UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

CASSAVA SCIENCES, INC., Plaintiff, -against- DAVID BREDT, GEOFFREY PITT, et al., Defendants.	:	22-CV-9409 (GHW) (OTW) **REPORT & RECOMMENDATION TO THE HONORABLE GREGORY H. WOODS**

ONA T. WANG, **United States Magistrate Judge**:

I. INTRODUCTION

This is a defamation and civil conspiracy case brought by Cassava Sciences, Inc. ("Cassava" or "Plaintiff"), a clinical-stage neuroscience biotechnology company, against three groups[1] of short sellers of Cassava stock, who published (and republished) allegedly defamatory statements about Cassava's development of simufilam, a drug intended to treat Alzheimer's disease ("Alzheimer's" or "AD"). All three groups of defendants have moved to dismiss the First Amended Complaint ("FAC") (ECF 30). This Report and Recommendation addresses the motion to dismiss filed by Defendants David Bredt, M.D., Ph.D., and Geoffrey Pitt M.D., Ph.D. (collectively, the "Neuroscientist Defendants"). (*See* ECF 74).[2] For the reasons below, I respectfully recommend that the Neuroscientist Defendants' motion be **GRANTED**.

[1] The three groups are (1) the Neuroscientist Defendants (*see* ECF 74); (2) Quintessential Capital Management LLC (*see* ECF Nos. 77 and 78); and (3) the "Dot.Com defendants" Adrian Heilbut, Jesse Brodkin, Enea Milioris, and Patrick Markey (*see* ECF Nos. 86 and 87).

[2] The briefing on the Neuroscientist Defendants' motion to dismiss is located at ECF Nos. 74-1, 80 and 81.

II. FACTUAL BACKGROUND

Certain proteins, such as amyloid and tau, have been found to lose their shape and function, resulting in misfolded proteins in the brains of people with Alzheimer's disease. (FAC ¶ 41). These misfolded proteins[3] can then clump together and form plaques and tangles in the brain, which are believed to disrupt normal function and communication between neurons (nerve cells), destroy synapses (the junctions between neurons), and contribute to neuron death, causing much of the Alzheimer's symptomology. *Id*. at ¶¶ 41–42. As relevant to this case, "phosphorylated tau," or "p-tau181" ("p-tau") is believed to be a major component of the plaques and tangles found in the brains of people with Alzheimer's. *Id*. at ¶ 75. Indeed, in many of the foundational papers cited to support Cassava's research, levels of p-tau and their reduction (or not) are measured as a correlate to Alzheimer's disease. *Id*. Filamin A ("FLNA") is another key protein found in an altered form in the Alzheimer's brain. *Id*. at 38, 42.

A. Cassava's Studies of Simufilam

Plaintiff is currently in Stage 3 (typically the last of three sequential phases for clinical studies in the United States) trials of a prospective drug, simufilam (also called "PTI-125" in the scientific papers), that is believed to work by binding to FLNA and "restoring" it to its normal shape. (FAC ¶¶ 43, 55, 63). The studies supporting this hypothesis and cited by Cassava are generally authored by Dr. Lindsay Burns, Cassava's Vice President of Neuroscience ("Dr. Burns"), and Dr. Hoau-Yan Wang, Associate Medical Professor at the City University of New York ("CUNY") and Cassava's "academic collaborator" ("Dr. Wang"). (*See* FAC ¶ 25; ECF 30-5 at 4; ECF

[3] Proteins can function to mediate necessary biological processes in the body and brain. (FAC ¶ 40). When they are misfolded, not only can they form plaques and tangles that can physically disrupt or interfere with other processes, but they also cannot perform their normal function. *Id*. at ¶ 41.

30-22, Exhibit 20 – Cassava Form 10-K, at 14).[4] Based on numerous studies conducted by Dr. Burns and Dr. Wang, Cassava asserts that "normal function" of certain receptors in the brain is restored when FLNA is restored to its normal shape. (FAC ¶ 42). In studies conducted in living mouse models conducted by Dr. Wang, Dr. Burns and others, use of simufilam is correlated with reduced neuro-inflammation, reduced amyloid and tau deposits, improved receptor signaling, and improved learning and memory. (FAC ¶ 44; *see also* ECF 30-22 at 15; ECF 36-9).

