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

2021

AD Target Population is Huge at 18M and Growing at 3.5% Annually

- Watch and Wait
- Cognitive Testing
- Ease into Dx

Dx

Only 10-20% see Neuro
Wait time can be weeks

Neuro 13K

- Confirm Dx (including PET/CSF tests)
- Consider Clinical Trials and Aducanumab

PCPs 140K

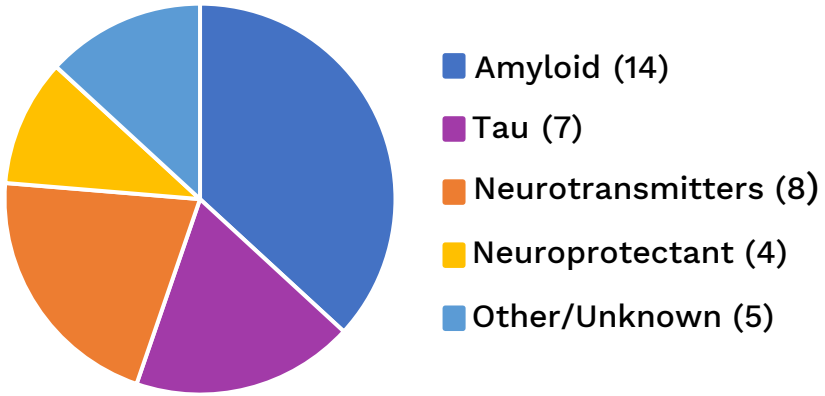
- Treat with Older AD Meds
- Manage Risk Factors

- 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 Tx to be mostly ineffective

Wave of New Therapies Will Overwhelm AD Healthcare System

New Treatments Coming to Market Between 2023-2027

- 38 Novel Tx 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.

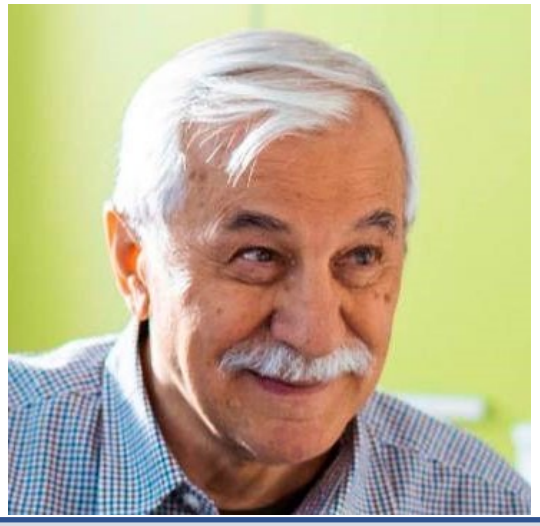
Cognoptix's Mission

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



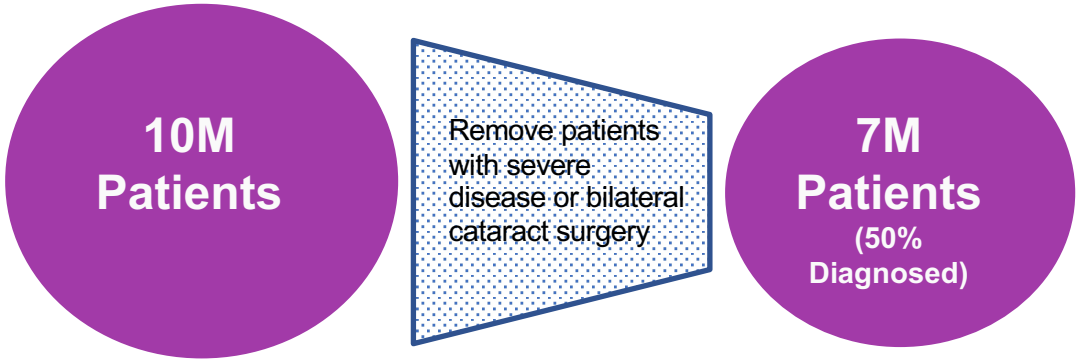
Patient Benefits

- Access to Early Treatment that Slow 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 2024 (US) :

