CASSAVA sciences

Corporate Overview

November 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. All statements other than statements of historical fact contained in this presentation including, but not limited to, statements regarding plans or timing for future clinical studies with sumifilam or SavaDx; plans to initiate a Phase 3 clinical study of sumifilam in 2021; the interpretation of prior or current results of our Phase 2 clinical studies, including the measured effects of sumifilam on biomarkers or cognition; plans to publish results in a peer-reviewed journal; plans to disclose an interim analysis of an open-label study of sumifilam; potential health benefits, if any, of changes in levels of biomarkers; verbal commentaries made by Cassava Sciences' employees; and potential benefits, if any, of the Company's product candidates for Alzheimer's disease, are all forward-looking statements.

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 may also 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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Meet the Company

- **We are a publicly-traded, clinical-stage biotechnology company based in Austin, TX.**

- **We are developing sumifilam, a proprietary drug candidate to treat Alzheimer's disease, and SavaDx, a blood-based diagnostic to detect Alzheimer's disease.**
  - Both are investigational product candidates substantially funded by competitive research grant awards from the National Institutes of Health (NIH).

- **Our scientific approach is unique, our clinical data is highly differentiated.**
  - ✓ In 2019, we announced positive results in an open-label Phase 2a study of sumifilam in Alzheimer's disease.
  - ✓ In 2020, we announced positive results of a randomized, placebo-controlled Phase 2b study of sumifilam in Alzheimer's disease.

Our goal is to initiate a Phase 3 study of sumifilam in Alzheimer's disease in 2021.

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Meet the Team

Leadership

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 elan 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

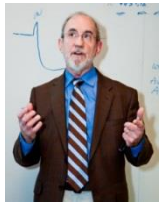
Independent Directors

Sanford Robertson

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

Robert Gussin, PhD

- Formerly, Johnson & Johnson, Chief Scientific Officer and Corporate VP, Science and Technology



Patrick Scannon, MD/PhD

- Formerly, Founder & CSO/CMO - XOMA Corporation

Michael O'Donnell

- Partner, Morrison & Foerster LLP

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Science & Technology

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Introduction to Sumifilam

- **Sumifilam is our proprietary, small molecule (oral) drug candidate to treat Alzheimer's disease (AD) and other neurodegenerative diseases.**
  - Discovered and developed in-house, 2008 to present.

- **Sumifilam binds a single target, has a dual mechanism of action:**
  - Reduces neurodegeneration *and* neuroinflammation.
  - Published preclinical data, mechanism of action studies support sumifilam's potential as a disease-modifying drug for AD that also provides symptomatic improvement.

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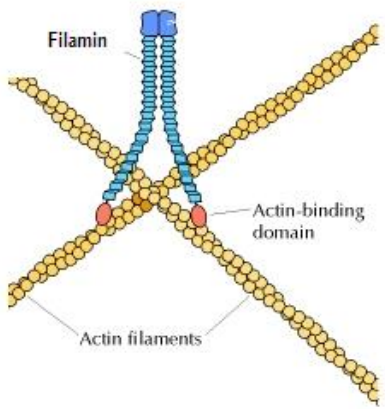
Sumifilam Mechanism of Action

The Target of Sumifilam is Altered Filamin A (FLNA)

Filamin A (FLNA) is a scaffolding protein highly expressed in the brain.



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.

Mechanism of Action

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

Altered FLNA <u>enables</u> $A\beta_{42}$ signaling via:

i. **α7-nicotinic acetylcholine receptor (α7nAChR)**
   → hyperphosphorylates tau

ii. **Toll-like receptor 4 (TLR4)**
   → releases inflammatory cytokines

Sumifilam binds altered FLNA, restores its proper shape/function, <u>disables</u> $A\beta_{42}$ signaling via α7nAChR and TLR4.

Through a single target, sumifilam reduces neurodegeneration and neuroinflammation.

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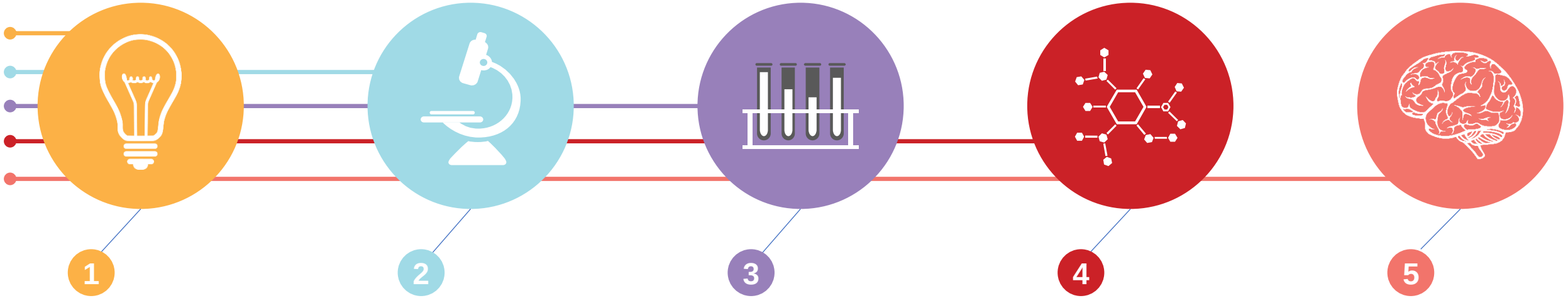
10+ Year In-house Discovery/Development Program



<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
Sumifilam (formerly, PTI-125) binds altered FLNA with high affinity, blocks α7nAChR/Aβ interactions. Preclinical testing of sumifilam.

2017 - present
IND filing. Clinical testing of sumifilam. Positive Phase 2 results reported in Alzheimer's patients.

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Summary of Preclinical Effects

Sumifilam	Intracerebro-ventricular (ICV) $A\beta_{42}$ infusion mouse model	Triple transgenic AD mouse model	Post-mortem human AD brain tissue	Post-mortem human age-matched control brain tissue treated with $A\beta_{42}$ in vitro
Reduced FLNA linkage to α7nAChR/TLR4	√	√	√	√
Reduced $A\beta_{42}$ bound to α7nAChR	√	√	√	√
Reduced amyloid deposits and NFTs	√	√	–	–
Reduced tau hyperphosphorylation	√	√	–	√
Improved function of α7nAChR, NMDAR and insulin receptors	√	√	√	√
Improved synaptic plasticity (activity-dependent Arc expression)	–	√	–	√
Reduced inflammatory cytokine levels	√	√	–	–
Improved cognition/behavior	–	√	–	–

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Clinical Hypothesis

Hypothesis

Phase 2a results, published mechanism of action studies and preclinical data all suggest sumifilam is a disease-modifying drug for AD that also provides symptomatic improvement.

Study Objective

Evaluate safety, biomarkers and cognition in a randomized, placebo-controlled Phase 2b clinical study of sumifilam.

