CASSAVA sciences

We Focus on Alzheimer's disease

December 2022

Forward-Looking Statements & Safe Harbor

This presentation from Cassava Sciences contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, that may include but are not limited to: our strategy and plans; the size and scope of our pivotal Phase 3 trial and its likelihood of success; the interpretation of clinical data generated in interim analyses of an open-label study; plans to announce clinical results of our open-label or CMS study and the timing thereof; the initiation and progression of a scientific inquiry undertaken by CUNY and the publication of its results; the treatment of Alzheimer's disease; the status of current and future clinical studies with simufilam; the safety or efficacy of simufilam in humans; our ability to expand therapeutic indications for simufilam outside of Alzheimer's disease; the development path for SavaDx and the use of mass spectrometry as an alternative method of detection; expected cash use in future periods; clinical data presented at the 2021 Alzheimer's Association International Conference (AAIC), including a subsequent erratum regarding visual errors not caught in proofing; a technical paper published in 2017 in Neurobiology of Aging and a subsequent erratum regarding a visual error not caught in proofing; verbal commentaries made by our employees; and potential benefits, if any, of the our product candidates. These statements may be identified by words such as "may," "anticipate," "believe," "could," "expect," "forecast," "intend," "plan," "possible," "potential," and other words and terms of similar meaning.

Simufilam and SavaDx are investigational product candidates that are not approved by any regulatory authority and their safety, efficacy or other desirable attributes have not been established. All clinical data from our open-label study are inherently exploratory in nature and, as with all open-label data, should be interpreted with caution. Data results from our open-label study does not constitute, and should not be interpreted as, evidence of therapeutic benefit for simufilam.

Drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in regulatory approval and subsequent commercialization of a product. In addition, our clinical results from earlier-stage clinical trials may not be indicative of full results or results from later-stage or larger scale clinical trials and do not ensure regulatory approval. Also, our interim data and analysis should not be relied upon as predictive of full study results for the open-label study, or any other study. You should not place undue reliance on these statements or any scientific data we present or publish.

Such statements are based 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, potential health benefits, if any, of changes in levels of biomarkers, the severity and duration of health care precautions given the COVID-19 pandemic, any unanticipated impacts of the pandemic on our business operations, including those described in the section entitled "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2021 and future reports to be filed with the SEC. The foregoing sets forth many, but not all, of the factors that could cause actual results to differ from expectations in any forward-looking statement. In light of these risks, uncertainties and assumptions, the forward-looking statements and events discussed in this presentation are inherently uncertain and may not occur, and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. Accordingly, you should not rely upon forward-looking statements as predictions of future events. Except as required by law, we disclaim any intention or responsibility for updating or revising any forward-looking statements contained in this presentation. For further information regarding these and other risks related to our business, investors should consult our filings with the SEC, which are available on the SEC's website at www.sec.gov.

This presentation may also contain statistical data and drug information 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 publicly available sources of data and information. Accordingly, we make no representations as to the accuracy or completeness of such data or information. You are cautioned not to give undue weight to such data.

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

Introduction to Cassava Sciences

We are developing a novel drug treatment for people with Alzheimer's disease.

Our science is based on stabilizing—but not removing—a critical protein in the brain.

Our lead drug candidate is in Phase 3 clinical trials.

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Cassava Sciences - Senior Management

Remi Barbier - Chairman, President & CEO

EXELIXIS® XOMA ARQULE®

Lindsay H. Burns, PhD - SVP Neuroscience

Abgenix élan UNIVERSITY OF CAMBRIDGE

Nadav Friedmann, PhD/MD - CMO, Board member

Eight FDA drug approvals prior to Cassava Sciences.

Johnson & Johnson Abbott Daiichi-Sankyo

Michael Zamloot - SVP Technical Operations

Four FDA drug approvals prior to Cassava Sciences.

Boehringer Ingelheim Ciba-Geigy

Jim Kupiec, MD – Chief Clinical Development Officer

Two FDA drug approvals prior to Cassava Sciences.

Pfizer SANOFI Ciba-Geigy

Chris Cook – SVP, General Counsel

Alcon JONES DAY®

Eric Schoen - Chief Financial Officer

ASPIRA LABS A VERMILLION COMPANY

PRICEWATERHOUSECOOPERS

Mike Marsman, PharmD - SVP Regulatory Affairs

Impax COR COR THERAPEUTICS, INC.

