Strategy

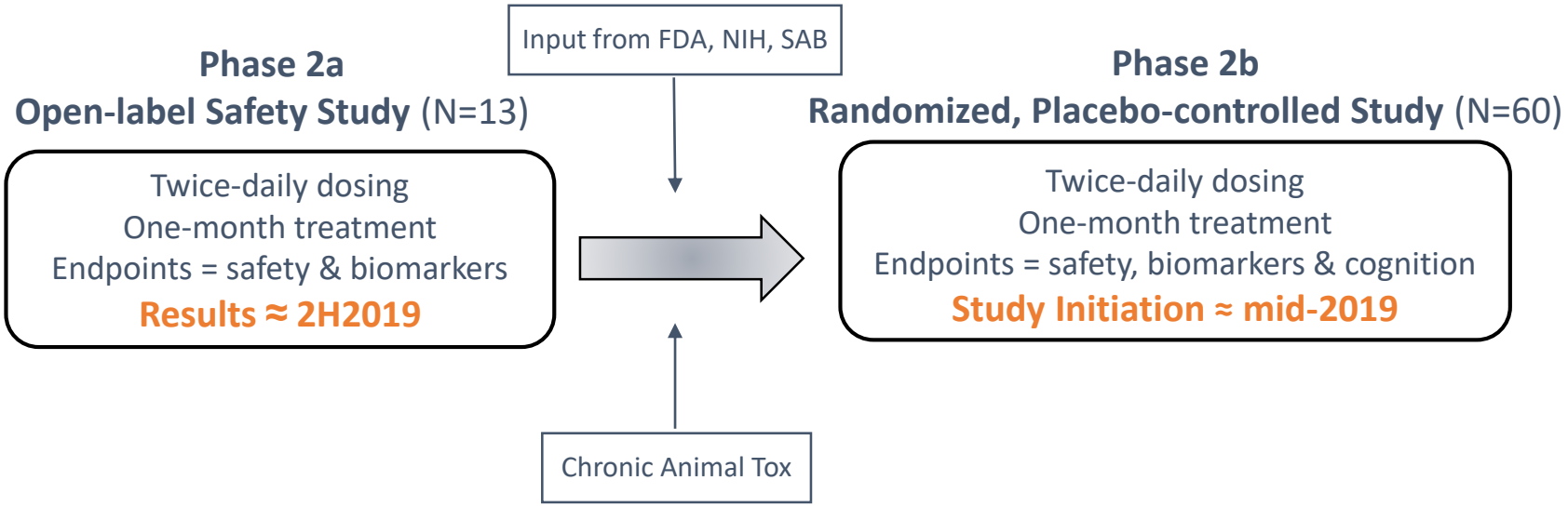
Our overall objective is to develop and gain regulatory approval for PTI-125 as a disease-modifying treatment for Alzheimer's.



On-going Phase 2 Clinical Program

A comprehensive, NIH funded, Phase 2 program with PTI-125 in patients with mild-to-moderate AD was developed in collaboration with FDA, NIH and our scientific advisors.

This program is intended to generate safety, tolerability and pharmacokinetics data; demonstrate target engagement; and prepare PTI-125 for a pivotal efficacy program.



Phase 2a Study Design

- **Objective:** Investigate safety, PK, biomarkers under an IND application filed with FDA
- **Study Design:** Multi-center, single-arm, open-label
- **Population:** Mild-to-moderate AD dementia, MMSE ≥ 16 ≤ 24, age 50-85
- **Enrollment:** Thirteen (13) patients, 4 male and 9 female
- **PTI-125 Dose:** 100 mg oral tablets, administered twice daily (BID)
- **AD Index:** CSF Total tau/Aβ42 ≥ 0.30, indicating AD
- **Treatment:** 28 days
- **Study Sites:** Five sites in the U.S.
- **Biomarkers:** CSF and plasma collected twice (screening and post-treatment)
- **Statistics:** Study was not powered to show statistical significance on any parameter

Upcoming Phase 2a Study Results

- In 2nd half 2019, we expect to announce results of a Phase 2a safety study with PTI-125 in AD patients.

- Consistent with >10 years of basic research + the drug's mechanism of action + preclinical data + Phase 1 results with PTI-125, in this Phase 2a study we expect evidence of:

    - Safety, tolerability and pharmacokinetics *and*
    - Validated biomarkers of Alzheimer's disease.

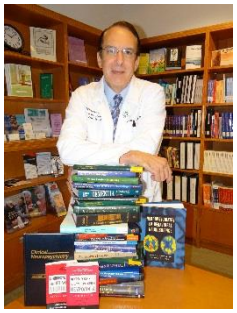
What Are Biomarkers of AD Pathology?

