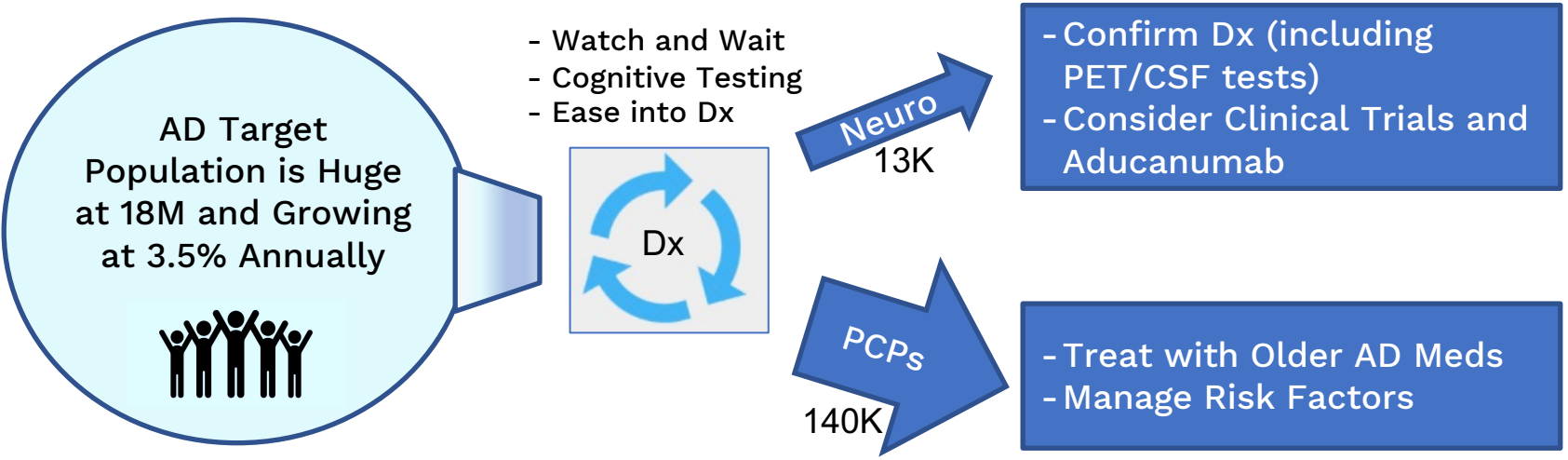
COGNOPTIX

A Simple Eye Scan

For
Early Detection of
Alzheimer's Disease

Current AD Care System Characterized by Delayed Dx and Lack of Treatment Options

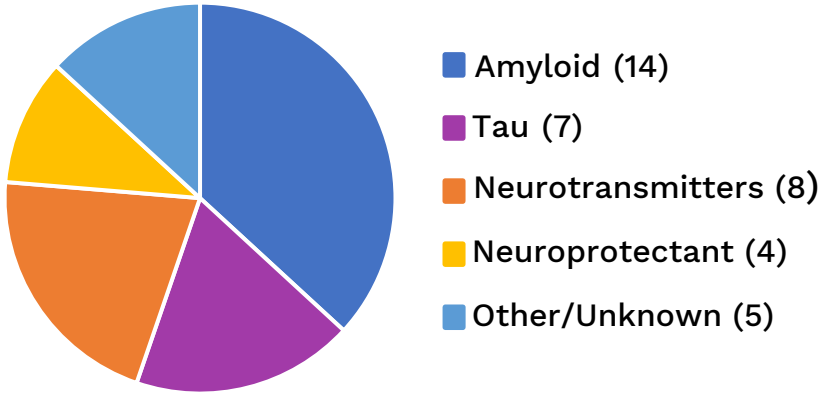


- Dx process slow and frustrating
  - Takes 2-3 years
  - Only 20% get Dx
  - Mostly done by PCPs
- Yields suboptimal outcomes
- However, system is functional because the impact of treatments is modest and Patient/PCPs perceive treatment to be mostly ineffective

Wave of New Therapies Will Overwhelm AD Healthcare System

New Treatments Coming to Market Between 2023-2027

- 38 Novel Treatments in Phase 2/3*
- 3 Anti-Amyloid Therapies in Phase 3



*As of Oct 2020

Patient Driven Demand will Overrun System

- Patients wait time to see Specialists could easily exceed 6 months
- Wait for Amyloid PET scan could triple
- As timely initiation of therapy is required for good outcomes, patient and MD frustration will rapidly escalate

A Breakthrough to Speed Dx is Required

- Ensuring Neuro time is used effectively is critical
- Ideal solution allows for rapid Dx in community-based PCP setting
- **Sapphire WILL FILL THIS NEED!!!**

Liu, Jodi L., et al. Assessing the Preparedness of the U.S. Health Care System Infrastructure for an Alzheimer's Treatment. Santa Monica, CA: RAND Corporation, 2017.