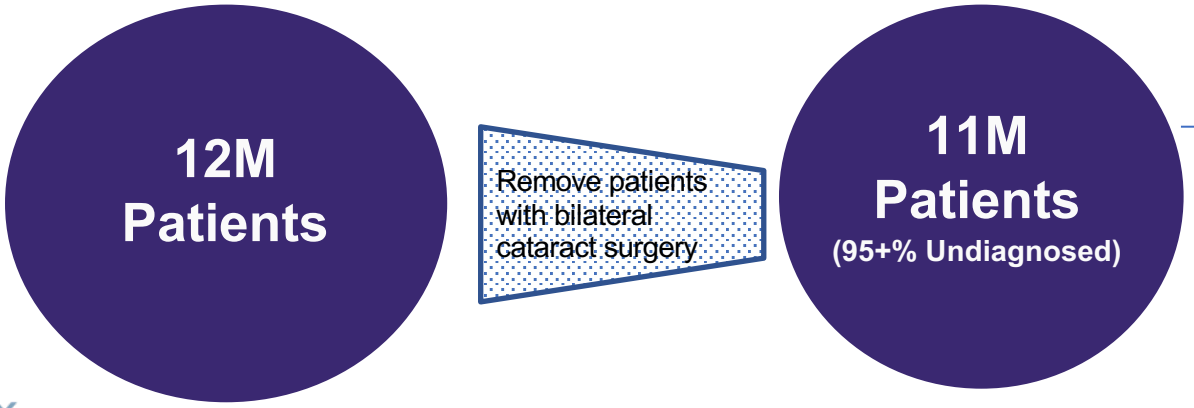
❖ Dementia



3.5M Diagnosed
- SAPPHIRE test can correct misdiagnosis by determining amyloid status

3.5M Undiagnosed
- SAPPHIRE test can aid diagnosis by determining amyloid status

❖ Mild Cognitive Impairment (MCI)



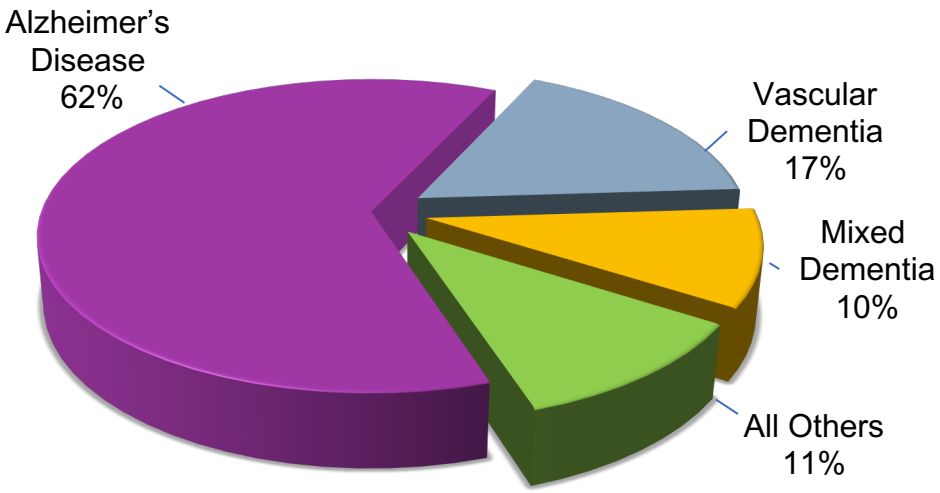
As new treatments for MCI stage gain traction, SAPPHIRE test can rule in/rule out AD.

TOTAL 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 II – Combination Product: Ointment + Device