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Why Consider Neuroscience?

Neurological diseases are among the world's most prevalent health conditions.[1] Global sales of CNS therapeutics were over $116 billion in 2020 and are on pace to reach $205.7 billion by 2028.[2]

An aging population needs new neurological treatments.

Private & public investments are fueling innovation.

Sources:
[1] iShares by BlackRock, August 26, 2022, Market Insights, https://www.ishares.com/us/insights/neuro
[2] See above and Grand View Research, "Central Nervous System Therapeutic Market Size, Share & Trends Analysis Report By Disease (Neurovascular Diseases, CNS Trauma, Mental Health, Neurodegenerative Diseases, Infectious Diseases), By Region, And Segment Forecasts, 2021 – 2028,"

Alzheimer's Disease: a Significant Unmet Need

Signature of Alois Alzheimer, circa 1915

Alzheimer's disease (AD) is a world-wide epidemic.

AD outranks cancer, stroke and heart attack as most-feared chronic disease by retirees, according to a study.[1]

Cassava Sciences sees an opportunity to create value.

"Alzheimer's disease represents one of the greatest medical challenges that face this century; the condition is becoming increasingly prevalent worldwide and as yet no effective treatments have been developed for this terminal disease."

Neurologic Clinics 2016 Nov 34(4)

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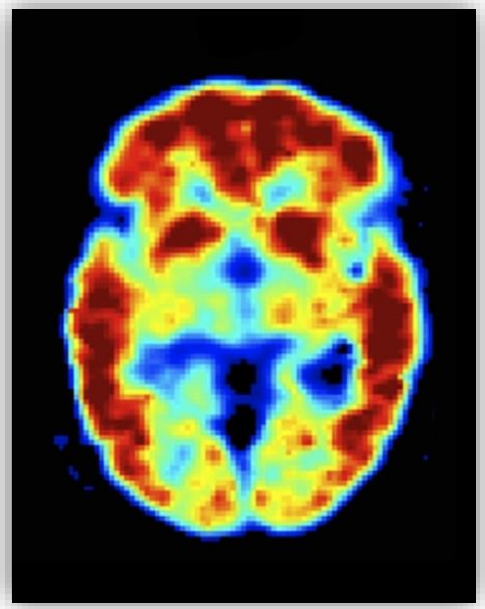
[1] Source: "*The Four Pillars of the New Retirement*", EdwardJones, accessed on-line November 2022.

Ultimately, a Fatal Disease



Alzheimer's disease (AD) is a progressive neurological disorder.

Results in memory loss, changes in behavior. Eventually, the AD patient is unable to perform daily functions.

Approved therapies slow cognitive decline modestly. Aducanumab; NMDA antagonist; enzyme blockers that may improve memory for some months, such as donepezil (Aricept®), galantamine (Razadyne®), rivastigmine (Exelon®).

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Simufilam for Alzheimer’s Disease

Not actual photo of simufilam.

Simufilam is Cassava Sciences’ wholly-owned, proprietary oral drug candidate for Alzheimer's disease.[1]

Simufilam is a small molecule aimed at stabilizing – but not removing – an altered protein in the Alzheimer’s brain.

We are evaluating simufilam in Alzheimer’s disease dementia in an on-going Phase 3 clinical program.

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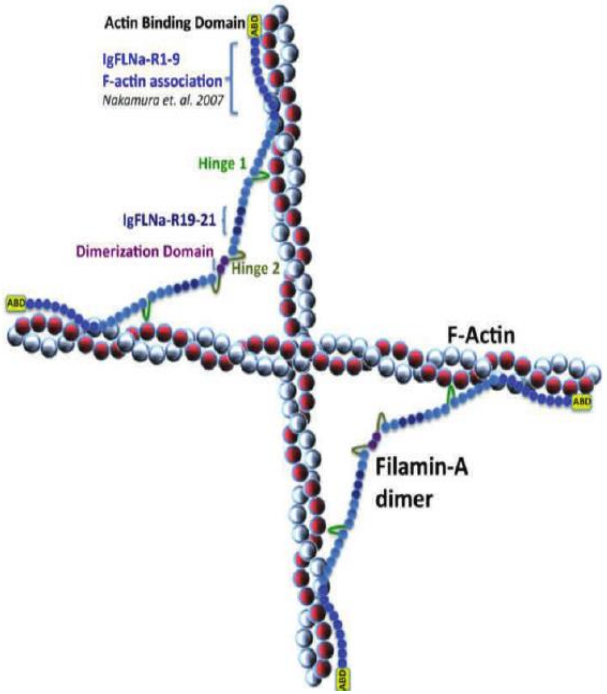
[1] Simufilam is an investigational drug that is not approved by any regulatory authority and its safety, efficacy or other desirable attributes have not been established.