As relevant to this case, earlier studies, and results from the Stage 2a and 2b trials of simufilam, were published and presented in various formats, including in peer-reviewed journals. (*See, e.g.*, FAC ¶ 311). In the Stage 2a trial, conducted in 2019, 13 Alzheimer's patients were given 100mg of simufilam twice daily for 28 days. *Id*. at ¶ 68. Cerebrospinal fluid ("CSF") was taken at the beginning and end of the 28-day period, and was analyzed to compare levels of 8 different biomarkers of Alzheimer's disease. *Id*. at ¶¶ 68–69. Cassava reported declines in the levels of all eight biomarkers, including statistically significant reductions of two forms of tau protein. *Id*. at ¶¶ 69–70.[5] In the Stage 2b trial, announced in 2020, 64 Alzheimer's patients across 9 sites were randomly divided into three treatment groups: placebo, 50mg or 100mg of simufilam treatment twice daily for 28 days. *Id*. at ¶ 71. This time, however, the initial bioanalysis of the CSF samples was conducted by "an outside lab, with whom [Cassava] had no work experience," and "showed unnaturally high variability and other problems." *Id*. at ¶ 73. Cassava "concluded that the data from this initial bioanalysis was anomalous" and "served no

[4] "Wang is a long-time member of Cassava's Scientific Advisory Board, one of its principal paid scientific consultants and its lead scientist responsible for the Company's Simufilam research . . . ." (ECF 30-6 at 7).

[5] The FAC and some of the research papers also discuss biomarker levels in plasma and lymphocytes – which are found in the blood but not CSF – but do not discuss when and how the plasma and lymphocytes were obtained or analyzed. (FAC ¶ 70). These markers may relate to Cassava's development of SavaDX, "a way to detect the presence of Alzheimer's disease from a small sample of blood." *Id*. at ¶ 37.

useful purpose," and sent "[b]ackup CSF samples" to Dr. Wang's lab at CUNY for a blinded reanalysis (the "re-do"). *Id*. at ¶ 73. From this reanalysis, Cassava reported that simufilam "significantly . . . improved an entire panel of biomarkers of [Alzheimer's] disease" when compared to results from the placebo group. *Id*. at ¶ 74. The Stage 2b results reported statistically significant changes in all biomarkers in both the 50mg and 100mg treatment groups when compared to the placebo group and apparently produced "directional" (but not statistically significant) improvements in memory in the 50mg and 100mg treatment groups when compared to the placebo group. *Id*. at ¶¶ 74–86.

B. Neuroscientist Defendants' Statements

At various dates in 2021, the Neuroscientist Defendants filed a Citizen Petition and sent publicly available letters to the Food and Drug Administration ("FDA") expressing "grave concerns about the quality and integrity of the laboratory-based studies surrounding" simufilam and claims about its efficacy. (ECF Nos. 30-5 at 3; ECF 80-1). The Neuroscientist Defendants accuse Drs. Burns and Wang (and others) of intentional data manipulation and misrepresentation in Cassava's preclinical and clinical studies, and request that the FDA halt the ongoing trials of simufilam pending an audit of these issues. (ECF Nos. 30-5; ECF 80-1). Cassava asserts that the Neuroscientist Defendants made allegedly defamatory statements in:

1. The Citizen Petition filed with the FDA on August 18, 2021 (ECF 30-5, the "CP" [6]);
2. The August 30 Letter to the FDA (ECF 30-6, the "August 30 FDA Letter");
3. The September 9 Letter to the FDA (ECF 30-7, the "September 9 FDA Letter"[7]);
4. The November 17 Letter to the FDA (ECF 30-11, the "November 17 FDA Letter"); and

[6] The FAC also references a press release dated August 26, 2021, that contained a link to the CP, but does not identify new or different statements by any Defendants. (FAC ¶ 123).

