UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the
Securities Exchange Act of 1934

Date of Report (Date of earliest event reported) September 14, 2020

Cassava Sciences, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**000-29959**	**91-1911336**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification Number)**

7801 N Capital of Texas Highway, Suite 260
Austin, Texas 78731
(Address of principal executive offices, including zip code)

(512) 501-2444
(Registrant's telephone number, including area code)

Not Applicable
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2 below):

☐ Written communication pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communication pursuant to Rule 14d-2(b) under the Exchange Act (17CFR 240.14d-2(b))

☐ Pre-commencement communication pursuant to Rule 13e-4(c) under the Exchange Act (17CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value	SAVA	NASDAQ Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).
Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐ ☐

Item 7.01. Regulation FD Disclosure.

A copy of the Cassava Sciences, Inc. Final Results of a Phase 2b Study of Sumifilam in Alzheimer's Disease presentation, dated September 14, 2020, is furnished as Exhibit 99.1 to this Form 8-K and is incorporated herein by reference.

Item 8.01. Other Events.

On September 14, 2020, Cassava Sciences, Inc. issued a press release, a copy of which is attached hereto as Exhibit 99.2 and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibit No. Description

99.1	Cassava Sciences, Inc. Final Results of a Phase 2b Study of Sumifilam in Alzheimer's Disease presentation, dated September 14, 2020
99.2	Cassava Sciences, Inc. press release dated September 14, 2020

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

CASSAVA SCIENCES, INC.
a Delaware corporation

Date: September 14, 2020

By: /s/ ERIC J. SCHOEN
Eric J. Schoen
Chief Financial Officer

Exhibit 99.1


CASSAVA
sciences
Final Results of a Phase 2b Study of Sumifilam in Alzheimer's Disease
September 14, 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 Phase 3 clinical studies with sumifilam; the interpretation of prior or current results of our Phase 2 clinical studies, including the measured effects of sumifilam on cognition; plans to publish results in a peer-reviewed journal; 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 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).

Company Presenters

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 élan UNIVERSITY OF CAMBRIDGE

Eric Schoen - Chief Financial Officer

VERMILLION PRICEWATERHOUSECOOPERS

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Guest Presenter

Dr. Gonzalez-Rojas, MD

Dr. Gonzalez-Rojas is Principal Investigator (PI) on the Phase 2b study of sumifilam, and PI on an ongoing, one-year open-label study of sumifilam in patients with Alzheimer's disease. Dr. Gonzalez-Rojas will be available for commentary during the Q&A session.

Background - Yaneicy Gonzalez-Rojas MD, Internal Medicine, is an ACRP-certified Principal Investigator working in Coral Gables, FL. Besides being an established medical practitioner treating hundreds of Alzheimer's patients annually, she has a keen interest in conducting quality clinical trials. Dr. Gonzalez-Rojas has participated in 13 clinical trials of various investigational drug agents for Alzheimer's disease.

Our Mission

Cassava Sciences is dedicated to the development of novel approaches to detect and to treat Alzheimer's disease.

Our Company

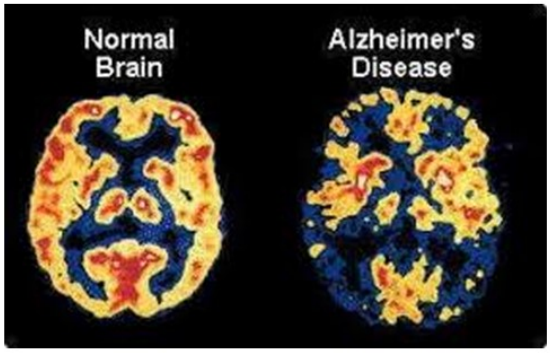
- Cassava Sciences is dedicated to the development of novel approaches to detect & treat Alzheimer's disease.
- Our initial focus is on developing **sumifilam**, a proprietary, investigational drug to treat Alzheimer's disease.
- Sumifilam is the first of a new class of drugs that target filamin proteins. Filamin-binding molecules are new to Alzheimer's research and may represent an important advance towards the goal of disease-modifying drugs.
- Sumifilam reduces neurodegeneration *and* neuroinflammation in Alzheimer's disease by binding a single target. The underlying science is published in peer-reviewed journals and benefits from long-term scientific and financial support from the National Institutes of Health (NIH).
- In 2019, we announced positive results of an open-label, Phase 2a study of sumifilam in Alzheimer's disease. In 2020, we completed a randomized, placebo-controlled Phase 2b study of sumifilam in Alzheimer's disease, funded by a research grant from the NIH (NIA grant #AG060878). The purpose of this presentation is to inform our stakeholders of the final clinical results of our Phase 2b study with sumifilam in Alzheimer's disease.

Our future goal is to conduct a Phase III efficacy program with sumifilam in Alzheimer's disease.

Alzheimer's Disease – Significant Unmet Needs

- Alzheimer's disease (AD) is a progressive brain disorder that destroys memory and thinking skills.
- AD is the largest potential drug market in the world, where diagnostic methods are currently limited, treatment options are inadequate and the ability to slow disease progression is non-existent.
- About 5-6 million people live with AD in the U.S. today; incidence is expected to grow dramatically.

There are no disease-modifying therapies for AD patients.



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First Bioanalysis – Invalid Data

As previously reported (May 2020), an outside lab conducted an initial bioanalysis of the Phase 2b study.

Biomarker data received from that lab made no sense. A post-hoc analysis showed significant data anomalies in patients who took placebo for 28 days.

Expected Observations for Patients Who Took Placebo		*Lab's Observations for Patients Who Took Placebo*
Small changes in levels of biomarkers over 28 days.	→	*Placebo patients showed large, dramatic swings (>100%) in levels of biomarkers over 28 days.*
Biomarkers generally move in the same direction.	→	*Biomarkers appeared to follow a random walk; some moved in opposite directions from each other in the same patient.*
Biomarkers that move in tandem show robust statistical correlations.	→	*Changes in levels of biomarkers are uncorrelated (R^2 = 0.06, on average) in placebo patients. See Appendix for more statistical data on placebo patients.*

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Second Bioanalysis – Valid Data