Simufilam Targets an Altered Protein

Plaques (Aβ) & tangles (tau) are neurotoxic hallmarks of Alzheimer's disease (AD).



Illustrative structure of a human FLNA and crosslinks to actin filaments into orthogonal networks.

Simufilam targets altered form of filamin A (FLNA) in AD.

i. Scaffolding proteins link other proteins into stable, healthy conformations.

ii. The AD brain has an altered form of FLNA, a scaffolding protein.

iii. Altered FLNA **enables** Aβ neurotoxicity – neuronal dysfunction/degeneration and neuroinflammation.

iv. Simufilam **disables** Aβ neurotoxicity by binding to altered FLNA, restoring its proper shape/function.

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Snapshot of On-going Clinical Activities

Phase 3 Clinical Program

Over 750 patients are now enrolled in Phase 3 studies of simufilam in Alzheimer's disease dementia.

- ✓ *Patients are being screened in clinical trial sites in the U.S., Puerto Rico, Canada, South Korea and Australia.*
- ✓ *Our Phase 3 studies have a relatively long & rigorous screening process to ensure only qualified patients are successfully enrolled.*
- ✓ *Alzheimer's patients who complete one of our P3 studies are eligible to enroll in an open-label extension study.*

Other Clinical Studies

Open-label study in Alzheimer's patients.

- ✓ *This study is fully-enrolled (>200 patients).*
- ✓ *Subjects have completed 1 yr of simufilam treatment.*

Upcoming data release, pending completion of an independent statistical analysis on the clinical dataset.

Randomized, placebo-controlled Cognition Maintenance Study (CMS) in Alzheimer's.

- ✓ *CMS is fully enrolled (>100 patients).*
- ✓ *Over 75 patients have completed this 6-month study.*
- ✓ *All clinical data remains blinded.*

Our goal is to announce top-line clinical results for the CMS approximately Q3 2023.

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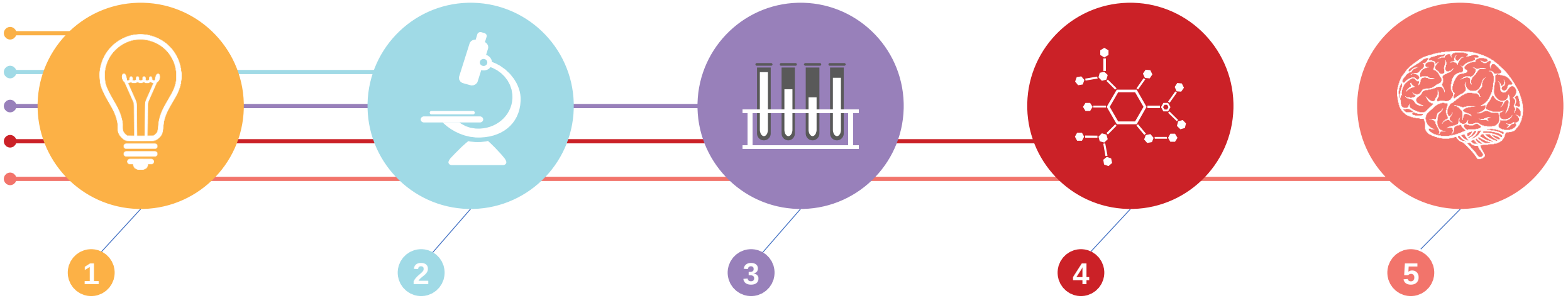
Science and Proof-of-Concept

Lindsay Burns, PhD – SVP Neuroscience

In-house Discovery/Development Program



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

2009
Discovery that altered FLNA links to α7nAChR when Aβ signals.

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

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

2017 - present
IND filing. Clinical testing of simufilam.