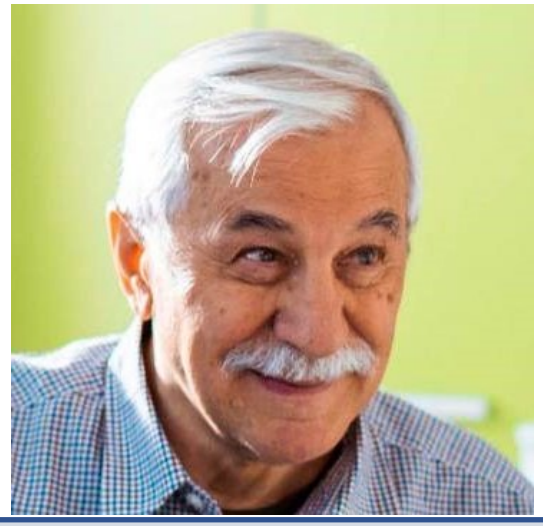
Cognoptix's Mission

Our Goal:

To enhance AD care and outcomes through early detection and intervention

Our Approach:

Accelerate successful delivery of our Sapphire solution into the marketplace by **actively pursuing partnering relationships** with companies, government agencies, AD-focused foundations, impact investors, and other organizations



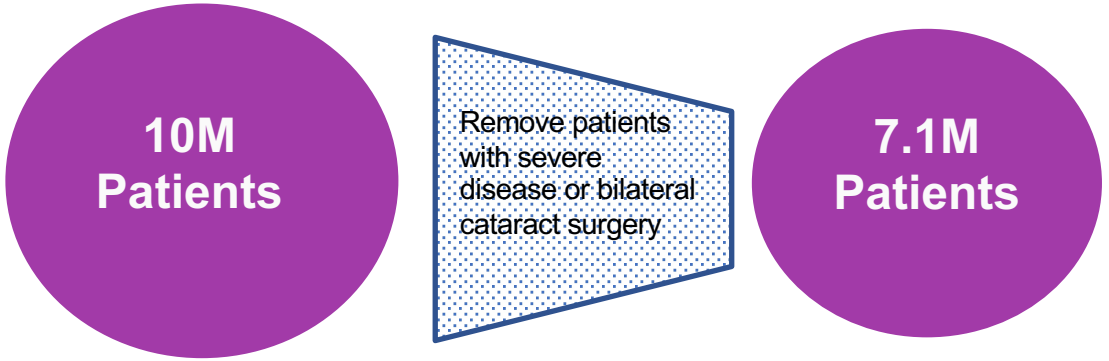
Patient Benefits

- Access to Early Treatment that Slows Disease
- "Value of Knowing"
  - Reduce Anxiety/Depression
  - More Open to Care
- Lifestyle Changes to Slow Progression
- Time to Plan Care

Large Opportunity: Improve Dx of AD in Dementia and MCI Populations

Target Population 2025 (US) :