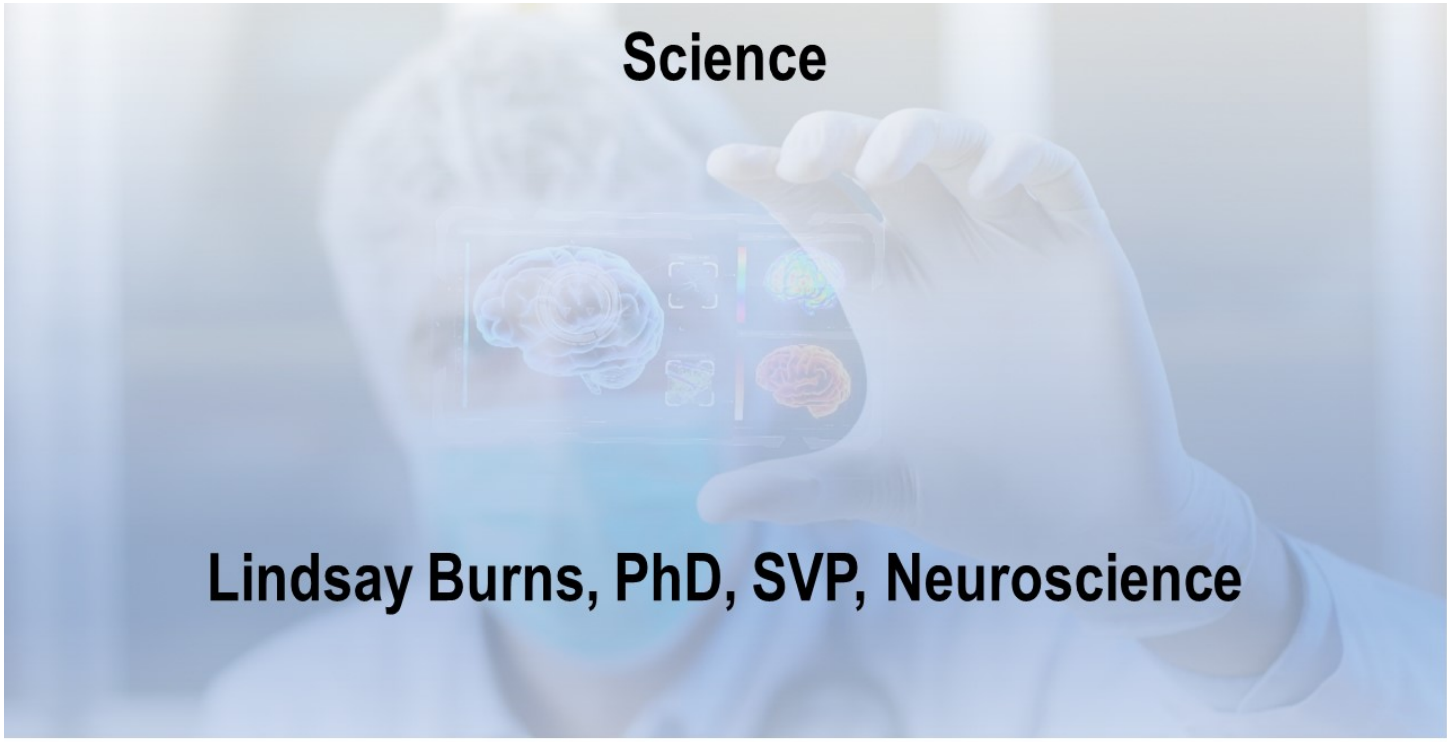
An academic lab conducted a second, final bioanalysis of the Phase 2b study.

The academic lab shows proper biomarker data in patients who took placebo for 28 days.

Data from the academic lab shows modest (4-6%, on average) changes in levels of biomarkers over 28 days; biomarkers that generally move in the same direction; robust statistical correlations (R^2 = 0.96, on average) among changes in levels of biomarkers; and negative correlation with Aβ42.

	Aβ42	Total Tau	P-tau181	NfL	Ng	YKL40	IL-6
Aβ42	1	-0.82	-0.89	-0.83	-0.86	-0.82	-0.85
Total Tau	-0.82	1	0.96	0.96	0.97	0.94	0.96
P-tau181	-0.89	0.96	1	0.96	0.97	0.94	0.95
NfL	-0.83	0.96	0.96	1	0.97	0.94	0.97
Ng	-0.86	0.97	0.97	0.97	1	0.92	0.96
YKL40	-0.82	0.94	0.94	0.94	0.92	1	0.96
IL-6	-0.85	0.96	0.95	0.97	0.96	0.96	1

Science



Lindsay Burns, PhD, SVP, Neuroscience

Sumifilam - A Novel Drug for Alzheimer's Disease

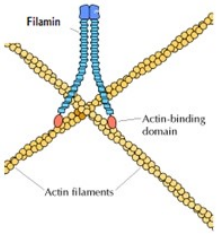
- **Sumifilam is our proprietary, small molecule drug candidate to treat Alzheimer's disease (AD) and other dementias and neurodegenerative diseases.**
  - Program benefits from long-term scientific & financial support from the National Institutes of Health (NIH).

- **Sumifilam reduces neurodegeneration *and* neuroinflammation by binding a single target.**

- **In 2020, we concluded a comprehensive Phase 2 clinical testing program of sumifilam in AD, in collaboration with clinical/scientific advisors and NIH.**

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.

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Sumifilam Mechanism of Action

- **The altered conformation of FLNA is a proteopathy in the AD brain.**

- **Altered FLNA enables $A\beta_{42}$ signaling via two different receptors:**
  1) **α7-nicotinic acetylcholine receptor (α7nAChR)** → hyperphosphorylates tau
  2) **Toll-like receptor 4 (TLR4)** → releases inflammatory cytokines

- **Sumifilam preferentially binds altered FLNA, restores its proper shape/function, potently suppressing $A\beta_{42}$ signaling via α7nAChR and TLR4.**
  - Through a single target, sumifilam reduces both neurodegeneration & neuroinflammation.

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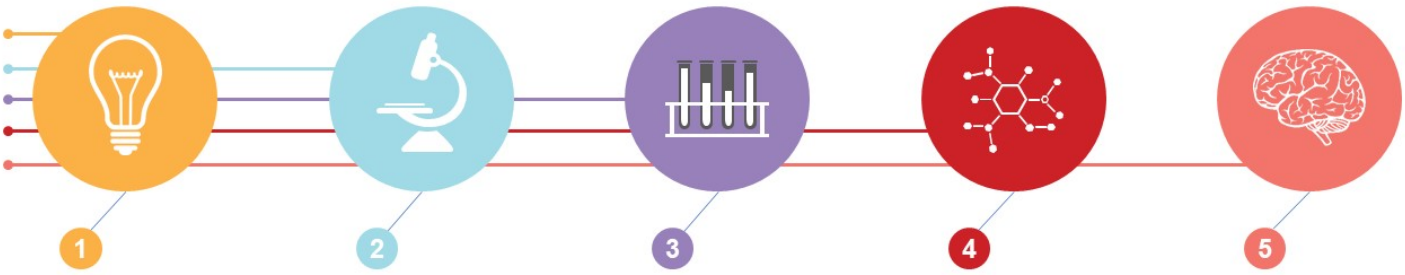
10+ Year Discovery/Development Program



<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
Clinical testing of sumifilam. Positive results reported in Alzheimer's patients.