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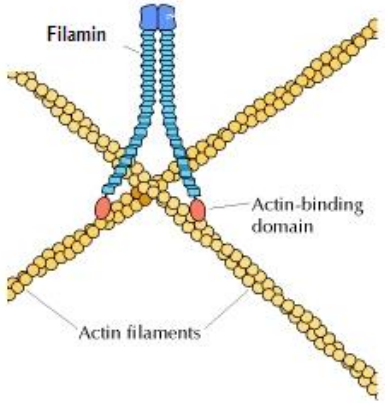
Simufilam Targets *Altered* Filamin A

Filamin A (FLNA) is a scaffolding protein anchored in the cell membrane.



FLNA cross-links actin to provide structure and motility, but also interacts with >90 proteins, influencing many signaling pathways.

The Alzheimer's brain carries an *altered* form of FLNA.

Altered FLNA is critical to amyloid beta toxicity.

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Proposed Mechanism of Action

The altered form of FLNA is a proteopathy in the AD brain.

Altered FLNA *enables* $A\beta_{42}$ signaling through two receptors by linking to them:

i. **α7nAChR ($A\beta_{42}$ binds with femtomolar affinity)** → hyper-phosphorylates tau
ii. **TLR4 ($A\beta_{42}$ binds CD14 co-receptor)** → persistent activation & chronic neuroinflammation

Simufilam preferentially binds *altered* FLNA:

i. ***restores*** **FLNA's normal shape,**
ii. ***disrupts*** **FLNA's aberrant linkages to α7nAChR and TLR4,**
iii. ***suppresses*** **$A\beta_{42}$ signaling through both receptors.**

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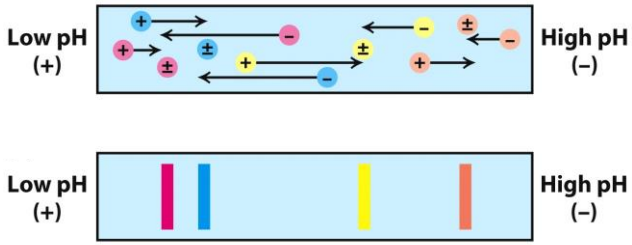
Evidence of Target Engagement

Evidence in patient lymphocytes from Day 0 to 14 and 28 by three methods

i. Reversal of altered conformation of FLNA

Assessed by isoelectric focusing point

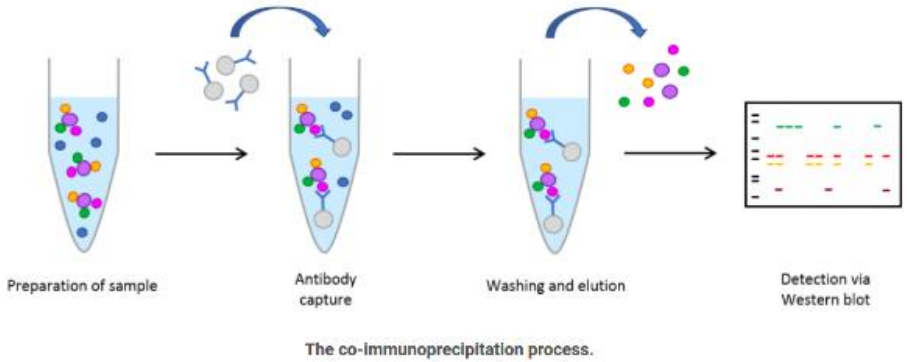


ii. Reduces FLNA linkages to α7nAChR and TLR4

Assessed by co-immunoprecipitation

iii. Reduced $A\beta_{42}$ complexed with α7nAChR and CD14

Assessed by co-immunoprecipitation



The co-immunoprecipitation process.

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Clinical Development Timelines for Simufilam

Completed

- ✓ *2017: Phase 1 dose-escalating safety study in human volunteers.*
- ✓ *2019: Phase 2a open-label safety study in Alzheimer's patients.*
- ✓ *2020: Phase 2b randomized, placebo-controlled study in Alzheimer's patients.*
- ✓ *2021: Interim analysis of open-label study in first 50 patients to complete 6, 9 & 12 months of treatment.*
- ✓ *2021: End-of-Phase 2 meeting with FDA.*
- ✓ *2021: Two FDA Special Protocol Assessments for Phase 3 clinical program.*

On-going

- ○ *Two Phase 3 studies in Alzheimer's patients.*
- ○ *Open-label safety study in Alzheimer's patients.*
- ○ *Open-label extension study for Phase 3 program.*
- ○ *Randomized, placebo-controlled Cognition Maintenance Study (CMS) in Alzheimer's patients.*

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On-going Open-label Study

We are conducting a one-year, open-label safety study of simufilam (100 mg BID) in up to 200 patients with mild-to-moderate Alzheimer's disease (MMSE 16 to 26).