[7] Again, although the Complaint is not clear, the allegations in the September 9 FDA Letter appear to add concerns about the data and results from the Stage 2a trial, the Stage 2b "redo," and Stage 3's reliance on the Stage 2a and 2b studies. (FAC ¶¶ 128–130).

5. The December 8 Letter to the FDA (ECF 30-13, the "December 8 FDA Letter"[8]).

The Neuroscientist Defendants' concerns fell into three general categories: (1) concerns related to "integrity of clinical biomarker data;" (2) integrity of Western blot data; and (3) integrity of analyses involving human brain tissue. (*See* ECF 30-5). In the Appendix to the CP, the Neuroscientist Defendants raise "six additional areas of concern." (*Id*. at 8–9, 30–48). I will summarize each of these in turn.

i. Integrity of Clinical Biomarker Data

Cassava's Stage 2b trials purported to test whether simufilam lowered the levels of certain biomarkers associated with Alzheimer's Disease in the CSF of 64 Alzheimer's patients. The CP points to two "significant problems" with this biomarker data. First, Cassava initially reported in May 2020 that the analysis of the biomarkers by an external lab[9] "missed its primary end points." (ECF 30-5 at 14; FAC ¶ 73). Four months later, Cassava reported that the bioassays done by an external group were in error, and that Cassava reanalyzed[10] "backup samples" – i.e., different samples of the same raw material drawn at the same time – and claimed statistically

[8] The December 8 FDA Letter supplemented the Neuroscientist Defendants' prior filings by describing their "recent re-inspection of the Methods section . . . shows seemingly irrefutable evidence of data manipulation/fabrication." (FAC ¶ 153).

[9] It is unclear who performed the initial analysis that missed its primary end points. Cassava apparently issued a press release on August 25, 2021, titled "Cassava Sciences Responds to Allegations," which stated that the plasma (not CSF) p-tau data presented in the July 26, 2021, poster was generated by Quanterix Corp. (*See* ECF 35-3, Exhibit 63, at 2). Two days later, according to the Neuroscientist Defendants, Quanterix issues a press release stating "Cassava previously engaged Quanterix' Accelerator laboratory to perform sample testing based on blinded samples provided by Cassava. **Quanterix or its employees did not interpret the test results or prepare the data charts presented by Cassava [in the July 2021 poster] . . . or otherwise**." (ECF 30-6 at 12) (emphasis in original). Cassava issued another press release on August 27, 2021, which asserted that Quanterix conducted sample testing by measuring p-tau in plasma testing, and then sent the raw data to Cassava "for analysis of treatment effects." (ECF 35-4 at 2).

[10] In the August 30 FDA Letter, Defendants explain that Cassava's reanalysis of "backup samples" of CSF were done at Dr. Wang's lab at CUNY, while Cassava's December 31, 2020, Form 10-K reports that the samples "were subsequently sent to a second outside lab for bioanalysis. . . . [and] conducted under blinded conditions to eliminate any possibility of bias." (ECF 30-6 at 6–7).

significant improvement in the biomarker levels in the CSF of patients who had been given the 50mg and 100mg simufilam regimen for 28 days. (ECF 30-5 at 14; FAC ¶¶ 73–74). Cassava asserted that this reanalysis was necessary because "the initial biomarker data showed high levels of inconsistent values without explanation for the high level or variation," and that such reanalyzing is "common and accepted practice." (FAC ¶ 402). Second, two figures in a poster presented by Cassava at the Alzheimer's Association International Conference ("AAIC"), reporting on the biomarker levels from simufilam's Stage 2 studies, are internally inconsistent. (ECF 30-5 at 13–15).