1. Administer Imaging Ointment

24 hours later

2. Conduct SAPPHIRE II scan

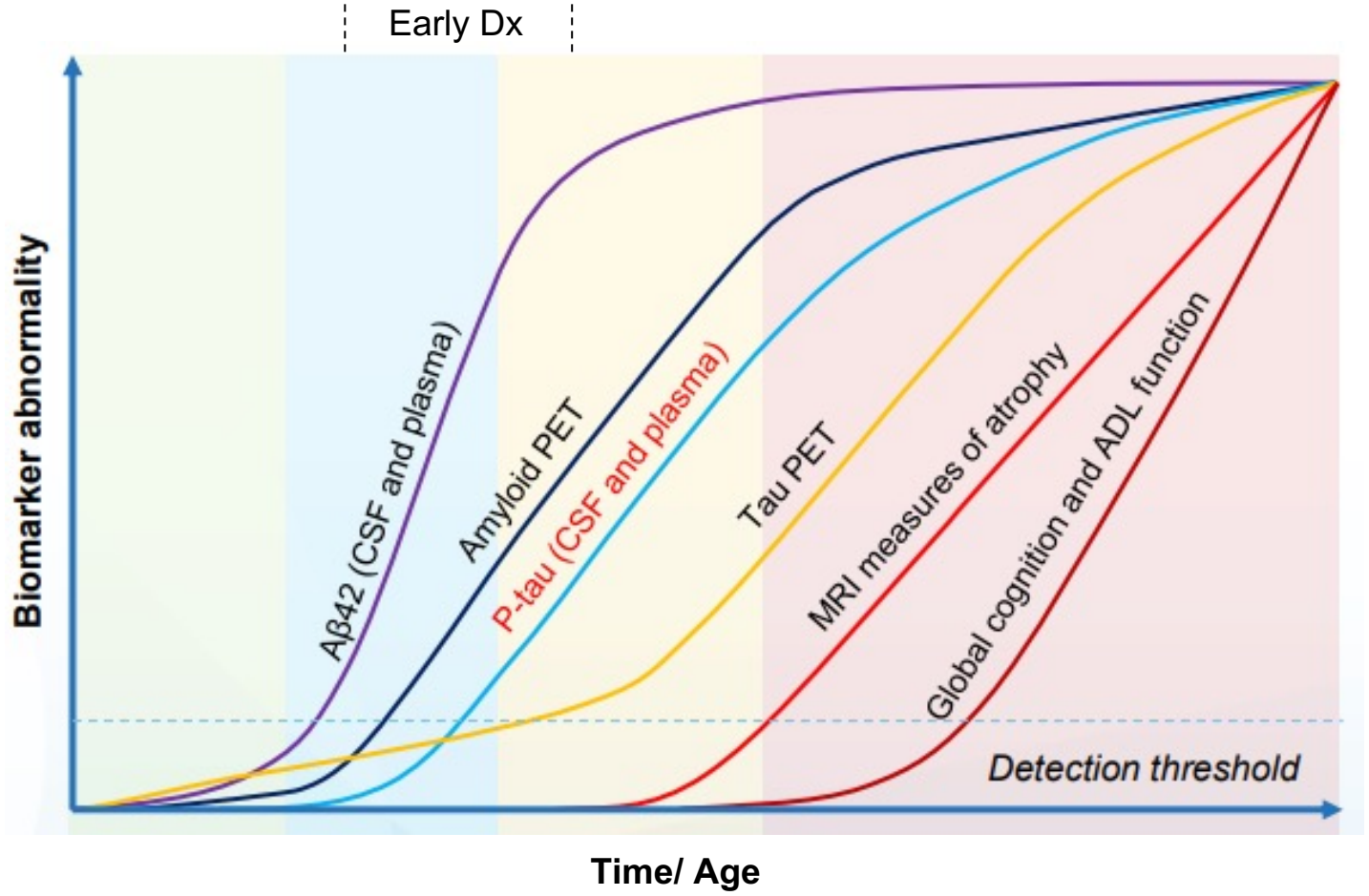
Cognoptix Exclusive Imaging Ointment:
Fluorescent β Amyloid specific binding compound (Aftobetin-HCL)

Cognoptix Exclusive Sapphire II Imaging Instrument

Results: < 5 min

Easy	Accessible	Very Well Tolerated	Non-Invasive	Affordable

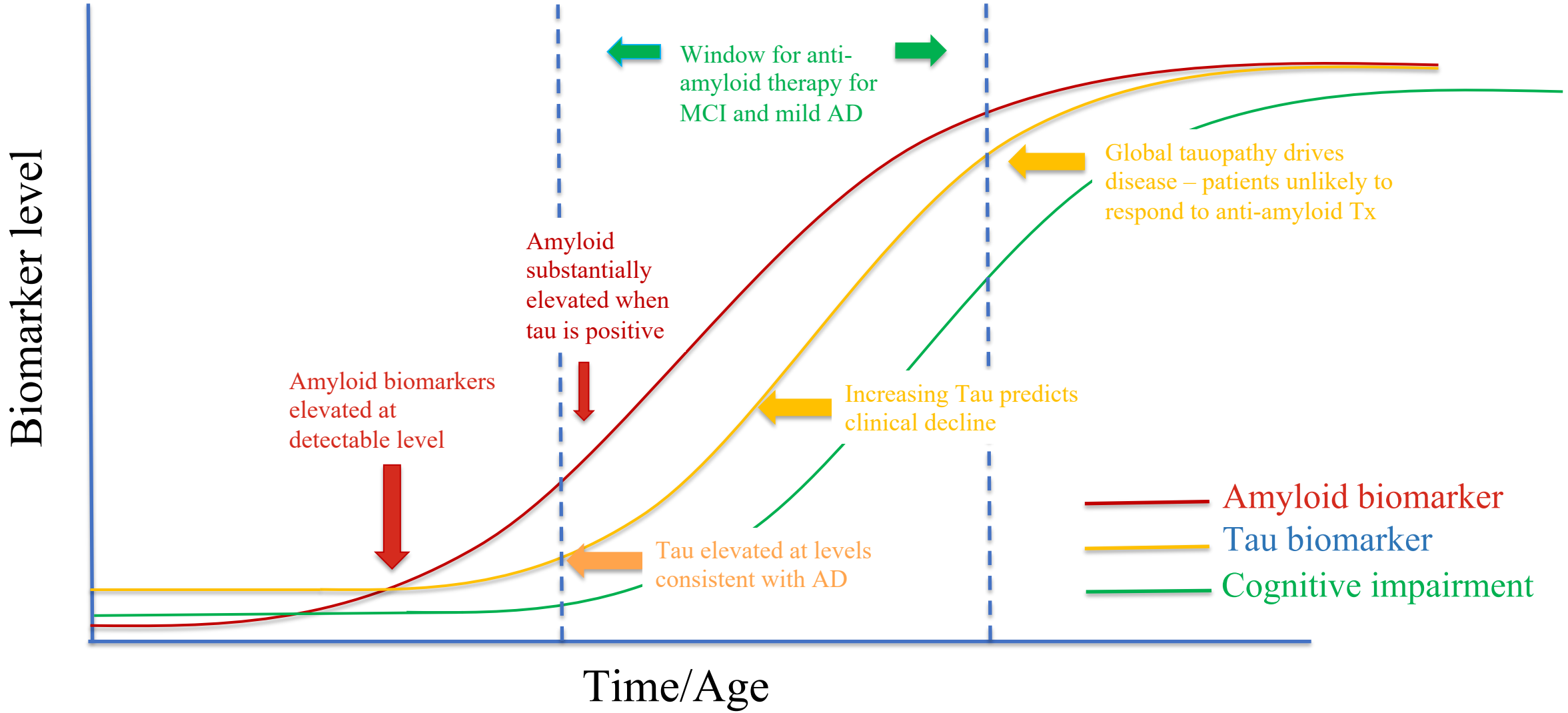
Biomarkers will Enable Early Dx and Intervention