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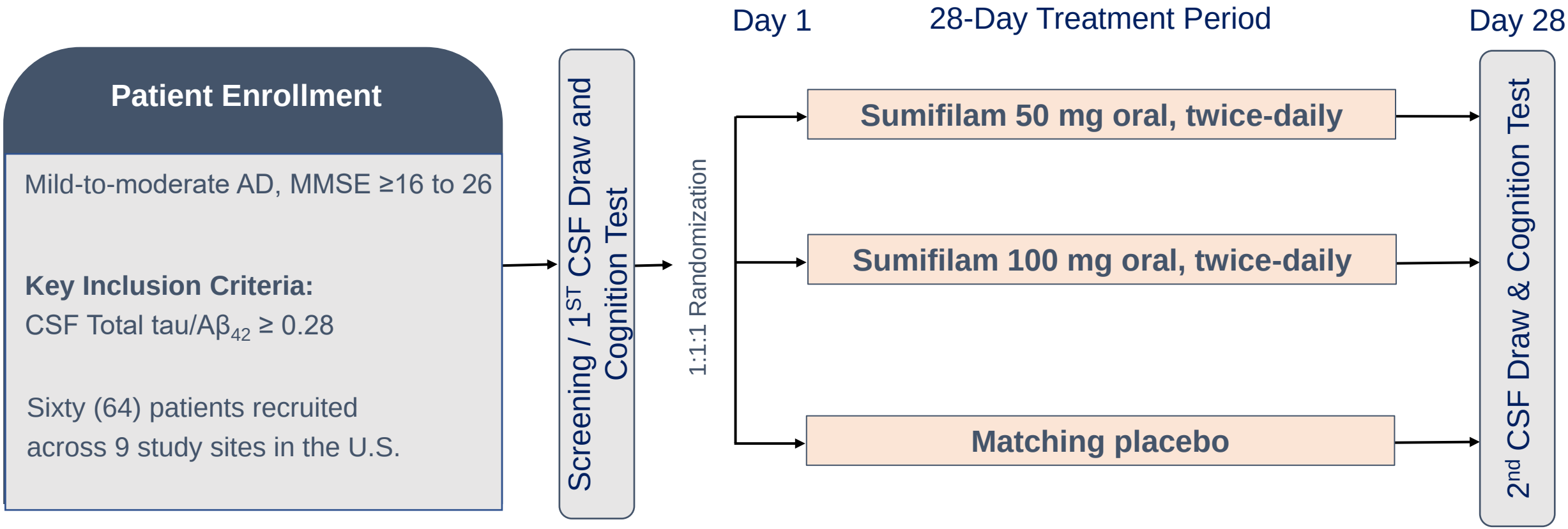
Phase 2b - Study Design

Randomized, Double-blind, Placebo-controlled, Multi-center



Primary Endpoint: **Biomarkers of disease**

Secondary Endpoint: **Cognition**

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Phase 2b Results – Safety & Baseline

- **Sumifilam was safe and well-tolerated**
- **No serious adverse events**
- **No drug-related patient discontinuation**
- **No drug-related adverse events**
  - Common, non-persistent side-effects observed in placebo & drug groups
- **Baseline characteristics were well-balanced between treatment groups, assigned through (1:1:1) randomization.**

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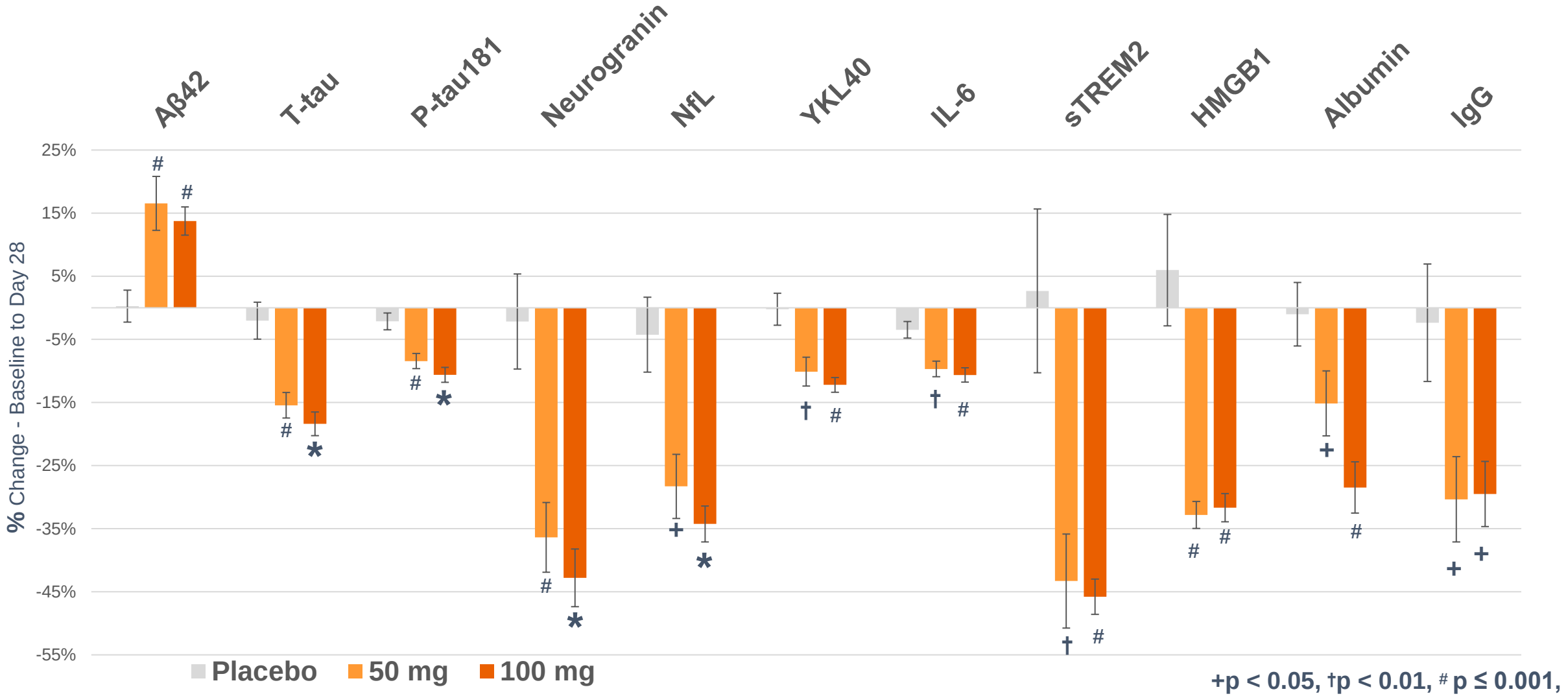
Phase 2b Summary of Results - CSF Biomarkers