Dementia

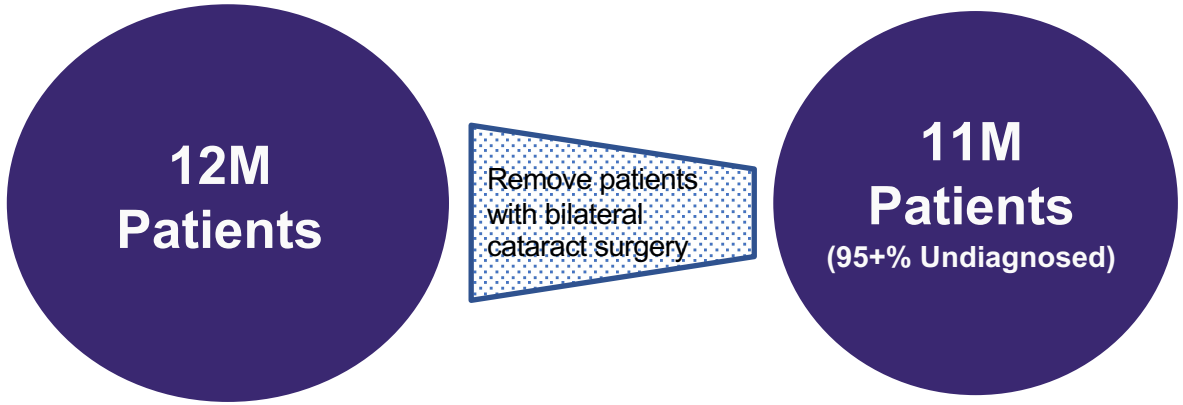


3.4M Diagnosed
- SAPPHIRE test can correct misdiagnosis by determining amyloid status

3.7M Undiagnosed/New
- SAPPHIRE test can aid diagnosis by determining amyloid status

Correcting misdiagnosis and driving Dx among patients already under MD care is critical to a successful launch

Mild Cognitive Impairment (MCI)



Sapphire test can rule in/rule out AD.

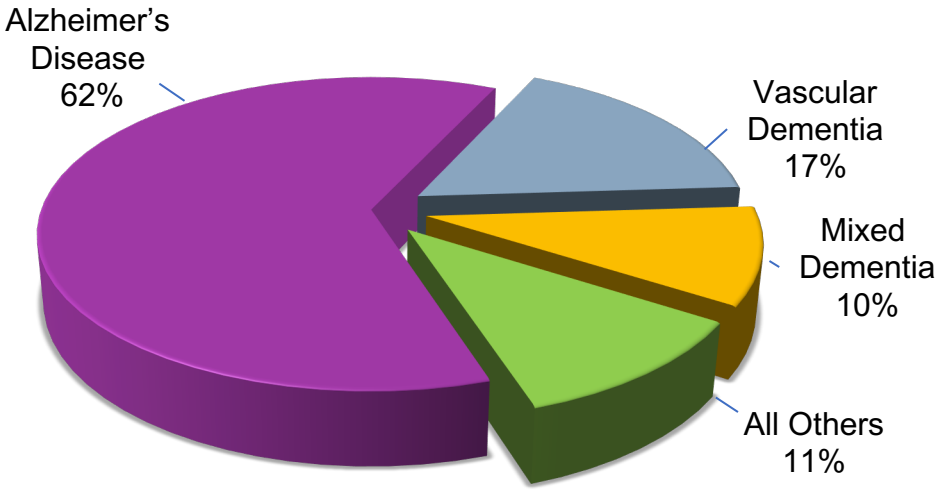
Use in MCI Dx will drive long term success

TOTAL US TARGET POPULATION 18M

Sources: US Alz Association Facts and Figures

Unmet Need: Improve Dx Accuracy & Outcomes via Amyloid Test in Diagnostic Workup

Dementia Can Have Many Causes



- Only patients positive for Amyloid have AD

Benefits of Adding an Amyloid Test

- **Underdiagnosis and misdiagnosis is common**
  - Clinical diagnosis of AD is difficult
  - Up to 30% dementia patients with a Dx are misdiagnosed
- **Objective test for AD pathology improves diagnostic accuracy and patient acceptance of the Dx**
- **Amyloid test helps patients get best care**

POSITIVE	NEGATIVE
AD Treatments and Risk Factor Modification can slow cognitive loss and facilitate appropriate life planning	Patient care significantly different than for AD Dementia; more tests needed to find Dx

Source: McGill-Carter, Tammi. "Market Analysis Alzheimer's Disease 2020". AAIC 2020. *J. Psychiatry*. 2020 Vol(22) Issue 6.

Our Solution: SAPPHIRE II Allows Easy Detection of Amyloid in Lens

Cognoptix's Key Discoveries

- β-amyloid aggregates in AD occur in the lens as well as the brain
- Lens deposits are much easier to detect

Sapphire – Combination Product: Ointment + Device

1. Administer Imaging Ointment

Cognoptix Exclusive Imaging Ointment:
Fluorescent β Amyloid specific binding compound (Aftobetin-HCL)