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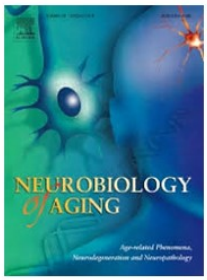
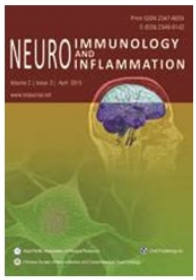
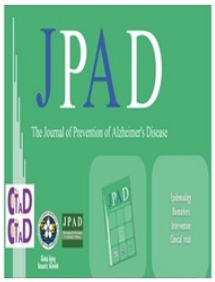
Peer-reviewed Science

The underlying science for sumifilam has been subject to the scrutiny of many experts in the field……







….including NIH, which has awarded our science programs >$10 million in research grant awards.

NIH National Institutes of Health

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Hypothesis and Objective

Clinical Hypothesis

AD patients desperately need disease-modifying drug therapies.

Published pre-clinical data support sumifilam's potential as a disease-modifying drug for AD.

Can sumifilam provide early clinical evidence of disease-modifying effects in a well-controlled study?

Phase 2b Study Objective

Evaluate safety, biomarkers and cognition following 28-day treatment with sumifilam, a new, first-in-class therapy.

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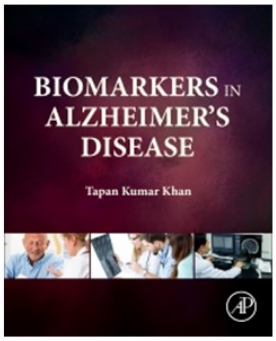
Bring on the Biomarkers



- *Biological markers ('biomarkers') refers to objective measures of Alzheimer's disease at the level of biology.*
- *Biomarkers present hard evidence for the presence and progression of Alzheimer's disease.*
- *Alzheimer's disease can take a decade or more to present. Over that time certain biomarkers rise dramatically, while cognition and health decline.*

One drug, one biomarker is the traditional paradigm in AD research.

Sumifilam's goal is to improve an entire panel of biomarkers of AD pathology, neuroinflammation and neurodegeneration.

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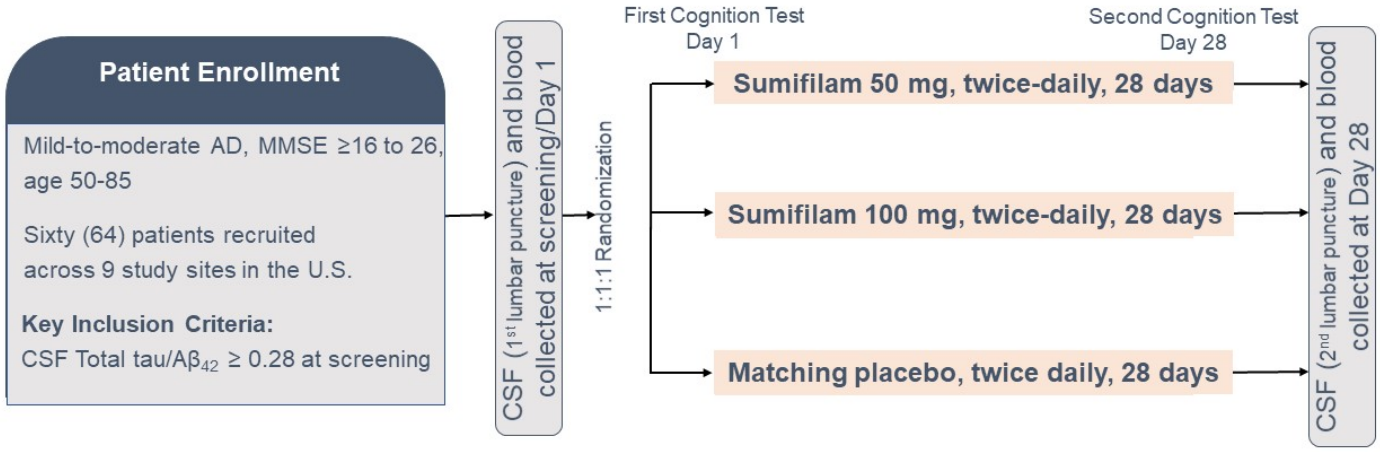
Clinical Results

Nadav Friedmann, PhD/MD, Chief Medical Officer

Lindsay Burns, PhD, SVP, Neuroscience

Phase 2b - Study Design

Randomized, Double-blind, Placebo-controlled, Multicenter Clinical Study



Primary Endpoint: biomarkers of disease

Secondary Endpoint: cognition

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Phase 2b - Safety

- **Sumifilam was safe and well-tolerated**
- **No serious adverse events**
- **No drug-related adverse events**
  - Common, non-persistent side-effects observed in placebo & drug groups
- **No drug-related patient discontinuation**

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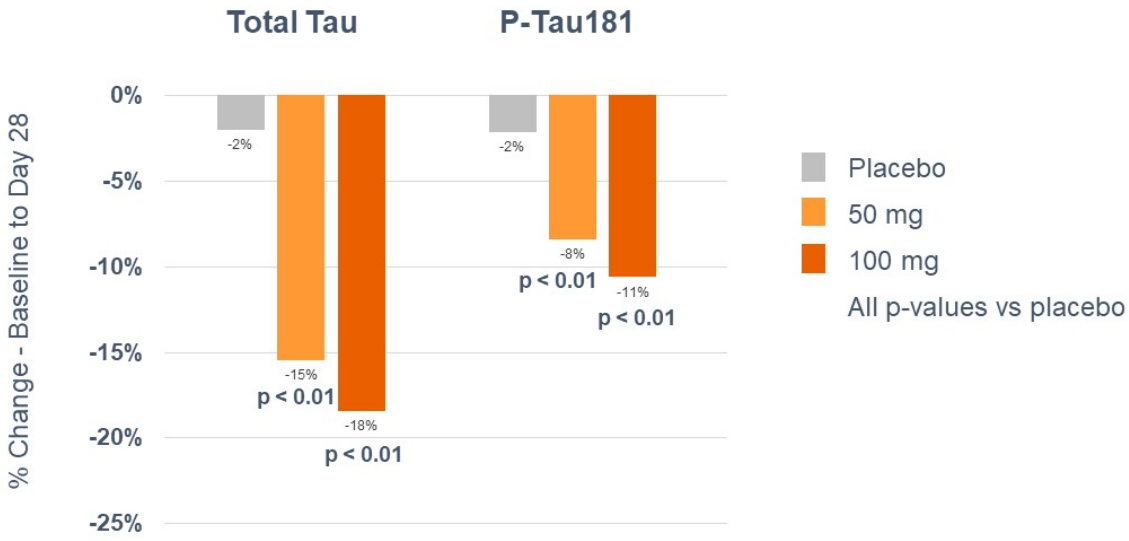
Phase 2b - AD Pathology Decreased Significantly

Levels of CSF Tau Proteins Decreased Significantly in Both Drug Groups



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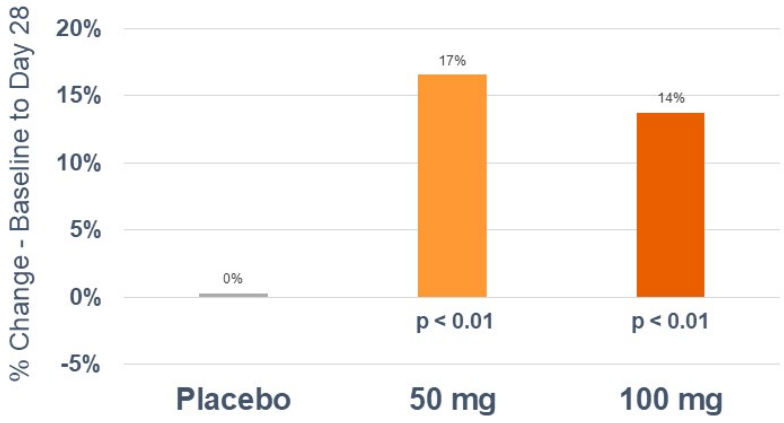
Phase 2b - $A\beta_{42}$, Low in AD, Increased Significantly

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.