- **All study participants have now completed drug treatment.**
- **Upcoming data release, pending completion of statistical analysis.**
- **To ensure the highest integrity of data analysis, outside biostatisticians with specific expertise in Alzheimer's disease will conduct an independent statistical analysis on the clinical dataset.**

All clinical data from our open-label study are inherently exploratory in nature and, as with all open-label data, should be interpreted with caution. Data results from our open-label study does not constitute, and should not be interpreted as, evidence of therapeutic benefit for simufilam.

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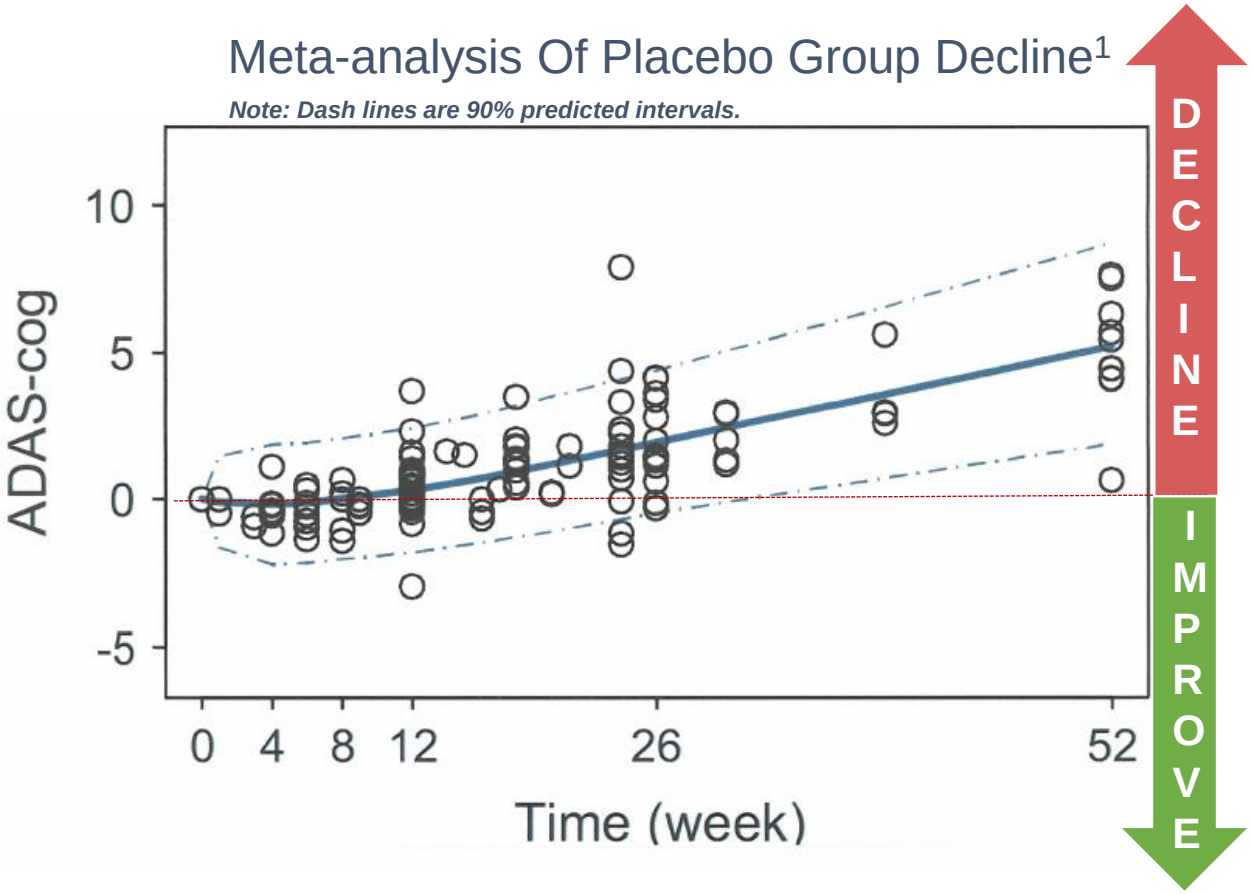
Expected Rate of Cognitive Decline in AD - Literature