Specifically, Figure 5 of the July 2021 poster, presented by Dr. Wang,[11] shows spaghetti plots of the three treatment groups: placebo, 50mg, and 100mg. (ECF 30-5 at 14). Each line on the plot represents the change between day 1 and day 28 of p-tau levels in the CSF of each (living) human subject. *Id.* If the line slopes up, the amount of p-tau in that person's CSF was higher on day 28 than it was on day 1, and vice versa if the line slopes down. *Id.* In all three plots in Figure 5, some lines go up and some go down. *Id.* Figure 4 purports to present the same data (levels of p-tau on day 1 versus day 28) in a different way: now, each line that slopes up or down is represented by a dot that represents the amount of increase or decrease of p-tau on day 28 as compared to that person's p-tau level on day 1. *Id.* Dots falling below the horizontal line corresponding to "0" represent decreases in levels of the biomarker after 28 days, while dots above the "0" line represent increases. *Id.* Figure 4 reports a statistically significant decrease for both groups that received simufilam as compared to a mean (average) 20% change

[11] The CP explicitly draws an inference that the re-test was done in Dr. Wang's lab based on the poster presented by Dr. Wang in 2021 describing the Stage 2b results. (ECF 30-5). Later filings confirm that the data in the poster are results from Dr. Wang's Stage 2b "re-do." (*See* ECF 30-6 at 7–8).

from baseline[12] for the placebo group. *Id.* The CP points out that there is a line in the spaghetti plot that represents an Alzheimer's patient who received the 100mg dose of simufilam whose biomarker level increased by 235% over baseline, which does not have a corresponding dot in Figure 4. *Id.* at 15. The Neuroscientist Defendants infer, then, that if that data point had been included in the analysis represented in Figure 4, "any beneficial effect of 100mg simufilam would likely have been negated." *Id.* at 15; *see also* ECF 30-6 at 7 (recalculating and finding no statistical difference from placebo once all data points were included). The September 9 FDA letter further notes that the baseline levels of three of the biomarkers tested in the Stage 2b "re-do" were "far outside expectations," which the Neuroscientist Defendants assert is a sign of "major lab errors or manipulation." (ECF 30-7 at 7).

ii. Integrity of Western Blot Data

The western blot is a technique for detecting the presence – and assessing relative amounts – of proteins in a sample.[13] Photographs of western blot analyses are often presented in scientific publications to support inferences whether certain proteins are present or not, and

[12] Figure 4 also reports that the mean 20% increase in the placebo group was "(driven by an outlier)," which presumably is the uppermost dot above the "0" line in Figure 4. (ECF 30-5 at 14). The CP does not suggest how the 20% increase, and its comparison to the 50mg and 100mg results, might have changed (to Cassava's detriment) if that outlier had been omitted; the August 30 FDA Letter provides a summary of a new statistical analysis done by a different scientist using all the data points in Figure 4. That new statistical analysis reports that the differences between the treatment and placebo groups would not be statistically significant. (ECF 30-6 at 7).

[13] In short, via a multi-step process, proteins present in a sample move across a substrate, and the distance they move depends on their molecular weight and other factors. The presence of the proteins can be visualized and the identity of the protein(s) in the sample and their relative amounts can be inferred by the presence, location and visibility, respectively, on the image of the blot. Typically, several "lanes" are run on the same substrate, at the same time, and compared to one lane on the substrate that contains the protein(s) sought to be detected, or which acts as a guide or calibrator to the molecular weights of certain proteins. Then, if a stripe representing protein is found to have moved the same distance as the corresponding stripe in the control lane, one could infer that the substances were of the same molecular weight, and thus the protein sought to be detected was present in the test sample. *See, e.g.*, Tahrin Mahmood & Ping-Chang Yang, *Western Blot: Technique, Theory, and Trouble Shooting*, 4(9) N. AM. J. MED. SCI. 429–34 (2012).

sometimes to compare their relative amounts. The stripes found in a western blot are not generally uniform in shape or density. (ECF 30-5 at 15–16). The general allegation here – that Western blot images in publications related to the development of simufilam may have been manipulated – is sadly not uncommon now, and has been found in other publications unrelated to Drs. Wang and Burns and unrelated to simufilam. (ECF 30-5 at 16; *see also* ECF 30-6 at 8–10).