All p-values vs placebo

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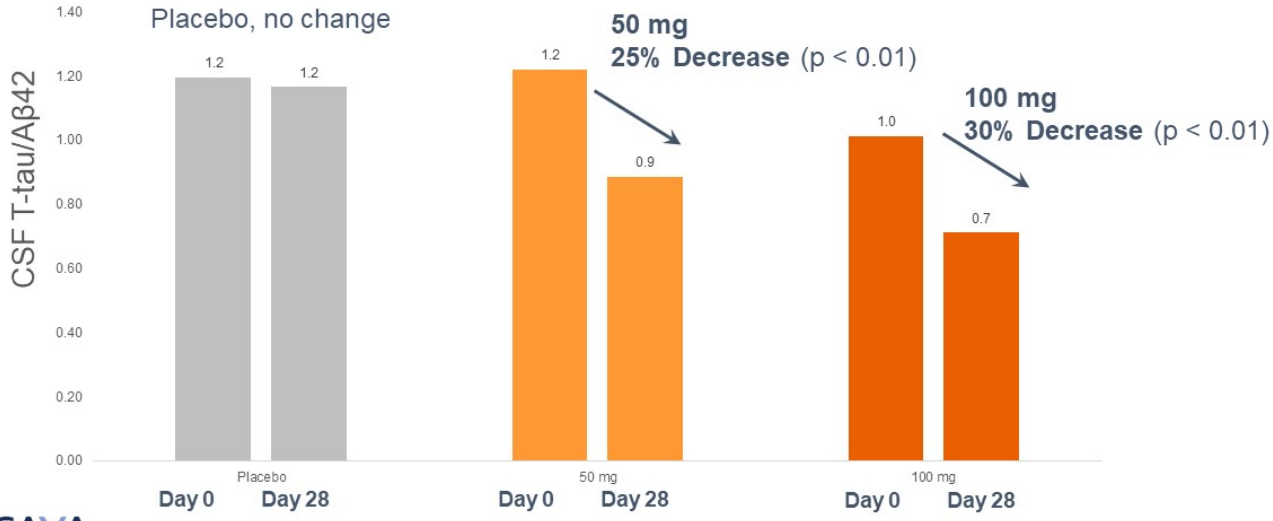
Phase 2b - Total tau/$A\beta_{42}$ Dropped Significantly

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

Change in Ratio of CSF T-tau/$A\beta_{42}$ Day 0 to Day 28



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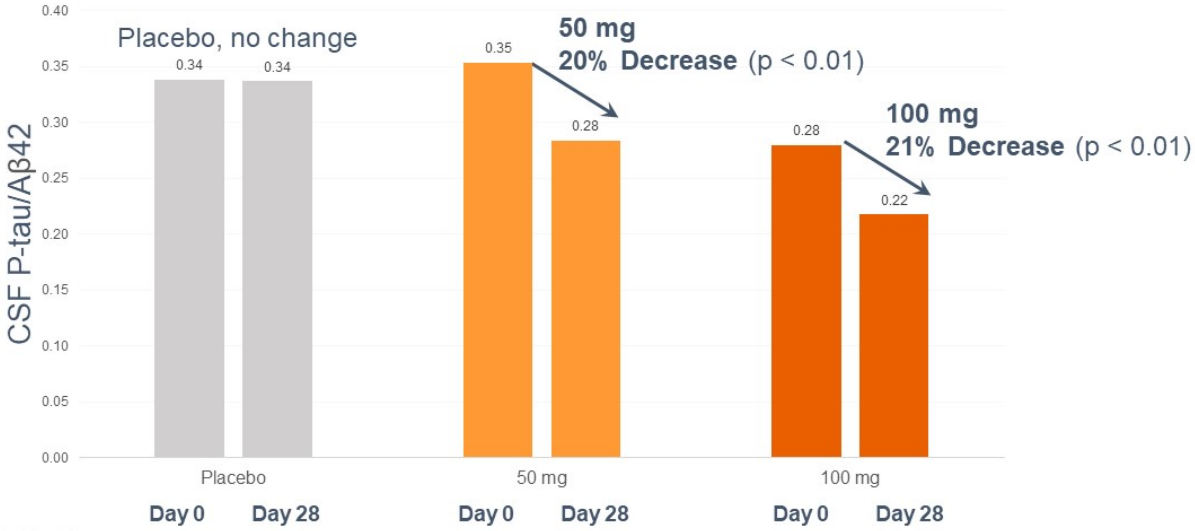
Phase 2b - P-tau/$A\beta_{42}$ Dropped Significantly

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

Change in Ratio of CSF P-tau/$A\beta_{42}$ Day 0 to Day 28



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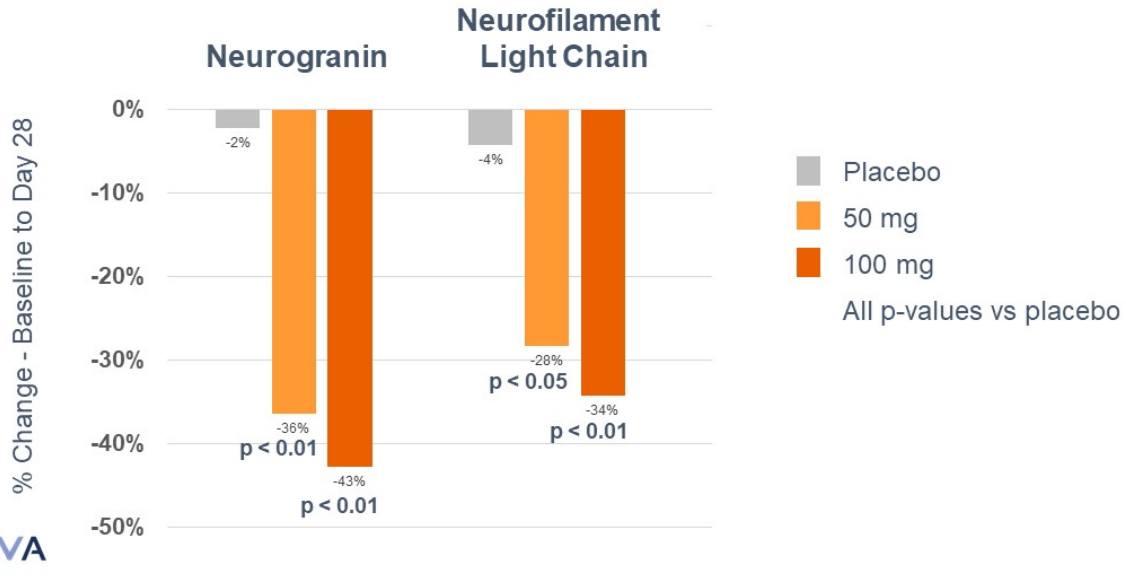
Phase 2b - Neurodegeneration Decreased