24 hours later

2. Conduct Sapphire scan

Cognoptix Exclusive Sapphire Imaging Instrument

Results: < 5 min

Easy	Accessible	Very Well Tolerated	Non-Invasive	Affordable

Eye has Shown Promise as a Non-Invasive Avenue for Detecting AD Pathology

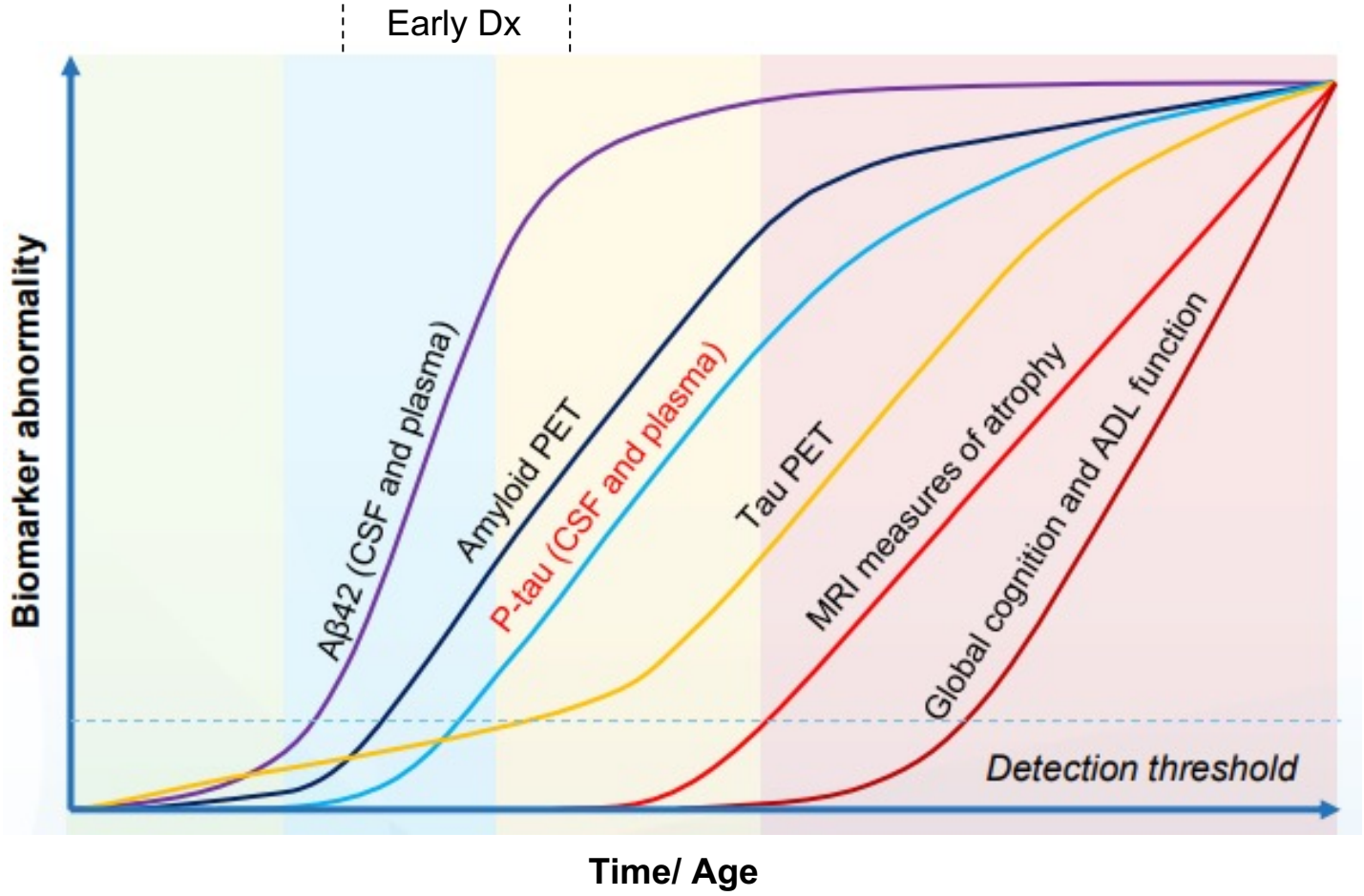
- Components of the eye share structural and pathogenic pathways with the CNS, including the cerebral microvasculature and neural cells

- Many efforts have focused on the retina because of the precedent for using it to detect evidence of other conditions (Diabetes, CV etc.)