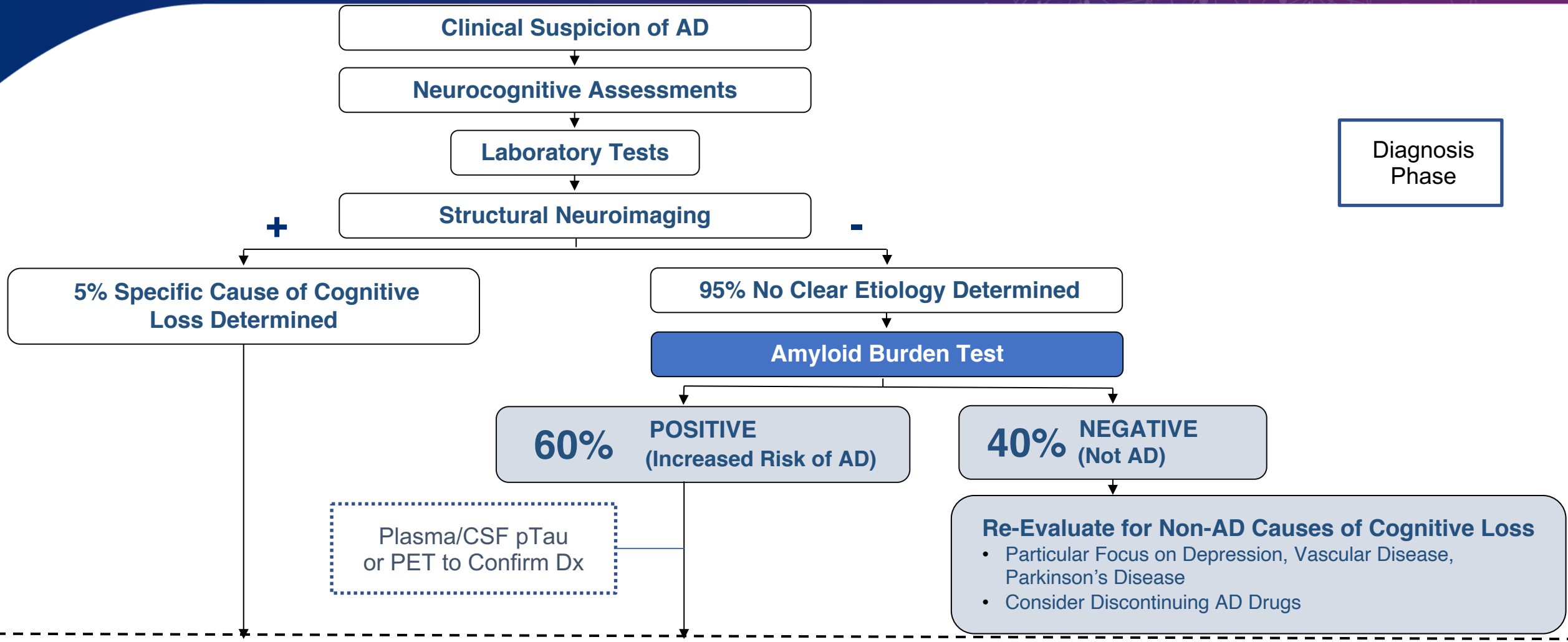
- Aβ and Tau are the defining biomarkers for AD
- Minimally invasive and affordable detection of Aβ accumulation is essential
  - Plasma
  - Eye (Lens/Retina)
- Detection of pTau in plasma may be useful and complimentary to early Aβ detection

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

Biomarker Progression and a Window for Therapy



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



KOL Feedback on Plasma Aβ and pTau Assays

Questions:

1) Provide feedback on three potentially serious problems with plasma Aβ
   - ❖ Limited dynamic range
   - ❖ Impact of co-morbidities
   - ❖ Harmonization & variability

2) Received unsolicited feedback on pTau assays

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.