+p < 0.05, †p < 0.01, # p ≤ 0.001,
*p < 0.0001 vs. placebo

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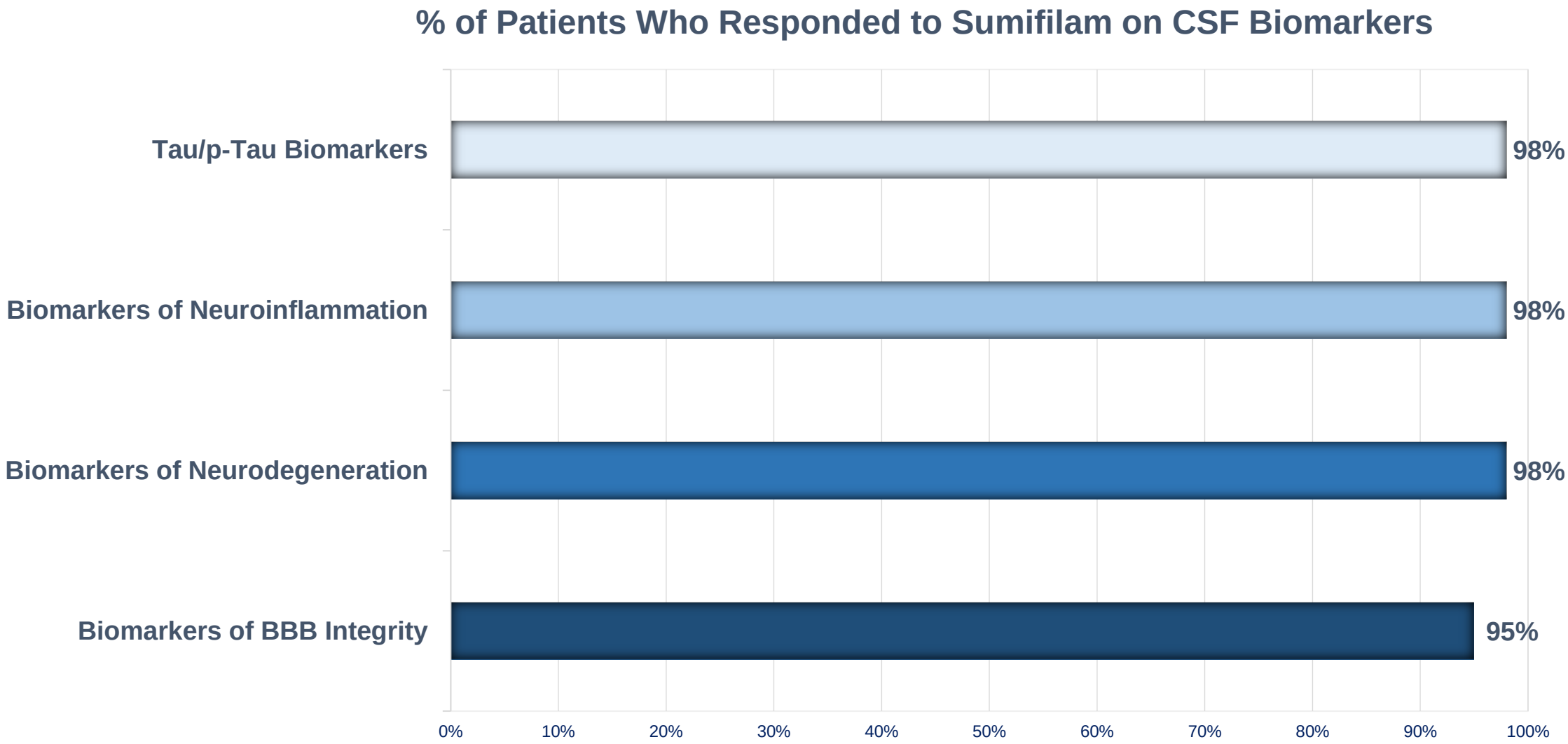
Phase 2b Results – Patient Responder Analysis



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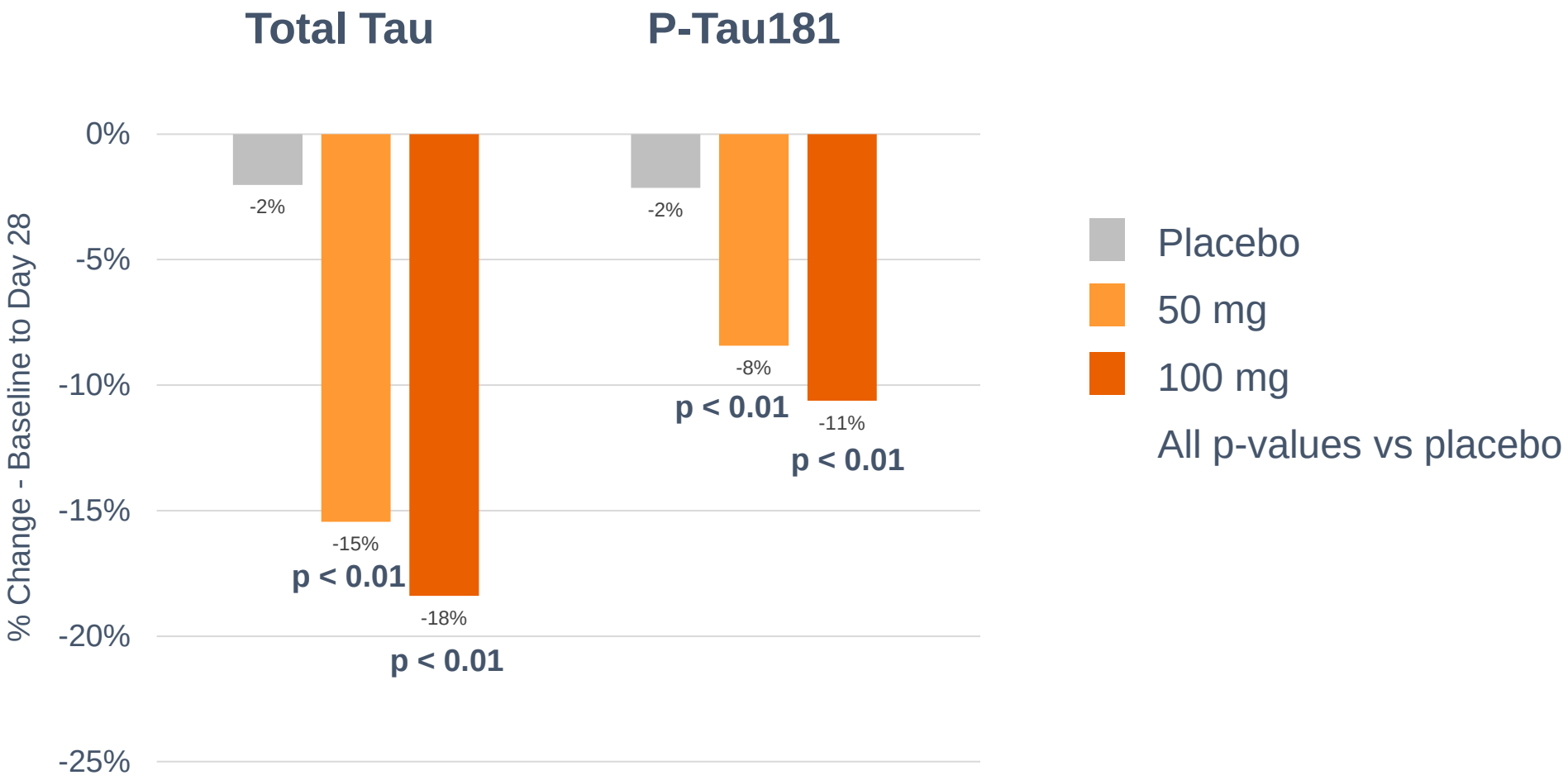
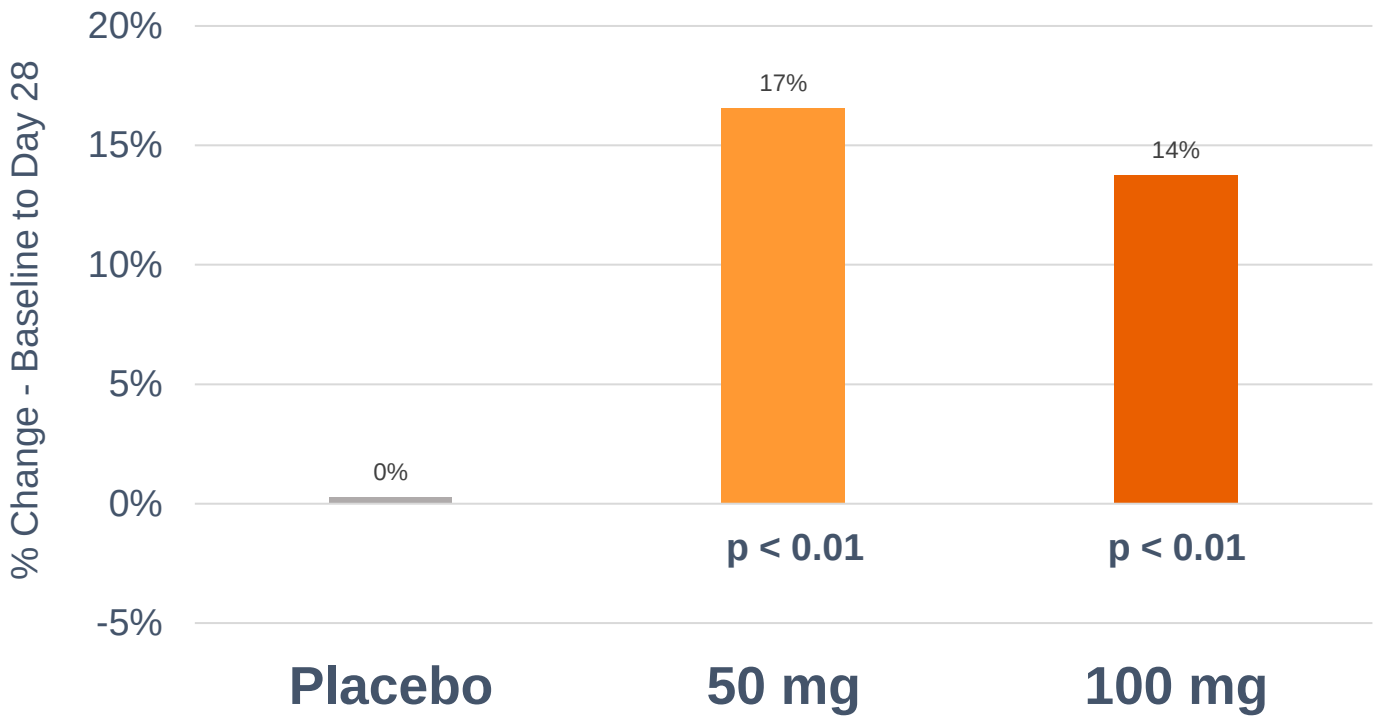
Phase 2b Results – CSF Total Tau and P-Tau181 Decreased