- Utilizing the lens is novel but may have important advantages
  - Lens and Brain come from same embryonic structure (ectoderm)
  - Pathology unaffected by common systemic conditions (e.g., cardiovascular and cerebrovascular) and eye diseases (glaucoma, AMD)
  - Long life of lens fibers preserves evidence of abnormal protein accumulation

Snyder, PJ, Alber, J, Alt, C, et al. Retinal imaging in Alzheimer's and neurodegenerative diseases. *Alzheimer's Dement*. 2021; 17: 103– 111.
Goldstein, LE et al. "Cytosolic Amyloid deposition and supranuclear cataracts in lenses from people with Alzheimer's Disease" The Lancet. 2003. 361: 1258-65

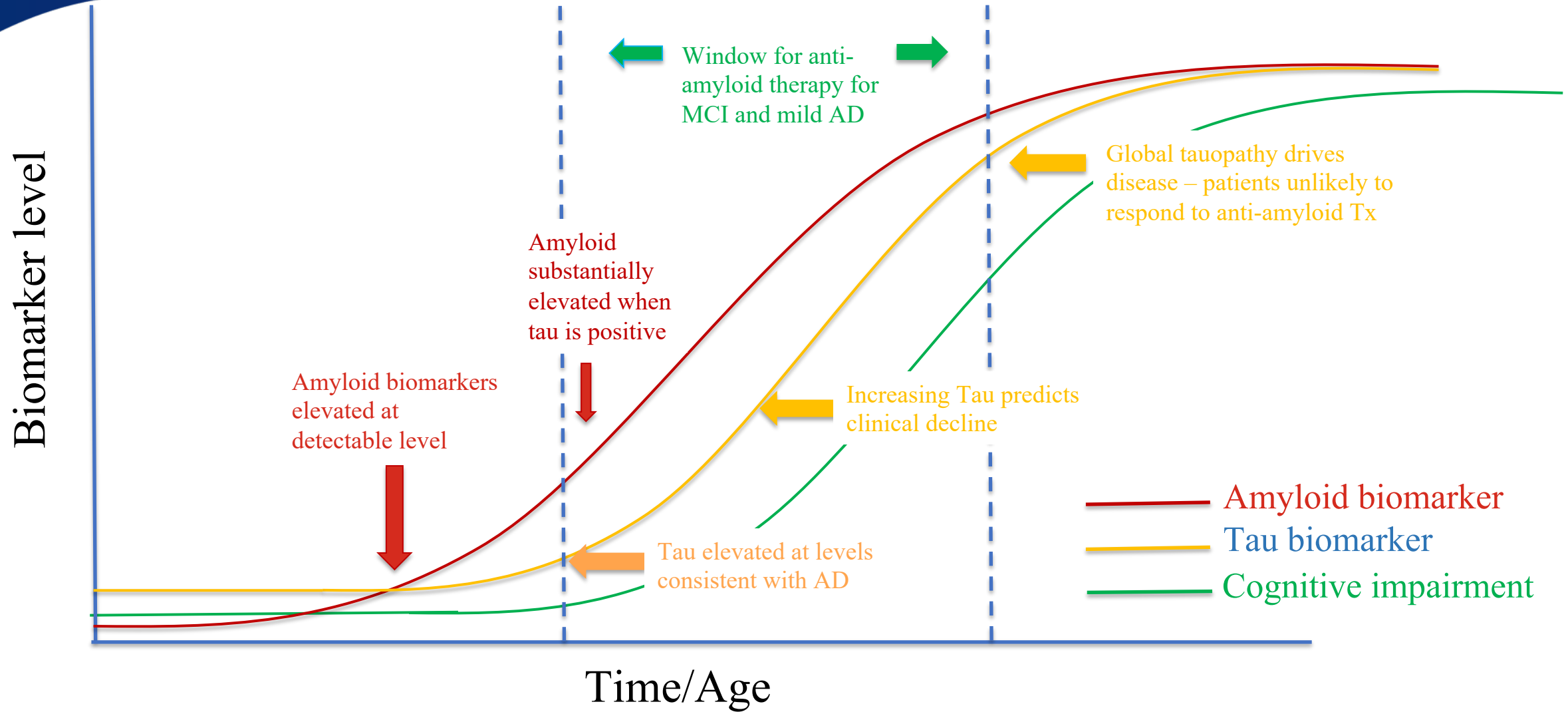
Biomarkers Enable Early Dx and Intervention



- Aβ and Tau are the defining biomarkers for AD
- Minimally invasive and affordable detection of Aβ accumulation is essential
  - Plasma
  - Eye (Lens/Retina)
- Detection of pTau in plasma may be useful and complimentary to early Aβ detection

Adapted from: Hansson, O. Biomarkers for neurodegenerative diseases. *Nat Med* **27,** 954–963 (2021).