- **Cognitive decline was reported in a published, meta-analysis of 20,000 patients with mild-to-moderate AD in randomized, controlled trials[1].**
  5.5 point average decline over 12 months on ADAS-Cog among study subjects who were administered placebo in randomized, controlled trials.

- **Cognitive decline was reported in two P3 studies of Biogen's aducanumab in patients with early AD[2]:**
  5.2 point average decline over 18 months on ADAS-Cog among study subjects who were administered placebo in randomized, controlled trials.

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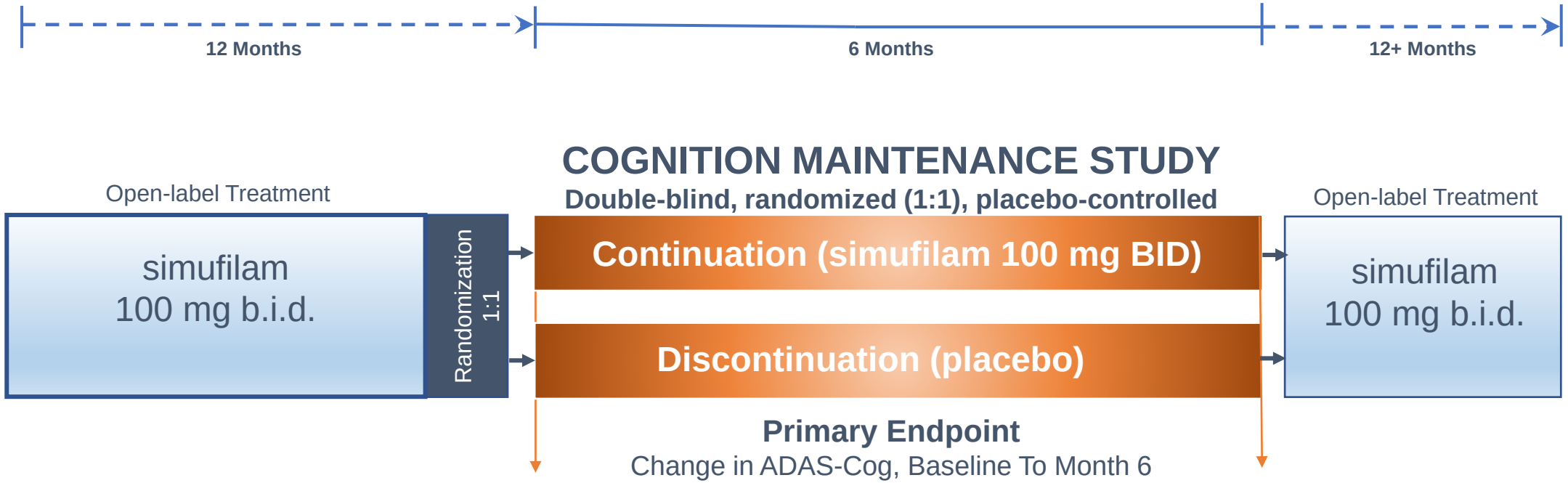
[1] *Disease Progression Meta-analysis Model in Alzheimer's disease* (Ito, et al., Pfizer Global Research), Alzheimer's & Dementia 6 (2010) 39-53
[2] *EMERGE and ENGAGE Topline Results (2020), https://investors.biogen.com/static-files/f91e95d9-2fce-46ce-9115-0628cfe96e83*

Cognition Maintenance Study (CMS)

Goal is to compare cognition in ≈ 100 AD patients who continue vs. discontinue simufilam treatment over 6 months, following 1-year open-label treatment.



Over 75 patients have completed the CMS as of December 1, 2022.

Our goal is to announce CMS results approximately Q3 2023.