Phase 2b Results – CSF $A\beta_{42}$, Increased, As Expected

Change in Levels of CSF Amyloid-β_{42} Day 0 to Day 28



Note: CSF amyloid-β_{42} levels are low in early stages of dementia in patients with Alzheimer's disease.

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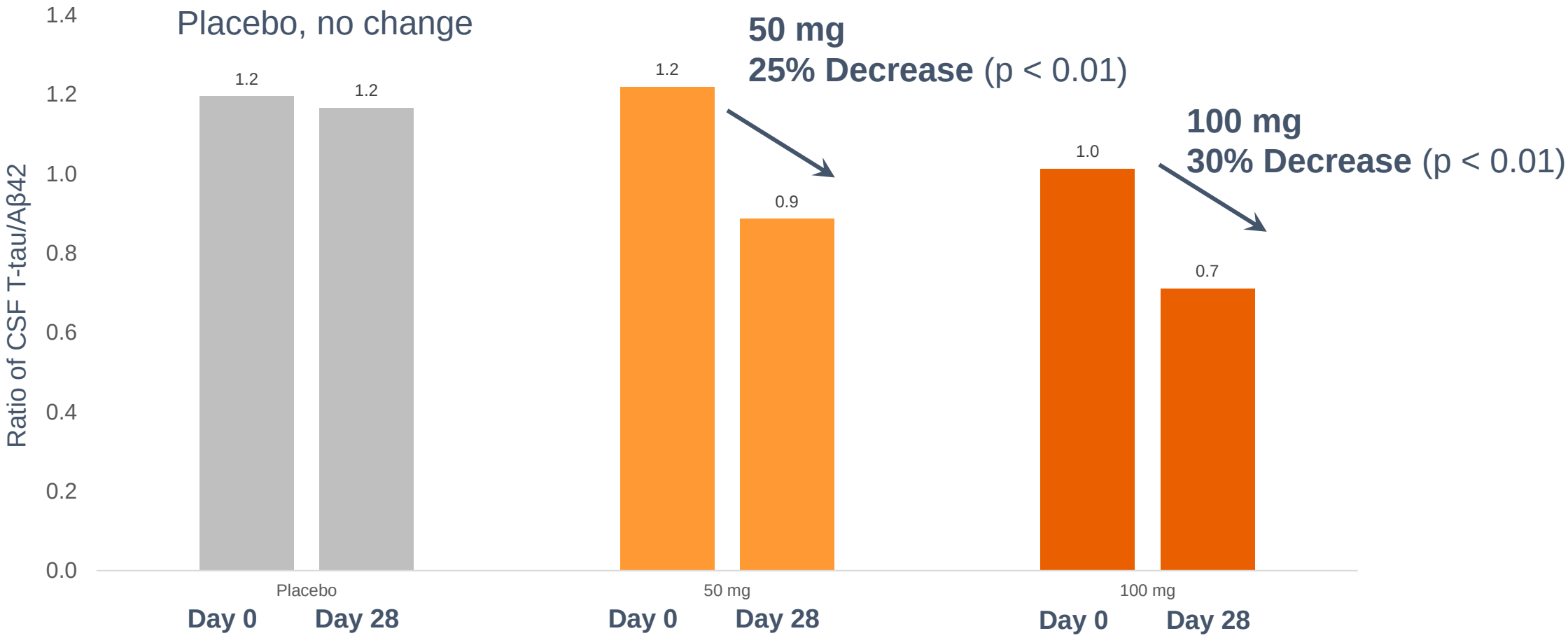
Phase 2b Results - Total tau/Aβ_{42} Decreased Significantly

A Key Diagnostic Criteria for AD Decreased Significantly in Both Drug Groups

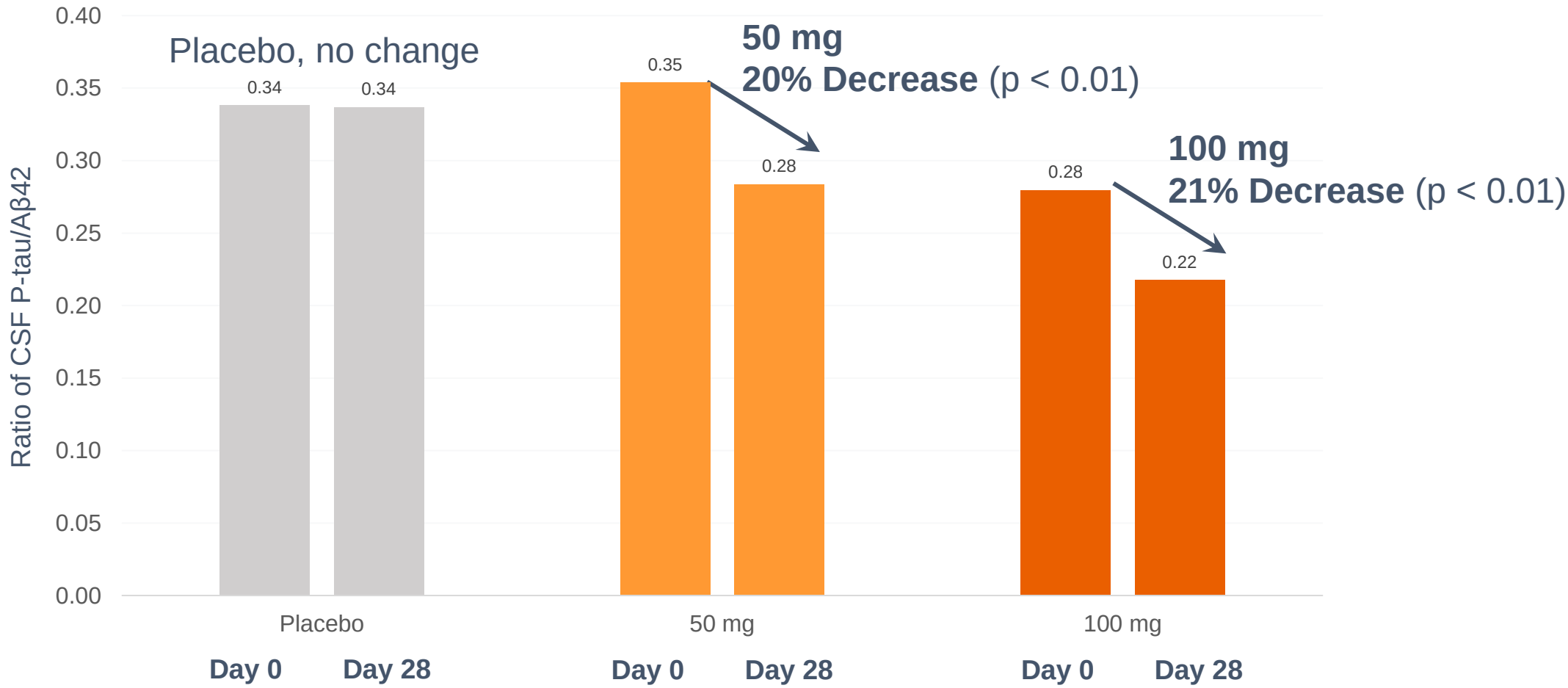
Change in Ratio of CSF T-tau/Aβ_{42} Day 0 to Day 28