Biomarker Progression and a Window for Therapy



Adapted from: Pontecorvo MJ. Tau and neuroinflammation Imaging - Next Steps Forward? High Country Nuclear Medicine Conference 2018, Vail CO
Devous MD Sr. Tau Imaging in Alzheimer's Disease Clinical Trials and in AD Research. 13th Annual Meeting Clinical Trials on Alzheimer's Disease (CTAD) October 2020

Routine Amyloid Testing Will Transform Dx and Tx of Alzheimer's Disease

Diagnosis Phase

Clinical Suspicion of AD

↓

Neurocognitive Assessments

↓

Laboratory Tests

↓

Structural Neuroimaging

+

5% Specific Cause of Cognitive Loss Determined

-

95% No Clear Etiology Determined

↓

Amyloid Burden Test

60% POSITIVE (Increased Risk of AD)

Plasma/CSF pTau or PET to Confirm Dx

40% NEGATIVE (Not AD)

Re-Evaluate for Non-AD Causes of Cognitive Loss

- Particular Focus on Depression, Vascular Disease, Parkinson's Disease
- Consider Discontinuing AD Drugs

Treatment Phase

Treatment of Underlying Disease

- B12 Deficiency
- Depression etc.

AD Treatment Options Considered

- Consider AD Rx Treatment
- Treat Risk Factors
- Consider Clinical Trials
- Initiate Dietary Changes
- Exercise Program
- Consider Cognitive Stimulation
- Avoid Social Isolation
- Monitor and Plan for Future Care

KOL Feedback on Plasma Aβ Assays

Question:

Provide feedback on three potentially serious problems with plasma Aβ

- Limited dynamic range
- Impact of co-morbidities
- Harmonization & variability

Feedback on Plasma Aβ

KOL #1:

- Narrow dynamic range of plasma Aβ is problem for these assays, will always make this measurement a challenge.
- Effects of BMI, CKD and other co-morbidities will confound this less as it is used as a ratio.
- Harmonization to minimize variability across different lab sites is still work in progress.

KOL #2:

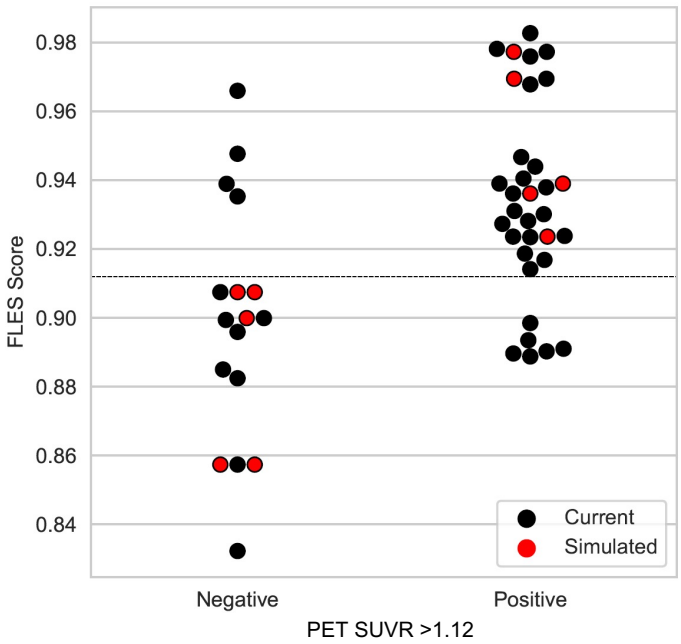
- Plasma Aβ42/Aβ40 might be difficult to implement in clinical practice because levels in plasma only reduced by 8-12% in amyloid+ patients.
- Some effects of kidney function, BMI, etc. on blood biomarker levels can mostly be ignored.
- Even minor drifts in the assay performance might have profound effects on classification of people into normal vs. abnormal results.