Biomarkers of Neurodegeneration Decreased Significantly in Both Drug Groups

Change in Levels of CSF Ng and NfL Day 0 to Day 28



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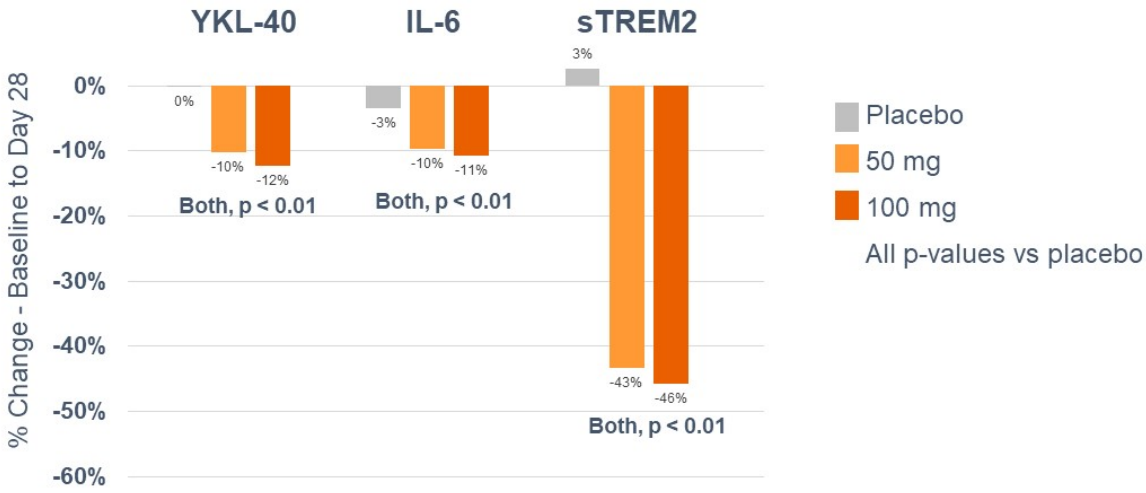
Phase 2b - Neuroinflammation Decreased

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



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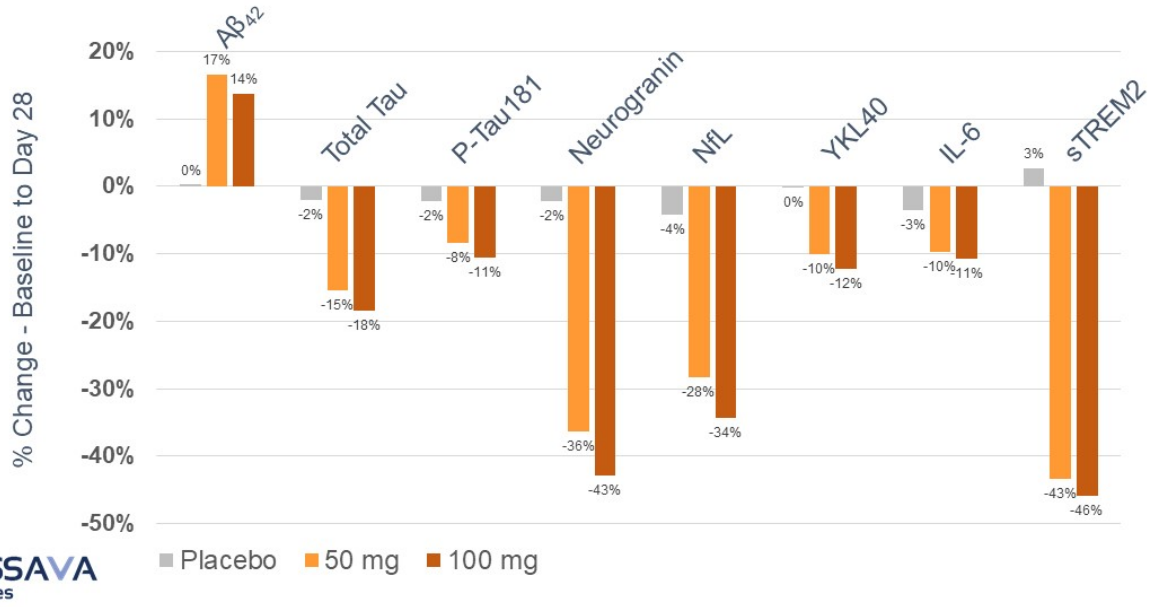
Phase 2b - Summary of CSF Results

Sumifilam Significantly Improved An Entire Panel of AD-related Biomarkers



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Phase 2b - Cognition

- **CANTAB (Cambridge Neuropsychological Test Automated Battery) is a widely used, computer-based battery of memory tests sensitive to subtle changes in cognition.**
  - Tests are independent of language skills, speed, gender or education.

- **Cognitive assessments were made on Day 1 (pre-dose) and again on Day 28.**

- **Patients were tested 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, so…….

Lower score is better!

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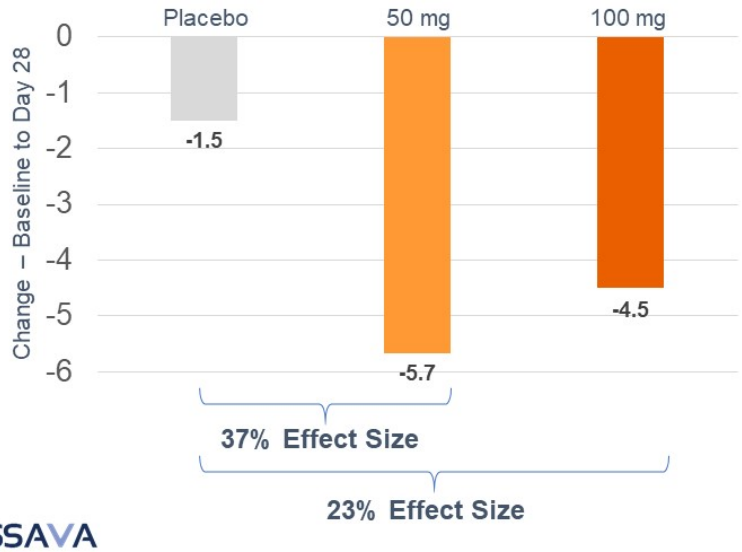
Phase 2b - Cognition

Drug Groups Show Directional Improvements in Episodic Memory



Episodic Memory Endpoint:

- **Lower score is better** on change from baseline in Total Errors on Paired Associates Learning (PAL).
- Effect sizes vs. placebo were calculated by Hedge's g after removing the most and least impaired subjects across all groups by baseline score.
- Effect size measures the magnitude of effect; in contrast, statistical significance measures the probability of effect occurring by chance.