Feedback on Plasma pTau

KOL #1: Did not comment on pTau.

KOL #2:
- Very optimistic when it comes to plasma pTau, especially pTau217, as plasma pTau assays are much more robust.
- Will take 1-2 years before assays are on fully-automated platforms that can be used in clinical practice, especially for pTau and NfL.

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

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

Assume that (1) we have 5 new PET negative and 5 new PET positive patients and (2) their FLES scores follow the same distribution as the FLES scores of the previous PET negative and PET positive patients whose PET results are congruent with the FLES results (example shown in Fig 1). Measure ROC AUC for the combined data of previous and new hypothetical patients. Simulate this 2000 times and check the distribution ROC AUC (Fig 2). FLES threshold: 0.912, SUVR threshold: 1.12

Fig 1. Sample Hypothetical Data and Resulting ROC curve

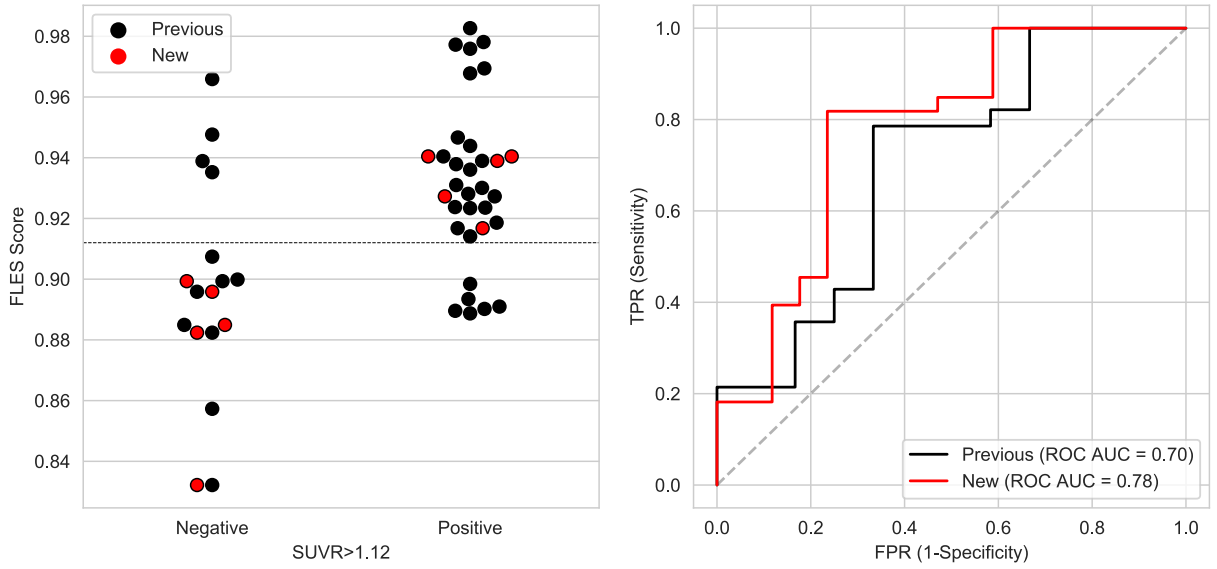
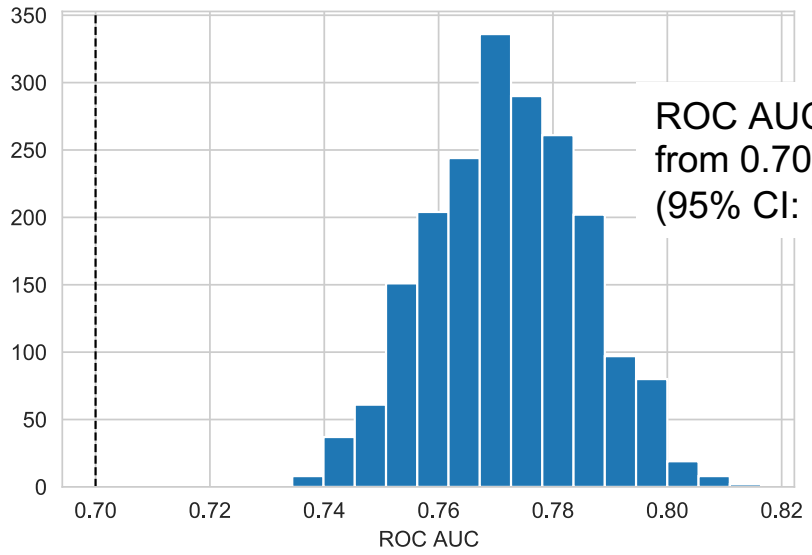