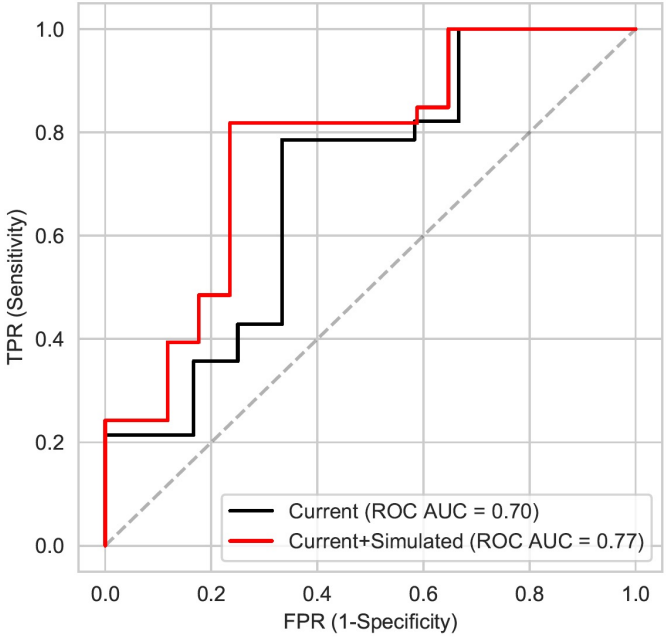
KOL #3:

- Concerns about scalability and reproducibility of the Aβ assays (p-Tau assays more robust in terms of effect sizes and scalability).
- Ultimately plasma may replace CSF, but will be complimentary to PET because plasma can't tell you about burden of pathology or topography.

Sapphire's Clinical Performance Will Improve as More Patients Are Studied

Results from a Single Simulation
(Current vs. Current + 10 Simulated New Patients)





- Completed clinical studies included 40 patients with comparative PET SUVR data
  - By chance, these studies over enrolled MCI patients
  - This likely led to us to understate the full performance potential of the Sapphire system
- Cognoptix's immediate next step is to expand its sample size by added 5 cognitively normal and 5 new AD patients
- Results of 2000 simulations predict that adding these 10 additional patients will raise the ROC AUC to 0.77 (95% C.I. 0.75-0.80)

Result from 2,000 Simulations	Sensitivity	Specificity	Accuracy	NPV	PPV	ROC/ AUC
Current	0.79	0.67	0.75	0.57	0.85	0.70
w/ Simulated Data	0.82	0.76	0.80	0.68	0.87	0.77

Competitive Landscape – AD Diagnostic Alternatives

	Sapphire II	PET	Plasma
Accuracy: AUC vs PET	0.70 → 0.80+	N/A	0.79 - 0.83
Clinical data source	Prospective study	N/A	Retrospective study
Cost	+++ $600	+ $5,000	++ $1,250
Accessibility	+++	+	+++
Ease of use	++ Room temperature	+	++ Refrigeration, centrifuging
Time to results	Next day	1-2 days	10 days
Income generating for physician	Yes	No	No
Free from radiation	+++	No	+++

Go-To-Market Strategy & Business Model

- Employ reagent-rental business model to minimize upfront investment for practices
- Initially launch to high volume Neurology and Geriatric practices
  - Year 1 Focus on 1,500 target MDs (Average 3.5 MDs/Practice)
  - Year 1 Goal is to place 60 devices
- Rapidly expand into Primary Care as SAPPHIRE gains traction with specialists
- Initial opportunity focuses on validating clinically diagnosed patients to correct misdiagnosis
  - Estimated to occur in ~30% patients. Patients are already under physician care so they are readily accessible.
- Driving diagnosis of MCI population will sustain longer term growth opportunity
  - Penetration is tightly linked to success of and promotional effort behind anti-amyloid and other disease modifying therapies (DMTs)

Financing History

Date	Description	$ Raised	Notes
2005-2014	Various Institutional Funders	$37MM	Generated positive data from a 48-patient clinical trial $76MM post-money valuation
2020	Series R	$2.615MM	Pre-money valuation of $4MM
2021	Convertible Note	$2.253MM	

11M
Patients

Primary Team Members

Team Member	Role
Donald Hawthorne	Acting Chief Executive Officer
Carl Sadowsky, MD	Chief Medical Officer
Dennis Nilan	VP of Operations
Michael Devous, PhD	Scientific Advisory Board (SAB)
Mike Kaswan	Chief Financial Officer
Barbara Hardwick	Commercialization Advisor
John Conley	Board Member
R. Gregg Stone	Board Member
Lee Goldstein, MD, PhD	Board Member, Co-Founder, SAB Chair

COGNOPTIX

Thank You