- **$A\beta_{42}$, tau, P-tau-181, neurogranin and neurofilament light chain (NfL) in cerebrospinal fluid (CSF) are objective, validated measurements of neurodegeneration.**

- **YKL-40, IL-6, IL-1β, and TNFα are objective, validated measurements of neuroinflammation.**

A beneficial drug effect in AD is expected to move one or both panels of biomarkers in the right direction.

Our Scientific Advisors



Jeff Cummings, MD

Director of Cleveland Clinic Lou Ruvo Center for Brain Health. Professor of Neurotherapeutics and Drug Development, Cleveland Clinic.

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

Medical Professor at CUNY Medical School.
Co-lead scientist on discovery & development of PTI-125.

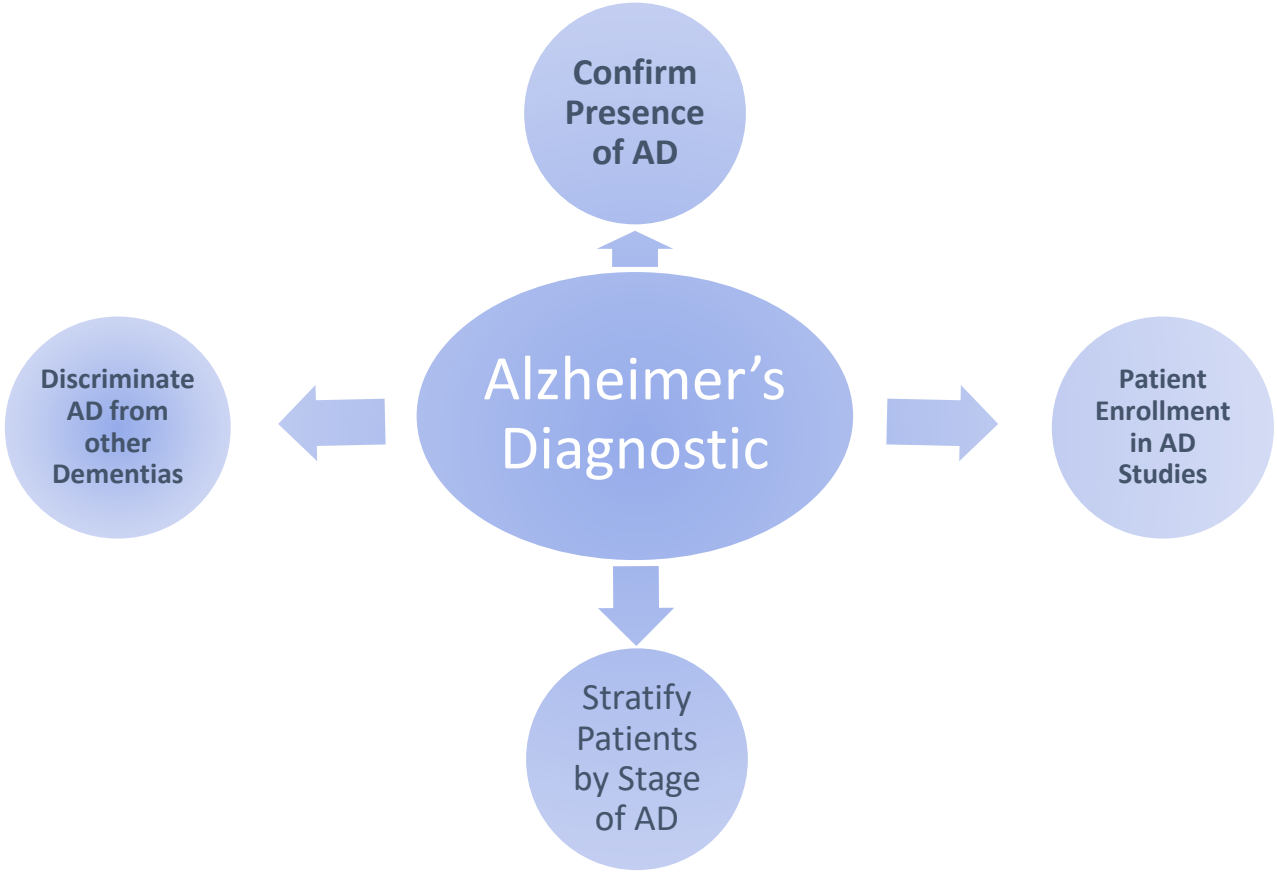
Steven E. Arnold, M.D.

Translational Neurology Head of the Interdisciplinary Brain Center, Massachusetts General Hospital, Harvard Medical School.

PTI-125Dx

PTI-125Dx is an investigational diagnostic to detect Alzheimer's disease with a simple blood test.