Fig 2. Distribution of ROC AUC Values from Simulation



ROC AUC increases from 0.70 to 0.77 (95% CI: [0.75,0.80])

Scenario	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

- Use FDA Breakthrough Device Designation granted in July 2021 to accelerate clinical & commercial progress
- Initially launch to Neurology
- Rapidly expand into Primary Care as SAPPHIRE gains traction with specialists
- Employ reagent-rental business model to minimize upfront investment for practices
- Leverage partnering across broad range of areas
  - Clinical trial participation/screening
  - KOL development
  - Scientific engagement, Congress activities
  - Device placement/servicing
  - Commercialization activities and execution

Use of Proceeds: Key Milestones Timing & Investment Requirements

March 2022

10- Patient Study Completed

- Preliminary Test Performance Validated
- $500K Incremental

Aug 2022

Pre-Pivotal Studies (0036/38) Completed

- Ready to Finalize Pivotal Design and Engage with FDA
- $2.9M Incremental
- ($1.6M Device Hardware & Software Development for Pivotal, externally funded)

Dec 2022

Finalize Pivotal Study Design & Materials

- Includes Commercial/ Regulatory Steps as well as Manufacturing First Batches of API & Ointment
- $1.2M Incremental

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

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	

COGNOPTIX

Thank You

COGNOPTIX

Appendix

Unmet Need: Current Amyloid "Gold Standard" Test Not Suitable for Community Practices

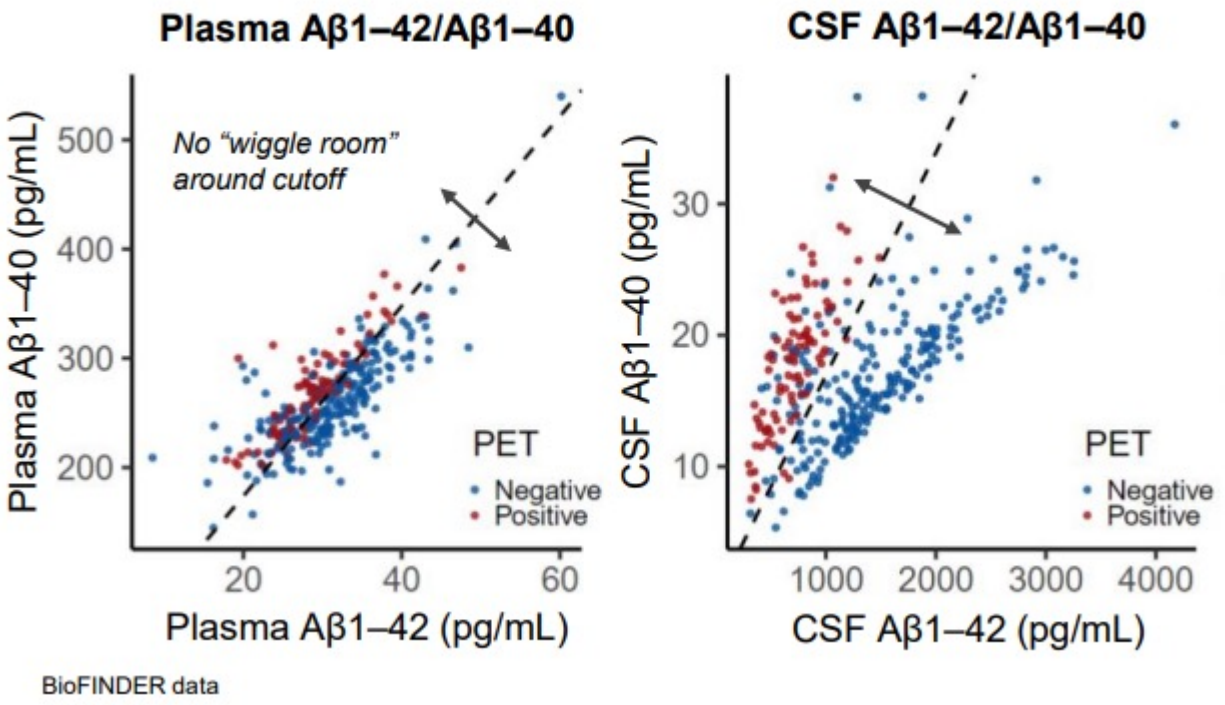
- Neurologists uniformly feel that knowing a patient's amyloid status would aid in the diagnosis of AD and allow them to select appropriate interventions
- Amyloid diagnostic tests are almost universally required for patient enrollment in AD clinical trials
- Unfortunately, PET Amyloid tests are not well suited for community use
  - Expensive ($5-6K on average) and not reimbursed
  - Expose patient to significant radiation
  - Not available in all communities; largely unavailable outside USA
  - Invasive and inconvenient for patients