Phase 2b Results - P-tau/Aβ$_{42}$ Decreased Significantly

A Key Diagnostic Criteria for AD Decreased Significantly in Both Drug Groups

Change in Ratio of CSF P-tau/Aβ$_{42}$ Day 0 to Day 28



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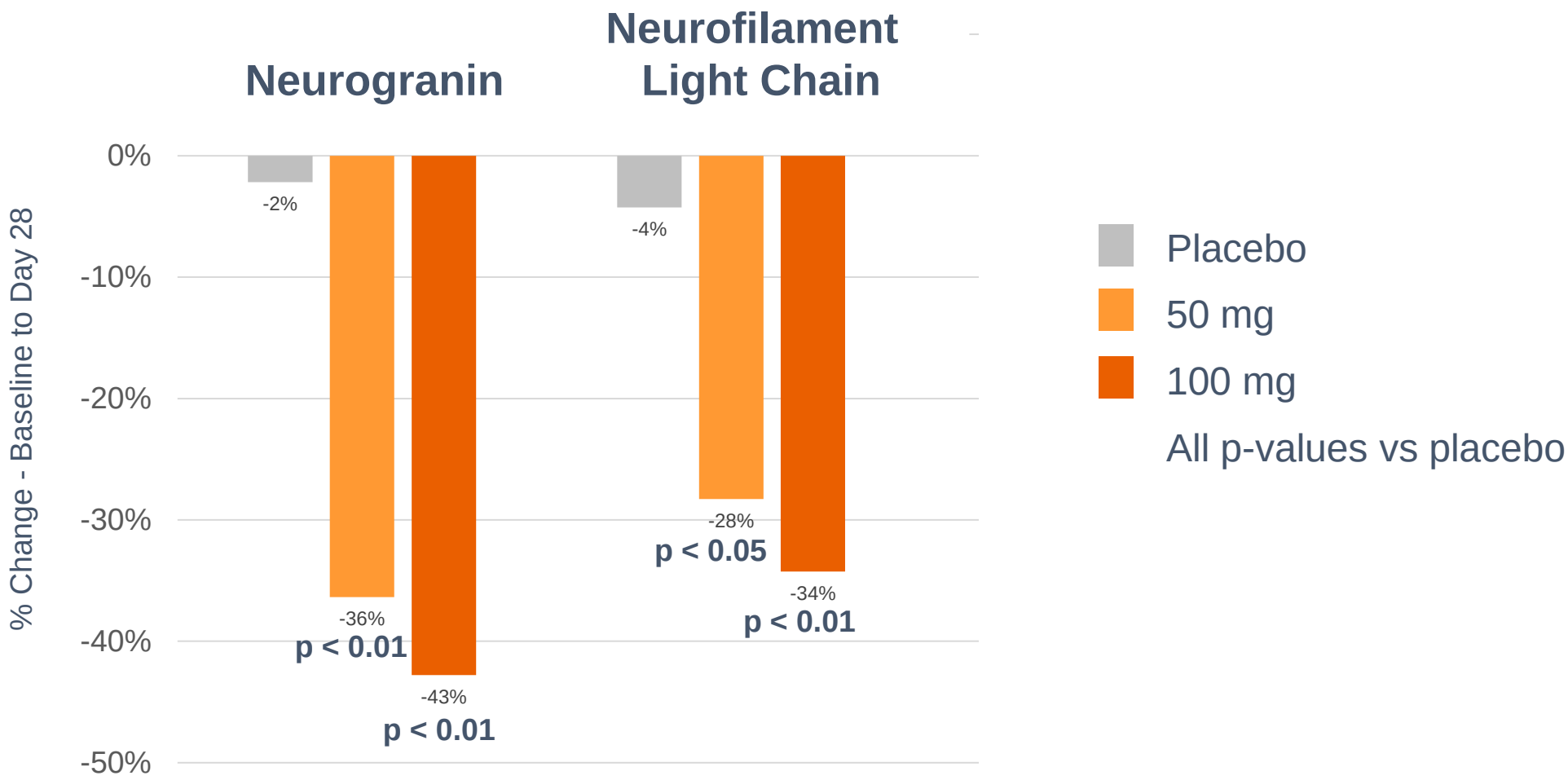
Phase 2b Results - Decrease in CSF Neurodegeneration



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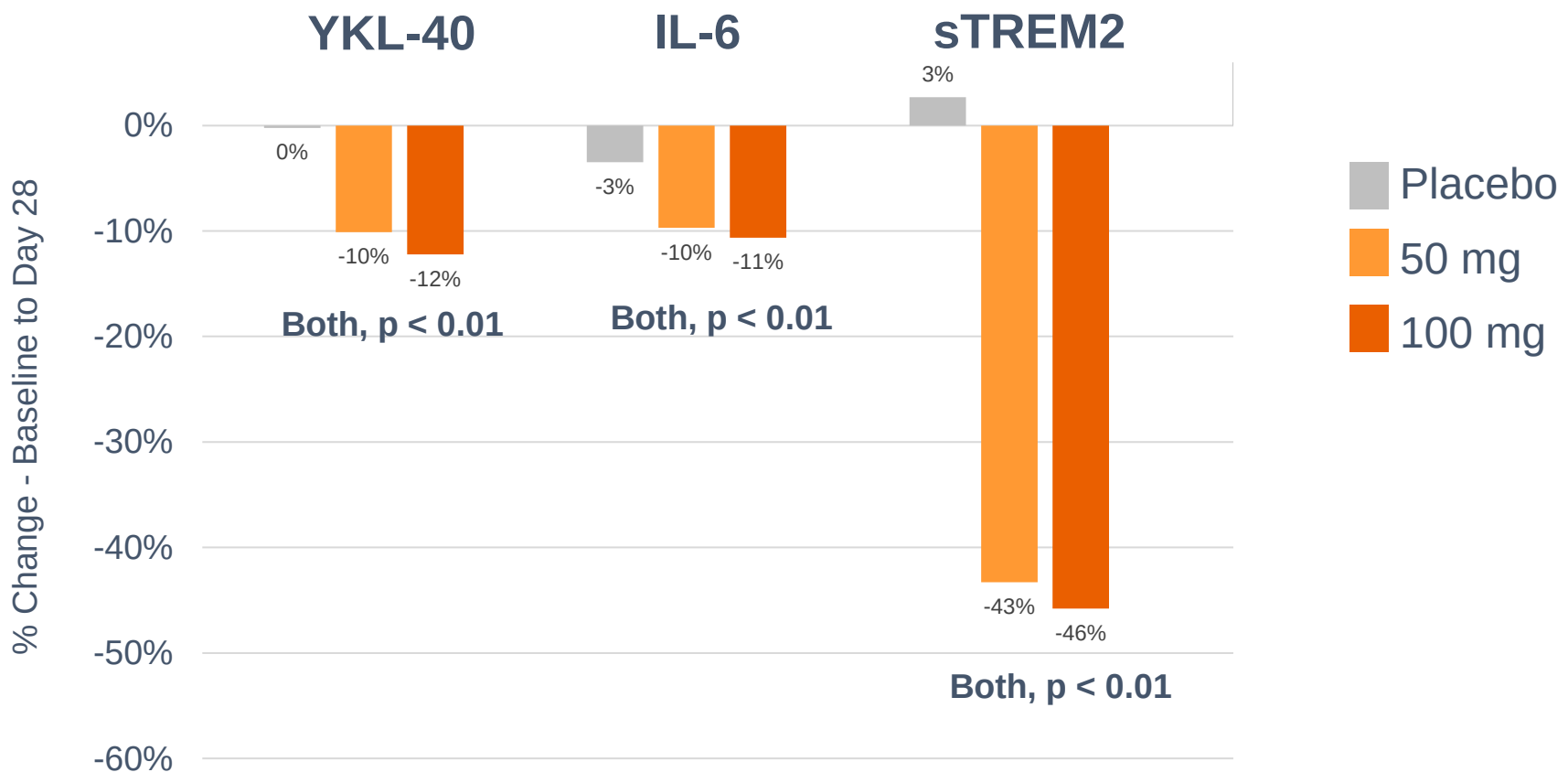
Phase 2b Results - Decrease in CSF Neuroinflammation