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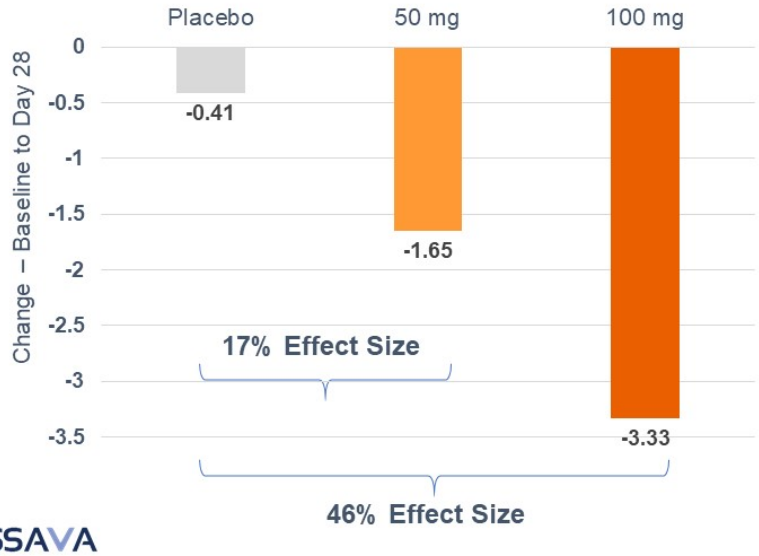
Phase 2b - Cognition

Drug Groups Show Directional Improvements in Spatial Working Memory



Spatial Working Memory Endpoint:

- **Lower score is better** on change from baseline in Total Errors on Spatial Working Memory task.
- Effect sizes vs. placebo were calculated by Hedge's g.
- Patients who did not take drug (no blood levels) were removed.

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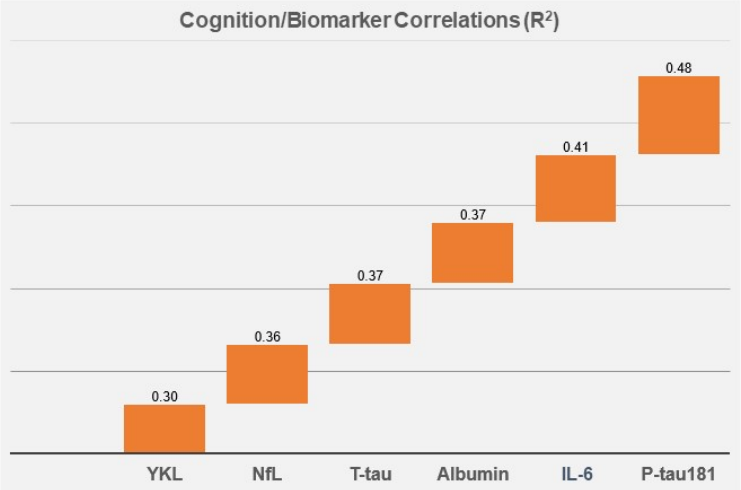
Phase 2b - Cognition/Biomarker Correlation

Cognitive Improvement Correlates 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 strongly with reduction in levels of P-tau^{181} (R^2 = 0.5)
- **Target engagement and mechanism of action were demonstrated in prior clinical and non-clinical studies and was demonstrated again in this Phase 2b.**

These data validate FLNA as a promising new therapeutic target for AD.

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Conclusions & Next Steps

Remi Barbier, President & CEO

Eric Schoen, Chief Financial Officer

Conclusions

- **A well-controlled Phase 2b study of sumifilam showed promising treatment effects in mild-to-moderate AD patients.**
  - No other clinical-stage drug candidate has improved an entire panel of biomarkers of disease pathology, neurodegeneration and neuroinflammation, and appears to benefit cognition.
- **Phase 2b drug effects are consistent with Phase 2a clinical results, preclinical data, mechanism of action and basic research.**
- **The dataset highlight sumifilam's potential as a disease-modifying drug candidate for Alzheimer's disease.**

Clinical data will need to be replicated in large, Phase 3 efficacy studies.

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Next Steps - Replicate Drug Effects in Phase 3

- Phase 2b publication, peer-reviewed journal.
- End-of-phase 2 (EOP2) meeting with FDA.
- Complete patient enrollment in on-going, open-label study of sumifilam.
- Develop study plan for Phase 3 efficacy program in Alzheimer's disease.
- Manufacture Phase 3 clinical trial supplies (drug substance + oral tablets).
- Initiate Phase 3 efficacy program, estimated 2021+

Intellectual Property

- **Sumifilam was discovered in-house. Cassava Sciences owns exclusive, worldwide rights to this and other drug asset and related technologies, without milestone or royalty obligations to any third party.**

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

- **Cassava Sciences' patent protection in this area currently runs beyond 2037, plus extensions, and includes seven issued patents and related patent filings and applications.**

Key Financials

Nasdaq ticker: SAVA	
Shares Outstanding	24.9 million
Warrants Outstanding	1.4 million
Total Shares Outstanding =	***26.3 million***
Unaudited Financials	
Cash Balance at June 30, 2020	≈ $25.3 million
Expected Net Cash Use Full-year 2020	≈ $ 5.0 million
No Debt	

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Clinical Discussion with Dr. Gonzalez-Rojas, MD, Principal Investigator

Yaneicy Gonzalez-Rojas MD, Internal Medicine, is an ACRP-certified Principal Investigator working in Coral Gables, FL. Besides being an established medical practitioner treating hundreds of Alzheimer's patients annually, she has a keen interest in conducting quality clinical trials. Dr. Gonzalez-Rojas has participated in 13 clinical trials of various investigational drug agents for Alzheimer's disease, including sumifilam.

Q & A Session


Thank you!
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sciences

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

Appendix - Biomarkers Generally Correlate!

AD biomarkers generally move in tandem as disease progresses. Therefore, a valid and sound bioanalysis should show data from placebo patients with robust statistical correlations among changes in biomarkers.

The first bioanalysis showed no correlation in the placebo samples (R^2=0.06, on average).

Correlation Values (R^2) Between Changes in CSF Biomarkers.
Placebo patients only – Baseline vs. Day 28.