< 3% AD Patients Receive an Amyloid Test

A "Better PET" would gain traction immediately with Neurologists

Plasma Aβ has a Narrow Dynamic Range

Only 8-12% Difference Between Plasma Aβ+ and Aβ- Patients

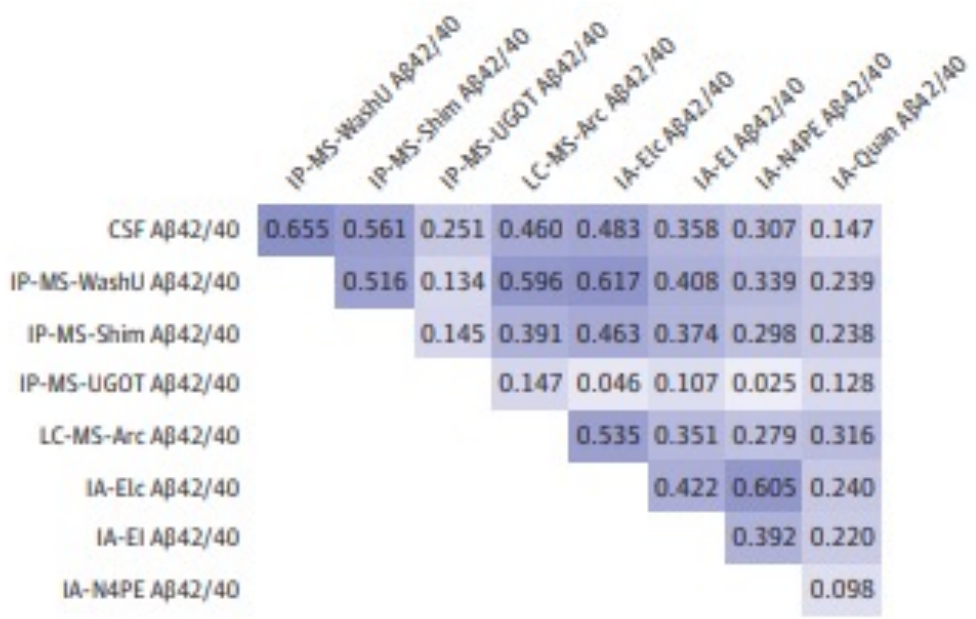


- Many plasma studies are retrospective and conducted in under protocols where sample collection and assay processing was very tightly controlled.
- High risk that a cutoff pre-specified based on one study would not be applicable to another
- Dynamic range is very limited
- May make application of plasma-based Aβ42/Aβ40 assays challenging in everyday clinical practice

Rabe, C et al. Poster: Utility of plasma Aβ1–42/Aβ1–40 as a screening tool is limited due to lack of robustness. CTAD 2021

...Perhaps Also a Reason for the Relatively Low Correlation Between Various Plasma Assays

Correlations Between CSF and Plasma Aβ42/40



Spearman correlations between plasma and CSF Aβ42/40 in a subcohort (n = 155) individuals where all plasma samples were analyzed using all 8 assays

- C2N (IP-MS-WashU) showed highest correlation with CSF
- Relatively low and inconsistent correlation between results from various plasma tests is concerning

Janelidze S, et al. *JAMA Neurol*. 2021 Nov 1;78(11):1375-1382.

Retina has Proven Challenging and Discovery Work Continues on Multiple Fronts

- **Multiple approaches have been explored**
  - OCT to measure thickening of RNFL (not specific to AD; glaucoma confounds results)
  - Aβ pathology (evidence of accumulation in humans is limited and inconsistent)
  - Hyperspectral Imaging ("blackbox" imaging approach, limited, retrospective studies)

> "These retinal imaging modalities require replication and neuropathological validation to move from the biomarker discovery to the biomarker validation phase" – Peter Snyder

Snyder, PJ, Alber, J, Alt, C, et al. Retinal imaging in Alzheimer's and neurodegenerative diseases. *Alzheimer's Dement*. 2021; 17: 103– 111.
Lemmens S, et al. Combination of snapshot hyperspectral retinal imaging and OCT to identify AD patients. Alzheimers Res Ther. 2020;12(1): 144

Simulation Results: Only MCI

Same methodology as MCI+ AD combined analysis shown on the previous slide, but using only MCI patients. The Simulation was run 2000 times and thresholds were as follows: FLES threshold: 0.912, SUVR threshold: 1.12.