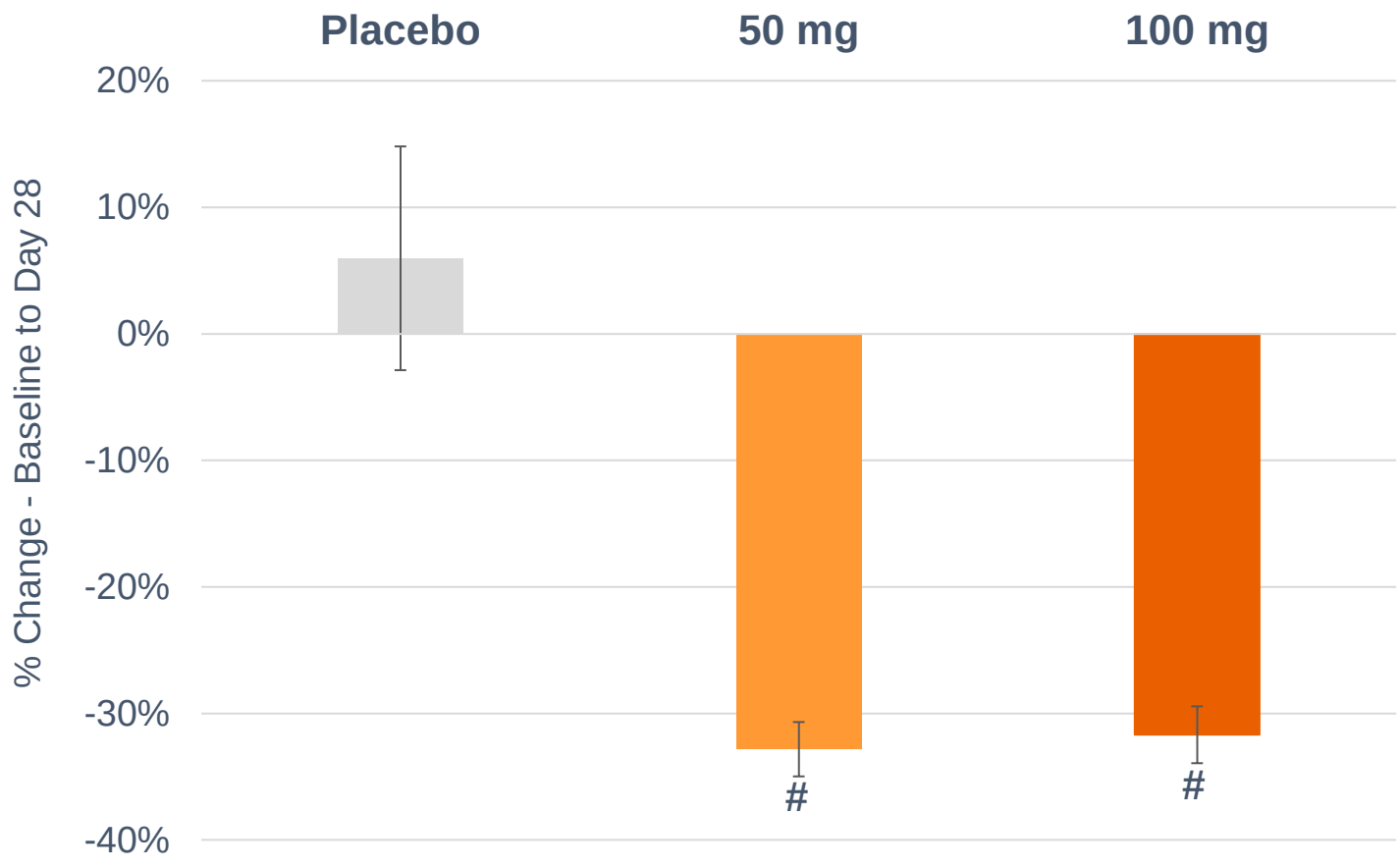
Biomarkers of Neuroinflammation Decreased Significantly in Both Drug Groups

Change in Levels of CSF YKL-40, IL-6 and soluble TREM2, Day 0 to Day 28



Phase 2b Results – CSF HMGB1 Decreased

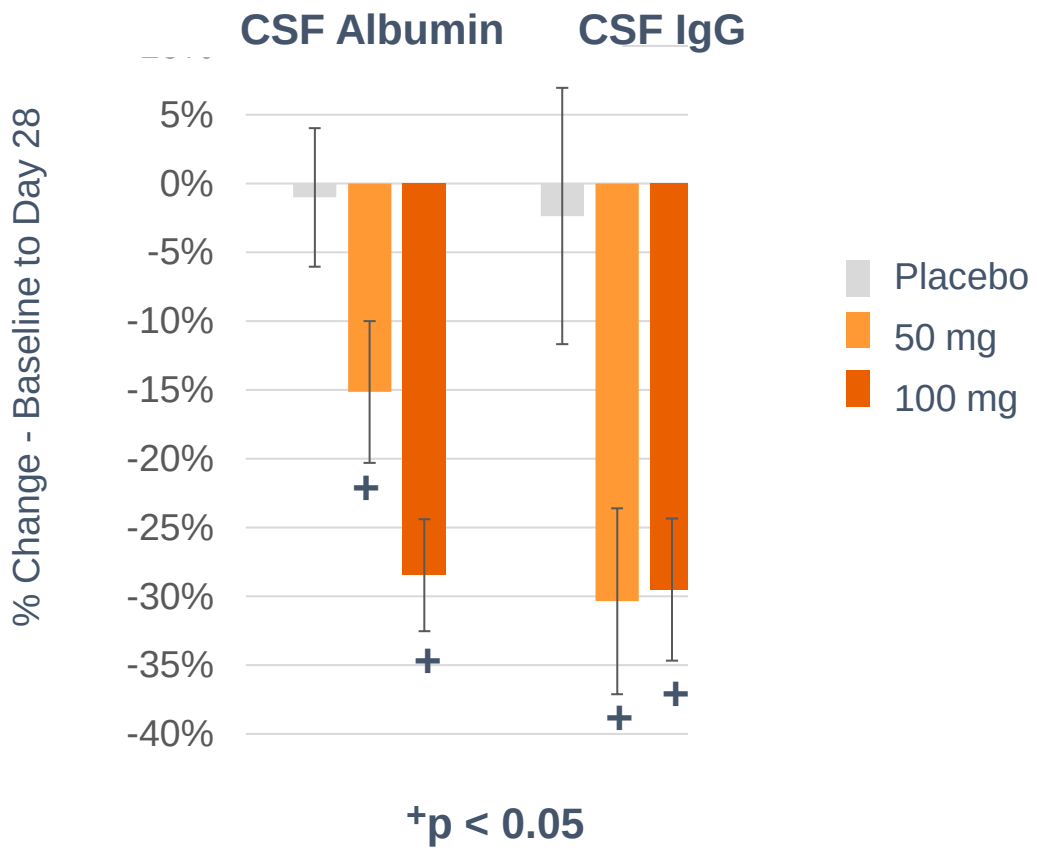
Elevated Levels of HMGB1 Triggers Neuroinflammation, Neurite Degeneration and Cell Death.