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Phase 1 and Phase 2 Clinical Data……

Appear promising because:

- ✓ Simufilam was safe, well tolerated in patients with Alzheimer's disease.
- ✓ The biology & preclinical data bridge back to the clinical data.
- ✓ High percentage of patients responded to drug treatment.

Viewed conservatively because:

- Drug treatment was open-label, except for Phase 2b study.
- The total number of patients exposed to simufilam in P1/P2 studies is small (N≈250).
- Evidence of simufilam's safety and efficacy still needs to be established.

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Phase 3 Program

Jim Kupiec, MD - Chief Clinical Development Officer

Nadav Friedmann, PhD/MD – Chief Medical Officer

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Regulatory Strategy

- **Successful End-of-phase 2 meeting with FDA.**
  - EOP2 meeting objectives were to gain general agreement around a Phase 3 clinical program and statutory requirements for a 505(b)(1) NDA submission and marketing approval of simufilam for the treatment of mild-to-moderate Alzheimer's disease.
  - FDA agrees that the completed Phase 2 program, together with well-defined Phase 3 clinical program, are sufficient to show evidence of clinical efficacy.
  - Agreement on use of co-primary efficacy endpoints to assess treatment benefits.

- **Agreement reached with FDA on two Special Protocol Assessments for Phase 3.**

Phase 3 Program Overview

Our Phase 3 program consists of two double-blind, randomized, placebo-controlled studies in patients with mild-to-moderate Alzheimer's disease.

>750 patients are enrolled in our Phase 3 studies as of December 1, 2022

				Co-Primary Endpoints		Secondary Endpoints	
	Enrollment Target	Simufilam Treatment	Length of Treatment	Cognition Scale	Function Scale	Cognition + Function Scale	Dementia-related Behavior Scale
1st Phase 3	~ 750 Subjects	100 mg	52-weeks	ADAS-Cog12	ADCS-ADL	iADRS	NPI_{12}
2nd Phase 3	~ 1,000 Subjects	100 mg or 50 mg	76-weeks	ADAS-Cog12	ADCS-ADL	iADRS	NPI_{12}

***ADAS-Cog** = The Alzheimer's Disease Assessment Scale – Cognitive Subscale, a measure of cognition*
***ADCS-ADL** = Alzheimer's Disease Cooperative Study – Activities of Daily Living, a measure of health function*
***iADRS** = integrated Alzheimer's Disease Rating Scale, a composite measure of cognition and health function*
***NPI** = Neuropsychiatric Inventory*

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Phase 3 Program Details

rethinkALZ
JOIN A CLINICAL STUDY TO **ADVANCE ALZHEIMER'S TREATMENT**

- 52-week Phase 3 study, initiated Fall 2021.
- ≈ 750 subjects, randomized (1:1) to simufilam 100 mg or placebo twice daily.
- Co-primary efficacy endpoints are ADAS-Cog12, a cognitive scale, and ADCS-ADL, a functional scale.
- A secondary efficacy endpoint is iADRS, a clinical tool that combines scores from ADAS-Cog & ADCS-ADL.
- Other secondary endpoints include plasma biomarkers of disease and NPI to assess dementia-related behavior.

refocusALZ
JOIN A CLINICAL STUDY TO **ADVANCE ALZHEIMER'S TREATMENT**

- 76-week Phase 3 study, initiated Fall 2021.
- ≈ 1,000 subjects, randomized (1:1:1) to simufilam 100 mg, 50 mg or placebo twice daily.
- Co-primary efficacy endpoints are ADAS-Cog12, a cognitive scale, and ADCS-ADL, a functional scale.
- A secondary efficacy endpoint is iADRS, a clinical tool that combines scores from ADAS-Cog & ADCS-ADL.
- Other secondary endpoints include CSF, plasma and imaging biomarkers of disease and NPI to assess dementia-related behavior.