The CP and subsequent filings with the FDA examine and note the following "anomalies" in the Western blot images in the scientific papers used by Cassava to support their research and initial findings:

a. 2005 Neuroscience Paper

The first example the Neuroscientist Defendants raise is from a 2005 *Neuroscience* paper authored by Drs. Wang and Burns, where the Neuroscientist Defendants claim evidence of cutting and pasting, or cropping an image, Figure 5a. (ECF 30-5 at 17). The CP itself does not draw any inferences about the anomaly or make statements about whether it is material. *Id*.

b. 2010 Biological Psychiatry Paper

The Neuroscientist Defendants identify four bands in Figure 1a in Dr. Wang's 2010 paper in *Biological Psychiatry* that show the same pattern of streaking as Figure 12a from the 2005 *Neuroscience* paper. (ECF 30-5 at 17–18). After expanding and enlarging the images of the four bands, the Neuroscientist Defendants claim that "the pattern of this streaking is identical in the two images." *Id*. at 18. The CP then asserts that "it is hard to imagine that the duplication was not intentional." *Id.* The CP then recommends that the authors produce, for independent review, the "original full-length images **with appropriate molecular weight markers** . . . to validate band migration." *Id.* (emphasis in original); *see also* ECF 30-6 at 9.

c. 2008 PLoS ONE Paper

In this 2008 paper in *PloS ONE*, authored by Drs. Wang and Burns, the CP identifies panels with irregularly-shaped blots in Figure 7a that are identical in shape, yet reported as different experiments. (ECF 30-5 at 19). The CP states that "[t]he similarity in these images could not have occurred by chance." *Id*. The CP again recommends validation of the original images. *Id*.; *see also* ECF 30-6 at 9.

d. 2012 Journal of Neuroscience Paper

The Neuroscientist Defendants state that this "foundational paper" in the *Journal of Neuroscience* (ECF 36-10), authored by Drs. Wang and Burns, is the one "**that links Filamin A and PTI-125** [simufilam] **to Alzheimer's Disease**." (ECF 30-5 at 20) (emphasis in original). The CP claims to present "only a small sampling" of "dozens of questionable image features," including blots that are of "low quality, over exposed and selectively cropped." *Id*. The CP identifies several bands in Figures 1a, 6b, 9a, and 11a that the Neuroscientist Defendants claim are identical, misaligned, and/or have white haloes around the bands that suggest image manipulation. *Id.* at 20–22. The link provided in the August 30 FDA Letter raises an additional concern in Figures 8a and 8b, which are not Western blots but stains of purportedly different brain tissue from different individuals subject to different treatments, but which appear to be duplicate images. (ECF 30-6 at 10, 12, images in link). Given the importance of this paper in Cassava's research, the CP suggests validating the results not only by reviewing images but by having the authors "produce full length unaltered gels with appropriate molecule weight markers to validate band migration, for all experiments in this paper." *Id*. at 22; *see also* 30-6 at 9.

The November 17 FDA Letter notes that although the *Journal of Neuroscience* issued an erratum to this 2012 paper on November 10, 2021 (ECF 30-11 at 18, link to erratum), the erratum did not address all of the images of concern, and that the "original" images in the erratum also appear to be altered.[14] *Id.* at 18–21.

e. 2020 Journal of Prevention of Alzheimer's Disease Paper

This 2020 publication in the *Journal of Prevention of Alzheimer's Disease* is first referenced in the August 30 FDA Letter. (ECF 30-6 at 8). This paper provides results and analysis from the Stage 2a clinical trial, and the link embedded in the August 30 FDA Letter raises some concerns regarding Western blot results, as well as a concern that the paper was approved for publication six days after it was submitted, which is an unusually short time for a peer-reviewed publication. (ECF 30-6 at 9). Dr. Wang is listed as the first author, and Dr. Burns, as well as her husband and Cassava's CEO, Remy Barbier, are also listed as authors. (ECF 30-6 at 8, link to publication provided).

The September 9 FDA Letter notes that Dr. Barbier stated[15] that Cassava did not have "the original films or images for the Western blots in question," noting instead that they were generated by Dr. Wang. (ECF 30-7 at 4).

[14] The November 17 FDA Letter also notes that Cassava halted trading of its stock on November 4, 2021, and issued a press release later that day entitled, "Review by Journal of Neuroscience Shows No Evidence of Data Manipulation in Technical Paper Foundational to Cassava Sciences' Lead Drug Candidate." (ECF 30-11 at 17, links to press release).