# p < 0.001 vs. placebo

Note: HMGB1 = High-Mobility Group Box 1

Phase 2b Results – Improved Blood-brain Barrier Integrity



Albumin Ratio by Treatment Group

	Day 0	Day 28	Change
Placebo	24	24	No change
50 mg sumifilam	25	20	- 5 (-20%)
100 mg sumifilam	25	18	- 7 (28%)

*Note: Albumin Ratio ((CSF/plasma)*100) is a clinical test for BBB permeability because albumin protein is not synthesized in CSF. Hence, albumin in CSF necessarily comes from plasma through the BBB.*

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Cognition

- **CANTAB** (Cambridge, England) **is a validated, computer-based battery of memory tests that are sensitive to subtle changes in cognition.**
  - Tests are independent of language skills, speed, gender or education.

- **Patients were assessed on ‘Episodic Memory’ and ‘Spatial Working Memory’.**
  - Patients advance through progressively more difficult levels.
  - Outcome measure = total errors, with errors imputed for more difficult levels not reached.
  - Lower score is better.

- **Patients were assessed on Day 1 (pre-dose) and Day 28.**

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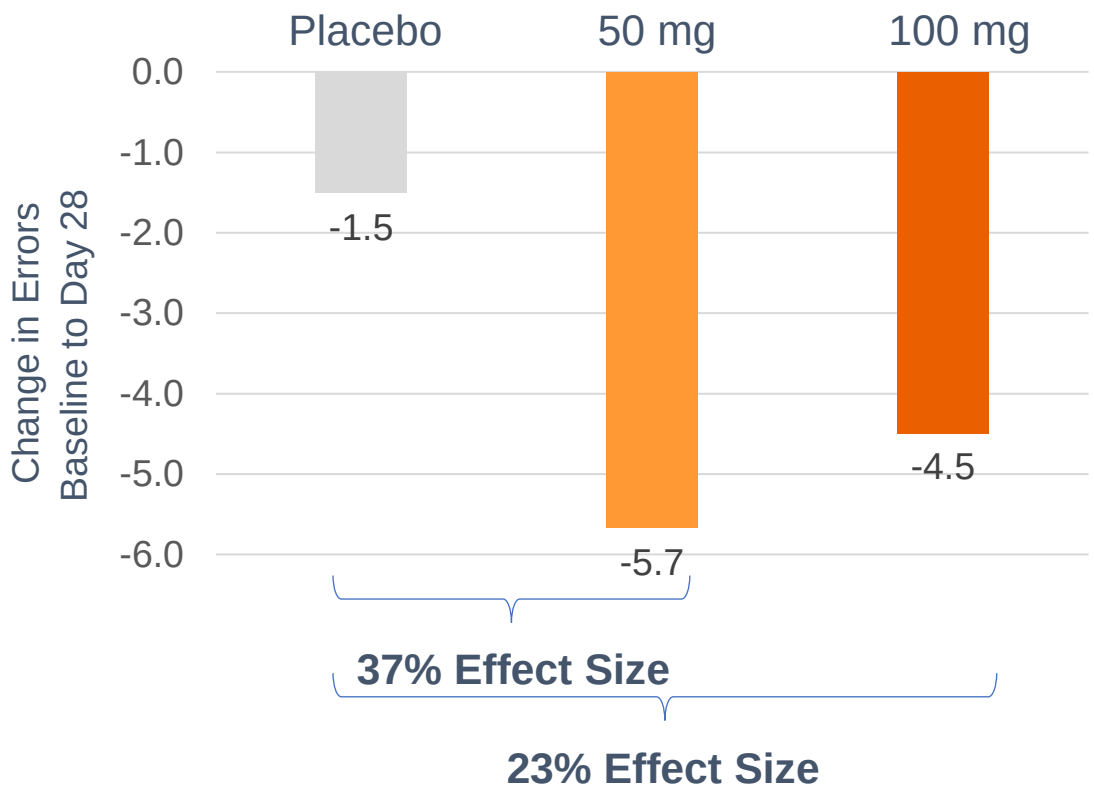
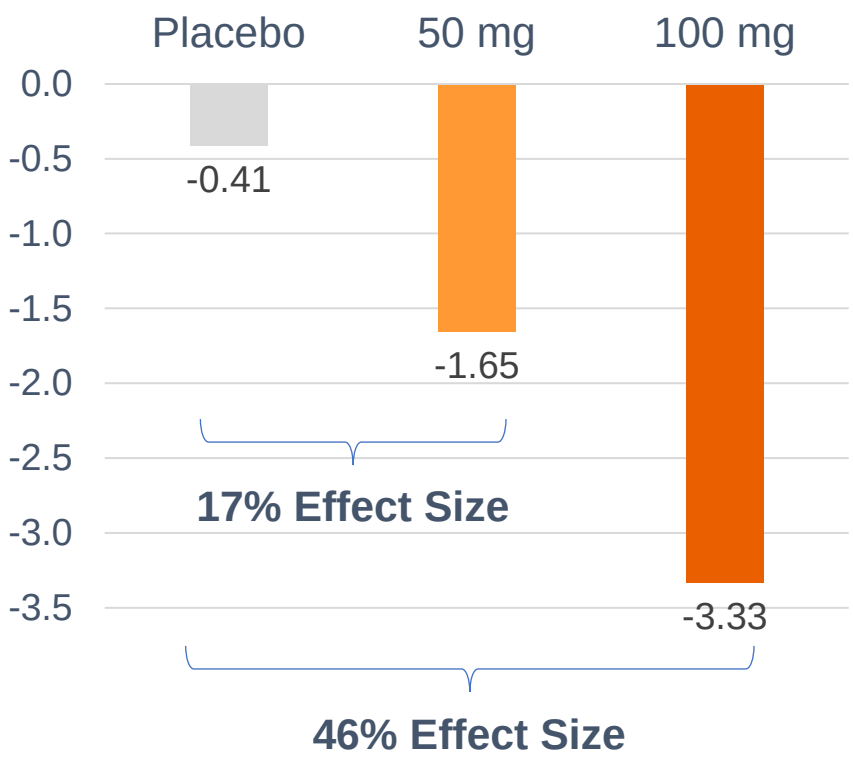
Phase 2b Results – Memory Measurements Improved