ADAS-Cog *= The Alzheimer's Disease Assessment Scale – Cognitive Subscale, a measure of cognition*
ADCS-ADL *= Alzheimer's Disease Cooperative Study – Activities of Daily Living, a measure of health function*
iADRS *= integrated Alzheimer's Disease Rating Scale, a composite measure of cognition and health function*
NPI *= Neuropsychiatric Inventory*

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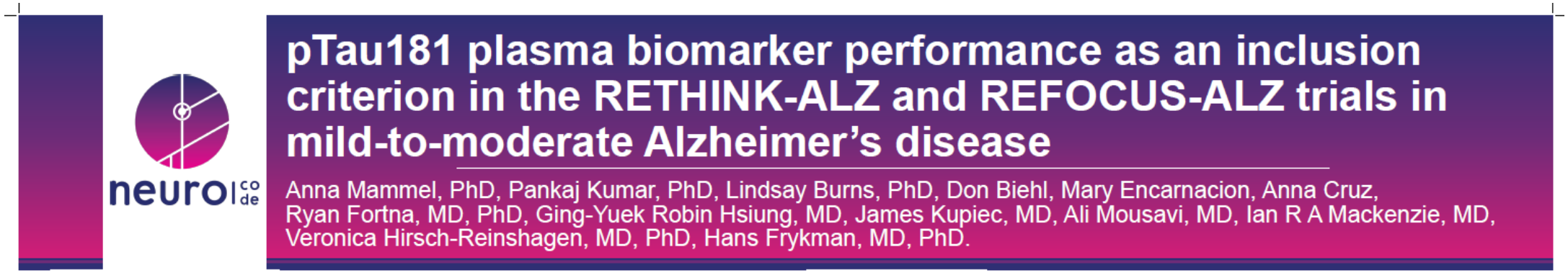
Phase 3 Entry Criteria Includes pTau Plasma Assay

- **Tau proteins can provide independent confirmation of AD neuropathology[1].**
- **ReTHINK-ALZ and ReFOCUS-ALZ Phase 3 studies use pTau181 plasma assay to qualify mild-to-moderate Alzheimer's patients.**
  - **30 ng/L cut-point showed 100% sensitivity and 88% specificity for AD diagnostic in 22 autopsy-confirmed samples[1].**
  - **2022 CTAD Poster presentation:** https://www.cassavasciences.com/static-files/d3e299ed-5d9b-4aaa-9e9b-8aada06a1a83



[1] Source: *pTau181 Plasma Biomarker Performance as an Inclusion Criterion in the RETHINK-ALZ and REFOCUS-ALZ trials in mild-to-moderate Alzheimer's disease,* Mammel et al., CTAD 2022

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SavaDx: An Investigational Diagnostic for Alzheimer's

- ***The underlying science for simufilam supports the development of a diagnostic technology to detect Alzheimer's disease with a simple blood test, called SavaDx.***
- ***SavaDx is an early-stage product candidate.***
- ***Working with third parties, we are evaluating the use of mass spectrometry to detect FLNA without the use of antibodies.***
- ***SavaDx is a lower priority program compared to simufilam.***

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Intellectual Property

- **Simufilam is a novel molecule. We own exclusive, worldwide rights to simufilam and related technologies, without financial obligations to any third party.**

- **Composition of matter patent protection for simufilam and other novel filamin-binding molecules includes over six issued patents. These currently run beyond 2033.**

- **We do not have issued patents in the U.S. for SavaDx, where we believe SavaDx may be protected by trade secrets, know-how and other proprietary rights technology.**

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Financials

Eric Schoen - Chief Financial Officer

$50,000,000 Capital Raise

- **On November 22, 2022, we closed a $50 million capital raise.**
- **We received approximately $47.3 million of net proceeds from the sale of 1.7 million common shares; all shares were placed with institutional investors.**
  - EcoR1 Capital (https://www.ecor1cap.com/) led this capital raise, taking >50% of the shares on offer.
- **Net proceeds to be used for working capital purposes, including continued development of simufilam.**

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Financials

Nasdaq ticker: SAVA	
Shares Outstanding	≈ 41.7 million[1]
Unaudited Financials at November 22, 2022	
Cash Balance	≈ $210 million[1]
Debt	none

Est. Cash Use for Operations in the 2nd Half of 2022 Guided to $45 to $55 million. Actual Cash Use Is Expected to be Under $45 Million for This Period.

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Footnote 1: Includes approximately $47.3 million of net proceeds received from the sale of 1.7 million common shares in a capital raise completed November 22, 2022.

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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/
Erratum: Figure 12 contains an image showing 12 control bands; it should show 13. This visual error was not caught in proofing. The data analysis was based on all 13 control bands. This error does not impact data conclusions.

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
Erratum: There is one duplicated panel in Figure 8; the publisher printed a correction. This error does not impact data conclusions.

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