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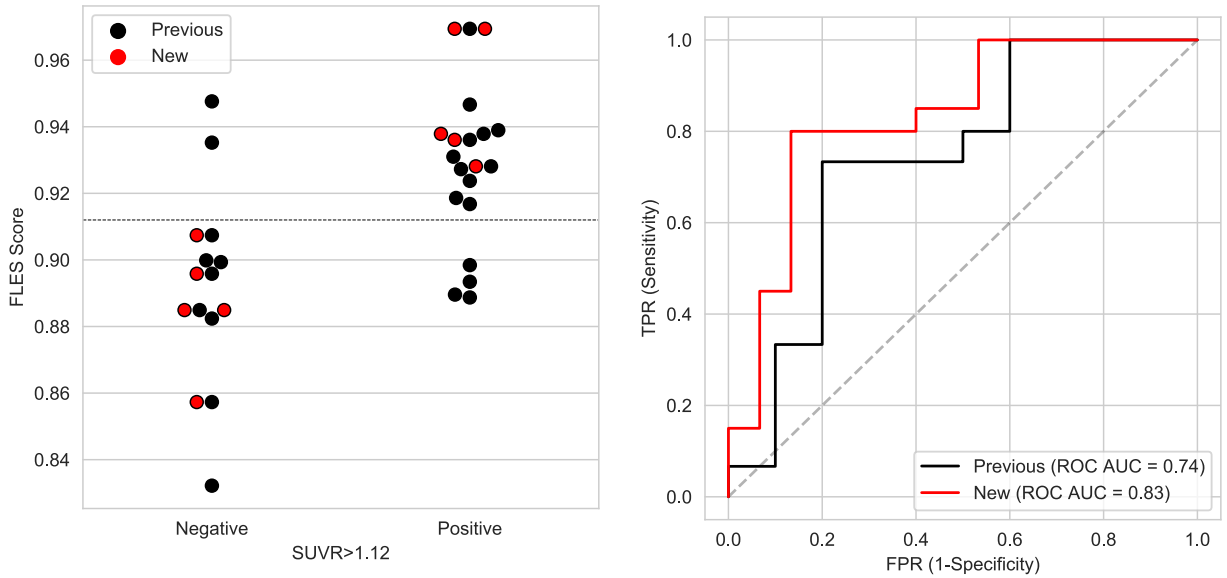

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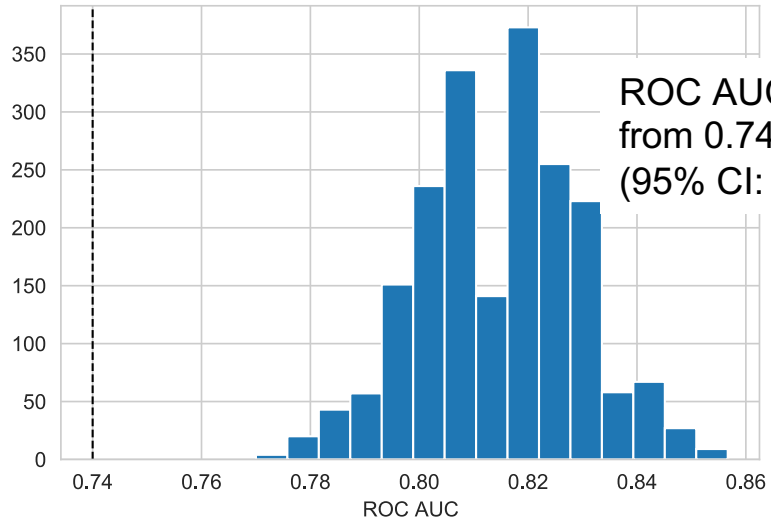

ROC AUC increases from 0.74 to 0.82 (95% CI: [0.74,0.82])

Scenario	Sensitivity	Specificity	Accuracy	NPV	PPV	ROC/ AUC
Current	0.73	0.80	0.76	0.67	0.85	0.74
w/ Simulated Data	0.80	0.87	0.83	0.76	0.89	0.82

2022-2023 Operating Plan Milestones & Costs

MILESTONES AND USE OF PROCEEDS	TIMING	BUDGET ESTIMATES
Baseline cash burn rate of $110K/month	**2022-2023**	**$1,320K/yr**
Clinical and Regulatory Investments		
10-Patient Study	Q1 2022	$215K
-0036 Study comparing Sapphire to PET	Q2-Q3 2022	$1,180K
-0038 Reproducibility Study	Q2-Q3 2022	$305K
FDA Pre-sub Meeting	Q4 2022	$25K
Pivotal Trial	2023	$10,000K
System Enhancements & Production		
Produce First Batch of API at Seqens	Q2-Q4 2022	$830K
Produce First Batch of Ointment at Cambrex	Q2-Q4 2022	$610K
Software Development and Device Build for Pivotal	TBD	$1,625K
Quality System ISO Certification	TBD	$600K
Produce 2nd and 3rd Batches of API and Ointment	2023	$620K
Commercial and Reimbursement		
Physician Market Research	Q3–Q4 2022	$75K
Brand Name Development	Q3- Q4 2022	$50K
Reimbursement Strategy	Q3- Q4 2022	$75K
Launch Preparations	2023	$500K