Episodic Memory Improved



Spatial Working Memory Improved



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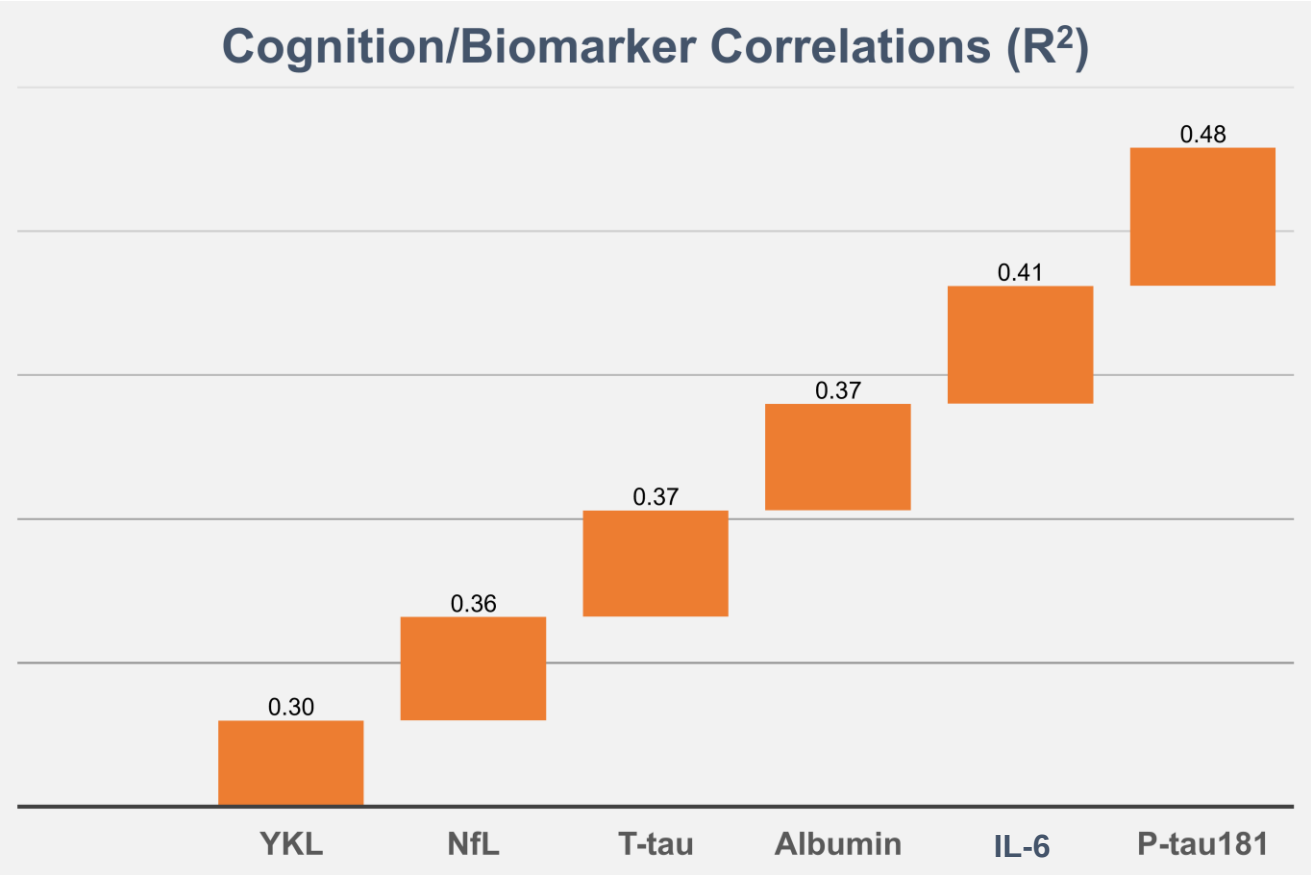
Phase 2b Results - Cognition/Biomarker Correlation

Cognitive Improvement Correlated Most ($R^2 = 0.5$) With Decreases in CSF P-tau181



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Summary of Drug Effects

- **98% of patients treated with sumifilam 50 mg or 100 mg b.i.d. for 28 days showed improvements in validated biomarkers of AD pathology, neuroinflammation, and neurodegeneration, with no safety issues.**

- **Sumifilam appears to stabilize or improve memory.**
  - 37% and 23% effect sizes in Episodic Memory vs placebo
  - 17% and 46% effect sizes in Spatial Working Memory vs placebo
  - Improved cognition correlated most with reduction in levels of P-tau^{181} (R^2 = 0.5)

- **Target engagement and mechanism of action were demonstrated in this Phase 2b and prior clinical and pre-clinical studies.**

The data validate FLNA as a new, promising and highly differentiated therapeutic target for Alzheimer's disease.

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Phase 2b Study Conclusions

- **A placebo-controlled study of sumifilam showed promising treatment effects in patients with mild-to-moderate Alzheimer's disease.**
- **Sumifilam improved a panel of validated biomarkers of disease pathology, neuroinflammation, and BBB integrity, and appeared to enhance cognition.**
- **Phase 2b data replicate prior clinical results and are consistent with published preclinical data and mechanism of action studies.**

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On-going Long-term Safety Study

- **We are conducting a one-year, open-label safety study of sumifilam to satisfy regulatory guidelines.**
- **Target enrollment is approximately 100 patients with mild-to-moderate AD.**
  - Initiated March 2020, now >60% enrolled.
- **Patients are evaluated for safety, cognition and behavior.**
  - Cognition is evaluated on ADAS-Cog11.
  - Behavior associated with dementia is evaluated on NPI (Neuropsychiatric Inventory).

Interim analysis on safety & cognition is expected in 1st Half 2021.

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Regulatory Status

- **End-of-phase 2 (EOP2) meeting with FDA is on calendar for January 2021.**

- **EOP2 meeting objectives are to gain general agreement around a Phase 3 clinical program and to identify outstanding data requirements, if any, to support the statutory requirements for a 505(b)(1) NDA submission and marketing approval of sumifilam for the treatment of mild-to-moderate Alzheimer's disease.**

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Phase 3 Development Goals

- **To show sumifilam's disease-modifying effects in AD.**
  - Goal is to show slower decline in AD patients treated with sumifilam compared to placebo.
- **To show sumifilam's effects on AD symptoms.**
  - Goal is to show symptomatic improvement in AD patients taking sumifilam vs placebo.
- **P3 study details TBA, pending End-of-Phase 2 meeting with FDA in January 2021.**

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SavaDx: Our Investigational Diagnostic for Alzheimer's

- The underlying science for sumifilam 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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Financials

Eric Schoen - Chief Financial Officer

Key Financials

Nasdaq ticker: SAVA	
Shares Outstanding	**35.0 million[1]**
Insider Ownership	*≈ 2.1 million*
Public Float	*≈ 32.9 million shares*
Warrants Outstanding (expire Feb 2021)	*≈ 0.8 million shares*
Unaudited Financials[1]	
Cash Balance @ November 17, 2020	**≈ $94.3 million[1]**
Expected Net Cash Use Full-year 2020	**≈ $ 5.0 million**

Footnote 1:
Pro forma balance includes unaudited, estimated net proceeds of $70.3 million received from the sale of 9.4 million common shares in a follow-on public offering completed November 13, 2020.

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Intellectual Property

- **Sumifilam is a novel molecule. Cassava Sciences owns composition of matter claims on sumifilam and other novel, filamin-binding molecules.**

- **Cassava Sciences' patent protection with respect to sumifilam (formerly known as PTI-125) and use of sumifilam for Alzheimer's disease and other neurodegenerative disease currently runs through 2033 and includes six issued patents and related patent filings and applications. The Company has no patents or patent applications with respect to SavaDx, which is protected by trade secrets, know-how and other proprietary rights technology.**

- **Cassava Sciences owns exclusive, worldwide rights to sumifilam and related technologies, without milestone or royalty obligations to any third party.**

Milestones

Our goal is to initiate a Phase 3 study of sumifilam in Alzheimer's disease in 2021.

- **End-of-phase 2 (EOP2) meeting with FDA in January 2021 to gain general agreement around a Phase 3 clinical program in Alzheimer's disease.**
- **Manufacture Phase 3 clinical trial supplies (drug substance + oral tablets).**
- **Interim analysis (safety & cognition) of on-going, open-label study of sumifilam.**
- **Complete patient enrollment of on-going, open-label study of sumifilam.**
- **Phase 2b publication, peer-reviewed journal.**
- **Initiate validation study with SavaDx.**

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Thank you!

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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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