	Total Tau	P-tau181	NfL	Ng	YKL40	IL-6
Total Tau	1.00	0.41	0.07	0.39	0.25	-0.05
P-tau181	0.41	1.00	-0.13	0.00	-0.04	0.26
NfL	0.07	-0.13	1.00	-0.05	-0.16	-0.07
Ng	0.39	0.00	-0.05	1.00	0.43	-0.21
YKL40	0.25	-0.04	-0.16	0.43	1.00	-0.15
IL-6	-0.05	0.26	-0.07	-0.21	-0.15	1.00

Cassava Sciences Announces Final Results of a Phase 2b Clinical Study of Sumifilam in Patients with Alzheimer's Disease

Alzheimer's Patients in Drug Groups Showed Statistically Significant Improvements in Biomarkers of Disease Compared to Placebo Group (P<0.05)

Alzheimer's Patients in Drug Groups Showed Improved Cognition Compared to Placebo Group (Effect Size 46-17%)

Sumifilam Was Safe and Well-Tolerated

COMPANY TO HOST CONFERENCE CALL TODAY AT 8:30 AM ET.

Conference Call Will Include Dr. Gonzalez-Rojas, MD, Principal Investigator on Both the Phase 2b Study of Sumifilam and an Ongoing, One-Year Open-Label Study of Sumifilam In Patients with Alzheimer's Disease

AUSTIN, TX – September 14, 2020 – Cassava Sciences, Inc. (Nasdaq: SAVA) today announced final results of a Phase 2b study with its lead drug candidate, sumifilam, in Alzheimer's disease. In a clinical study funded by the National Institutes of Health (NIH), sumifilam significantly improved an entire panel of validated biomarkers of disease in patients with Alzheimer's disease. The ability to improve multiple biomarkers from distinct biological pathways with one drug has never been shown before in patients with Alzheimer's disease. Study results are expected to be published in a peer-reviewed publication. Sumifilam is the first of a new class of drug compounds that bind to a protein called Filamin A.

"Filamin-binding molecules are new to Alzheimer's research and may represent an important advance if these data can be replicated in larger studies," said Jeffrey Cummings, M.D., Sc.D., Founding Director of the Cleveland Clinic Lou Ruvo Center for Brain Health, and Chambers Professor of Brain Science at the University of Nevada, Las Vegas. "I am pleased to see early evidence of disease-modifying effects in patients with this investigational drug. The data appear to represent a step forward toward urgently needed treatments for Alzheimer's disease."

In addition, Alzheimer's patients treated with sumifilam showed directional improvements in tests of remembering new information, versus patients on placebo. Improvements in cognition correlated most strongly with decreases in P-tau181, a biomarker that, when elevated, leads to tangles in the brain. Sumifilam decreased brain levels of Ptau-181 by 8-11%, versus placebo.

In this study, Alzheimer's patients treated with 50 mg or 100 mg of sumifilam twice-daily for 28 days showed statistically significant ($p<0.05$) improvements in biomarkers of disease pathology,

neurodegeneration and neuroinflammation, versus Alzheimer's patients who took placebo. In addition, Alzheimer's patients treated with sumifilam showed directional improvements in validated tests of episodic memory and spatial working memory, versus patients on placebo (Effect Sizes 46-17%). Cognitive improvements correlated most strongly (R^2=0.5) with decreases in P-tau181. The study achieved a 98% response rate, defined as the proportion of study participants taking sumifilam who showed improvements in biomarkers.

"The clinical data suggest sumifilam may be slowing disease progression in Alzheimer's patients," said Nadav Friedmann, PhD/MD, Chief Medical Officer, Cassava Sciences. "This exciting possibility will need to be evaluated in future collaborations with patients, physicians, advisors and others."

"Other than a few drugs to help ease the decline, there's really nothing out there to treat people with Alzheimer's," said Remi Barbier, Chairman, President & CEO, Cassava Sciences. "The improvement on multiple biomarkers in this clinical study is a first and offers hope that sumifilam has potential to become a transformative treatment for people with Alzheimer's disease."

Phase 2b Study Design
Phase 2b was a randomized, placebo-controlled, double-blind, multi-center clinical study of sumifilam (formerly, PTI-125). Sixty-four patients with mild-to-moderate Alzheimer's disease, age 50-85, were randomized (1:1:1) to 100 mg or 50 mg oral sumifilam or matching placebo. Treatment was administered twice daily for 28 days. Nine U.S. study sites enrolled patients. A clinical diagnosis of Alzheimer's disease was confirmed with the Mini-Mental State Examination (MMSE) ≥16 to ≤26 and a CSF T-tau/$A\beta_{42}$ ratio ≥0.28. Safety was assessed by ECGs, clinical labs, adverse event monitoring and physical examinations.

Phase 2b Study Results
In this study, drug was safe and well-tolerated, with no drug-related patient discontinuations. The study used biomarkers to measure drug effects. Biomarkers are objective biological endpoints used to track the progression of Alzheimer's disease. Molecular aberrations in the brain are reflected in biomarkers found in cerebrospinal fluid (CSF), a fluid that surrounds the brain. A key objective of this study was to measure changes in levels of CSF biomarkers in study participants before and after 28 days of treatment (i.e., percent change from baseline).

Key biomarker results include the following (all p-values versus placebo):

- Core markers of Alzheimer's pathology are total tau (T-tau), phosphorylated tau (P-tau181), and amyloid beta42 ($A\beta_{42}$). In Alzheimer's, tau and P-tau levels are elevated and $A\beta_{42}$ is low.
    - T-tau decreased 15% ($p<0.01$) for patients in the 50 mg drug group.
    - T-tau decreased 18% ($p<0.01$) for patients in the 100 mg drug group.
    - P-tau decreased 8% ($p<0.01$) for patients in the 50 mg drug group.
    - P-tau decreased 11% ($p<0.01$) for patients in the 100 mg drug group.
    - $A\beta_{42}$ increased 17% ($p<0.01$) for patients in the 50 mg drug group.
    - $A\beta_{42}$ increased 14% ($p<0.01$) for patients in the 100 mg drug group.

- Elevated CSF levels of two proteins, Neurogranin (Ng) and Neurofilament Light Chain (NfL) indicate neurodegeneration.

- Ng decreased 36% ($p<0.01$) for patients in the 50 mg drug group.
- Ng decreased 43% ($p<0.01$) for patients in the 100 mg drug group.
- NfL decreased 28% ($p<0.05$) for patients in the 50 mg drug group.
- NfL decreased 34% ($p<0.01$) for patients in the 100 mg drug group.

· Proinflammatory IL-6 (Interleukin 6) is produced in response to tissue stress and injury.

- IL-6 decreased 10% ($p<0.01$) for patients in the 50 mg drug group.
- IL-6 decreased 11% ($p<0.01$) for patients in the 100 mg drug group.

· Elevated levels of neuroinflammatory marker YKL-40 indicate microglial activation.

- YKL-40 decreased 10% ($p<0.01$) for patients in the 50 mg drug group.
- YKL-40 decreased 12% ($p<0.01$) for patients in the 100 mg drug group.

· sTREM2 is a neuroinflammation biomarker that has commanded substantial recent attention from researchers for its role in Alzheimer's disease and frontotemporal dementia.