Profound Need for a Diagnostic Test for Alzheimer's

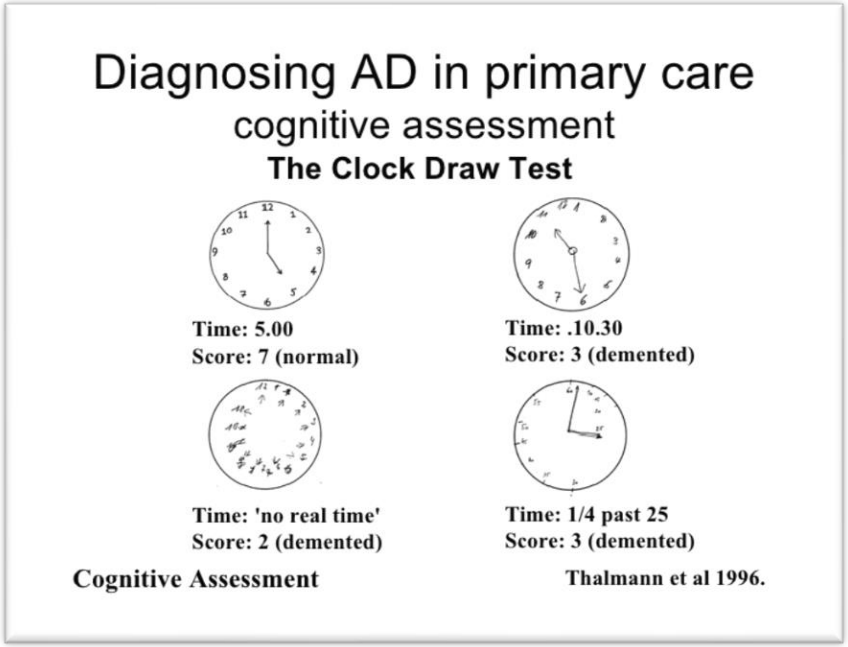


The ultimate goal is to identify people destined to develop Alzheimer's long before symptoms occur, and to cease -- or at least slow down -- brain damage before it is too late.

How Alzheimer's is Diagnosed Today

Right now, the only way to definitely diagnose Alzheimer's disease is through autopsy after death. Everything else is expensive, invasive, risky, uncomfortable or uncertain.

Plus, no one is tested until they show obvious cognitive decline.



Current approaches for diagnosing AD include measurement of amyloid-β (specifically Aβ42), total tau (T-tau) or phosphorylated tau (P-tau) levels in cerebrospinal fluid (CSF); structural neuroimaging techniques (MRI or CAT); PET imaging of brain amyloid (AmyVid®) or inflammation; and batteries of cognitive tests. Usually, a combination of more than one test is necessary to provide a working diagnosis.

Detecting Alzheimer's -- Simple as Getting a Blood Test?

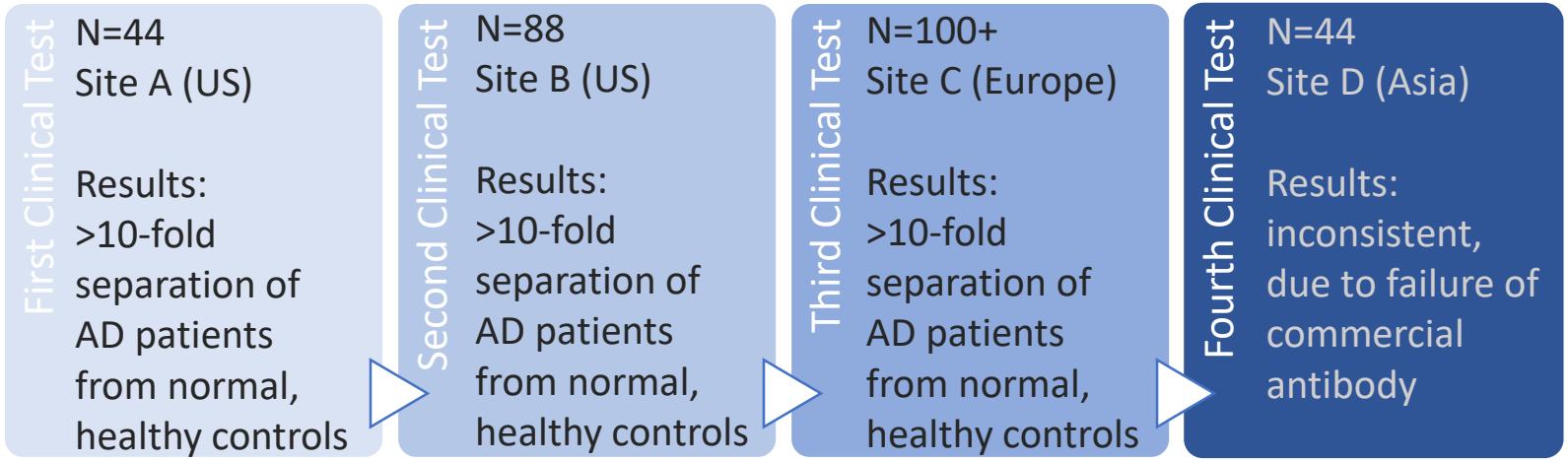
We are developing PTI-125Dx, an investigational diagnostic, to detect Alzheimer's disease in blood, potentially before the appearance of overt clinical symptoms.