- sTREM2 decreased 43% ($p<0.01$) for patients in the 50 mg drug group.
- sTREM2 decreased 46% ($P<0.01$) for patients in the 100 mg drug group.

A further objective of this study was to measure drug effects on cognition. Patients were tested at baseline and again on Day 28. Changes in episodic memory and spatial working memory were assessed on CANTAB, a validated, computer-based battery of tests. CANTAB is designed to measure cognitive skills regardless of the subject's language skills, speed, gender or education. Only directional trends are observed, due to limitations around study size (N=64).

Key cognition results include:

· Alzheimer's patients in both drug groups showed directional improvements on tests of episodic memory and spatial memory after 28 days of treatment, versus patients on placebo. Effect Sizes were 46-17% versus placebo.

· Episodic memory improved by -5.7 (lower score is better) for Alzheimer's patients in the 50 mg drug group, versus -1.5 for patients on placebo.

· Episodic memory improved by -4.3 (lower score is better) for Alzheimer's patients in the 100 mg drug group, versus -1.5 for patients on placebo.

· Spatial memory improved by -1.6 (lower score is better) for Alzheimer's patients in the 50 mg drug group, versus -0.4 for patients on placebo.

· Spatial memory improved by -3.3 (lower score is better) for Alzheimer's patients in the 100 mg drug group, versus -0.4 for patients on placebo.

· Improvements in cognition correlated most strongly (statistical $R^2=0.5$) with decreases in CSF P-tau181, a biomarker that, when elevated, leads to tangles in the brain. Sumifilam decreased brain levels of Ptau-181 by 8-11%, versus placebo.

Study Methods for Cerebrospinal Fluid (CSF) Bioanalysis

CSF was drawn from all study participants by lumbar puncture, an outpatient procedure used to remove a small sample of CSF from the lower spine. Study participants underwent two CSF draws: before treatment started and again after 28 continuous days of treatment. All CSF samples were sent to outside labs for bioanalysis. Bioanalysis refers to a set of laboratory tests that detect and measure very small amounts (pg/mL) of biomarkers in CSF. Bioanalyses were conducted under blinded conditions to eliminate any possibility of bias. An academic lab generated final results. The validity of final results is evidenced by robust correlations (R^2=0.96, on average) between biomarker movements over 28 days in the dataset for placebo samples, and only small changes in biomarkers in the placebo group, as expected.

As previously disclosed, an initial bioanalysis by a different lab showed highly anomalous data, e.g., huge swings (in both directions) in levels of biomarkers, as well as biomarkers moving in opposite directions in the same patients, all in the group who took placebo for 28 days. With its validity in question, the initial bioanalysis serves no useful purpose.

Phase 2b Study Conclusions
A small, well-controlled study of sumifilam showed promising treatment effects in patients with mild-to-moderate Alzheimer's disease. In this study, sumifilam treatment over 28 days improved an entire panel of validated biomarkers of Alzheimer's disease, decreased measurements of neuroinflammation, showed a 98% responder rate, appears safe and well-tolerated, and appears to benefit cognition. Importantly, the data are consistent with prior clinical and preclinical results, the drug's mechanism of action and over 10 years of basic research.

Ongoing Open Label Study
Cassava Sciences is conducting an ongoing, long-term, open-label, multi-center, extension study of sumifilam 100 mg twice-daily for 12 months. The study's target enrollment is approximately 100 patients with mild-to-moderate Alzheimer's disease, including patients from prior studies of sumifilam. The open-label study is currently over 50% enrolled.

About Alzheimer's Disease
Alzheimer's disease is a progressive brain disorder that destroys memory and thinking skills. Currently, there are no drug therapies to halt Alzheimer's disease, much less reverse its course. In the U.S. alone, approximately 5.8 million people are currently living with Alzheimer's disease, and approximately 487,000 people age 65 or older developed Alzheimer's in 2019.[1] The number of people living with Alzheimer's disease is expected to grow dramatically in the years ahead, resulting in a growing social and economic burden.[2]

1,2 Source: Alzheimer's Association. *2019 Alzheimer's Disease Facts and Figures*. Available online at: https://www.alz.org/media/documents/alzheimers-facts-and-figures-2019-r.pdf

About Sumifilam
Sumifilam is a proprietary, small molecule (oral) drug that restores the normal shape and function of altered filamin A (FLNA), a scaffolding protein, in the brain. Altered FLNA in the brain disrupts the normal function of neurons, leading to Alzheimer's pathology, neurodegeneration and neuroinflammation. The underlying science for sumifilam is published in peer-reviewed journals, including *Journal of Neuroscience*, *Neurobiology of Aging*, *Journal of Biological Chemistry, Neuroimmunology and Neuroinflammation* and *Journal of Prevention of Alzheimer's Disease.* The Company is also developing an investigational diagnostic, called SavaDx, to detect Alzheimer's disease with a simple blood test.

Sumifilam and SavaDx were both developed in-house. Both product candidates are substantially funded by peer-review research grant awards from the National Institutes of Health. Cassava Sciences owns worldwide development and commercial rights to its research programs in Alzheimer's disease, and related technologies, without royalty obligations to any third party. Patent protection in this area currently runs beyond 2037, plus extensions, and includes seven issued patents and related patent filings and applications.

About Cassava Sciences, Inc.
Cassava Sciences' mission is to discover and develop innovations for chronic, neurodegenerative conditions. Over the past 10 years, Cassava Sciences has combined state-of-the-art technology with new insights in neurobiology to develop novel solutions for Alzheimer's disease. For more information, please visit: https://www.CassavaSciences.com

For More Information Contact:
Eric Schoen, Chief Financial Officer
Cassava Sciences, Inc.
eschoen@CassavaSciences.com
(512) 501-2450

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The content of this press release is solely the responsibility of Cassava Sciences and does not necessarily represent the official views of the NIH/NIA.

Cautionary Note Regarding Forward-Looking Statements: *This press release contains "forward-looking statements" for purposes of the Private Securities Litigation Reform Act of 1995 (the Act). Cassava Sciences claims the protection of the Safe Harbor for forward-looking statements contained in the Act. All statements other than statements of historical fact contained in this press release including, but not limited to, statements regarding the status of current and future clinical studies with sumifilam; the interpretation of results of our Phase 2 clinical studies including cognition data and plans to publish results in a peer-reviewed journal; potential health benefits, if any, of changes in levels of biomarkers; verbal commentaries made by Cassava Sciences' employees and scientific advisors; and potential benefits, if any, of the Company's product candidates for Alzheimer's disease are forward-looking statements. Such statements are based largely on the Company's current expectations and projections about future events. Such statements speak only as of the date of this press release 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 COVID-19 pandemic, any unanticipated impacts of the pandemic on our business operations, and including those described in the section entitled "Risk Factors" in Cassava Sciences' 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, the forward-looking statements and events discussed in this press release 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, the Company disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this press release. 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.*

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