Altered Filamin A (FLNA) is a feature of Alzheimer's pathology in the brain. Its also appears in plasma. PTI-125Dx detects and quantifies this biomarker.

PTI-125Dx has strong scientific & financial support from NIA (National Institute on Aging) following multiple in-depth, peer-reviewed evaluations for scientific and technical merit.

Top-line Study Results with PTI-125Dx

PTI-125Dx detected more than 10-fold separation between AD patients and age-matched normal healthy controls or young cognitive intact subjects (N=232)**.**
All samples were blinded and analyzed by an outside lab.



Sensitivity is the proportion of subjects *with* Alzheimer's in whom the test is positive.

Specificity is the proportion of subjects *without* Alzheimer's in whom the test is negative.

Summary of Our Diagnostic/Biomarker Program

- ✓ With scientific and financial support from NIH, we are developing PTI-125Dx as a fast, accurate and quantitative method to detect the presence of Alzheimer's disease in plasma.
- ✓ Encouraging results to date indicate PTI-125Dx is a feasible program.
- ✓ In 3 blinded studies, PTI-125Dx detected >10-fold differences between AD patients and age-matched normal controls or young cognitively intact subjects (N=232).
  Study #4 indicate that commercial antibodies are not always properly validated.
- ✓ In 2019-2020, we are developing a proprietary antibody with well-defined affinity, specificity, etc.
- ✓ Even if there is not a precise cutoff value for Alzheimer's, it may be important to incorporate data from PTI-125Dx into a diagnostic framework for Alzheimer's. Repeat measurements taken over time with PTI-125Dx on the same subjects may provide a computational approach to disease progression.

Key Financials at 3/31/19

- $19.1 million of cash & cash equivalents
- $5-6.0 million net cash use expected in 2019
- 17.2 million shares outstanding
- 9.1 million warrants outstanding
- $78.7 million pre-tax NOLs
- No debt

Experienced Team

Remi Barbier - Chairman, President & CEO - 1998 to date.
- **Founder/co-founder, three public life science companies.**
- Trustee emeritus, *Carnegie Institution for Science*; *Santa Fe Institute; California Institute for Quantitative Biosciences.*

Nadav Friedmann, PhD, MD - Chief Medical Officer, 2001 to date; Board member.
- J&J; Daiichi Pharmaceuticals; Abbott Labs.
- **Eight FDA drug approvals prior to Cassava Sciences.**

Lindsay H. Burns, VP, Neuroscience, 2001 to date
- Neurex; Elan; Abgenix.
- PhD with Trevor Robbins, University of Cambridge.
- Post-doc in Parkinson's research, McLean hospital.

Eric Schoen, Chief Financial Officer, 2018 to date
- Vermillion, Inc; Borland Software.
- PricewaterhouseCoopers, Manager audit/assurance.

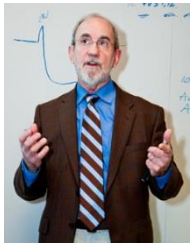
Michael Zamloot - Sr. VP, Tech. Operations, 2000 to date.
- Boehringer Mannheim; Athena; Ciba-Geigy.
- **Four FDA drug approvals prior to Cassava Sciences.**

Board of Directors

Sandy Robertson

Bob Gussin, PhD.

Saira Ramasastry



Patrick Scannon, MD, PhD

Mike O'Donnell

Summary

- Our scientific approach is to suppress neuroinflammation and restore the function of three key receptors in the Alzheimer's brain.

- In 2nd half 2019, we expect to announce results of a Phase 2a study with PTI-125 in patients with Alzheimer's.

- Consistent with >10 years of basic research + the drug's mechanism of action + preclinical data + Phase 1 results with PTI-125, in this Phase 2a study we expect evidence of:

    - Safety, tolerability and pharmacokinetics *and*
    - Validated biomarkers of Alzheimer's disease.

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NASDAQ: SAVA

THANK YOU!!

APPENDIX - Key Publications

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