[15] Based on the list of exhibits attached to the FAC, it is possible that ECF 35-5, Exhibit 65 – September 3, 2021, press release titled "Cassava Sciences Releases a Public Statement Regarding Recent Allegations," was intended to provide Dr. Barbier's public statements. The links provided in ECF 35-5, however, do not work.

f. 2007 Behavioural Pharmacology Paper

This 2007 publication in *Behavioural Pharmacology* is first referenced in the August 30 FDA Letter. (ECF 30-6 at 13, link to publication provided). The paper lists Dr. Wang as the second author and the link embedded in the August 30 FDA Letter raises numerous concerns about Western blot results. *Id*. This paper does not, on its face, concern clinical testing of simufilam.

g. 2021 Physiology & Behavior Paper

This publication is first referenced in the August 30 FDA Letter (ECF 30-6 at 13–14, link to publication provided). The paper lists Dr. Wang as the fifth author and the link embedded in the August 30 FDA Letter raises numerous concerns about Western blot results. *Id*. This paper does not, on its face, concern clinical testing of simufilam.

iii. Integrity of Human Brain Tissue Analyses

The Neuroscientist Defendants discuss three papers that purport to show simufilam's action in brain tissue taken from Alzheimer's patients post-mortem ("post-mortem brain tissue"). (ECF 30-5 at 23). The papers, published in 2009 and 2012 in *The Journal of Neuroscience* (ECF 36-10), and then in 2017 in *Neurobiology of Aging* (ECF 36-9), claim to detect chemical activity consistent with their hypothesis that simufilam binds to deformed or irregular FLNA in the Alzheimer's brain and "restores" its shape and function. First, the CP describes the chemical reactions[16] that purportedly occur in the brain specimens that were treated with simufilam, compared to the reactions (and end products observed) in the brain tissue that was

[16] Normal FLNA is believed to be associated with blocking the interaction of β-amyloid to the α7-nicotinic acetylcholine receptor, which in turn is believed to affect signaling between neurons in the brain, and decrease tau phosphorylation. (ECF 30-5 at 23). As reported in these papers, chopped postmortem brain tissue was exposed β-amyloid for an hour. In untreated brain tissue, exposure to β-amyloid for an hour without simufilam, resulted in "a massive increase in tau phosphorylation," while brain tissue exposed to β-amyloid and simufilam did not apparent show an increase in tau phosphorylation. *Id*.

not treated with simufilam. *Id*. In each of these experiments, post-mortem brain tissue had been harvested after Alzheimer's patients' deaths and stored at -80°C, warmed to -20°C, chopped and then treated with β-amyloid with and without simufilam for an hour at 4°C. (ECF 30-5 at 23). Dr. Wang, Dr. Burns and their colleagues used the same methodology to assess NMDA [N-methyl-D-aspartate] receptor signaling: combining minced human brain tissue from Alzheimer's patients, NMDA/glycine, and β-amyloid, with and without simufilam, to find that "NMDA signaling was . . . rescued" by simufilam. *Id*. at 23–24.

The CP challenges several aspects of these papers and their methodology. First, it notes that the temperature at which the brains and brain tissue were stored, processed, and at which the experiments were run, were far below human body temperature, where human enzymatic reactions "generally work best." (ECF 30-5 at 23). Chemical reactions generally proceed more slowly at lower temperatures because the molecules involved are moving more slowly. The CP then questions whether the enzymes necessary for these reactions would have survived the initial freezing to -80°C in the first instance, and whether they would likely be active at 4°C. *Id*.

Next, the CP notes that the methodology sections of all three papers describe brain tissue by "age and post-mortem interval" identically, so that it "is therefore reasonable to assume [that] the same human brain specimens were used across the studies from 2008 [to] 2017." (ECF 30-5 at 24). Drs. Burns and Wang, the authors of these papers, report that there was a "marked, rapid increase in the Arc protein observed as evidence of NMDA receptor activity with this approach." *Id*. In other words, Drs. Burns and Wang observed an increase in presence of the Arc protein, from which they infer that simufilam is responsible for rescuing

signaling in the NMDA receptor. *Id*.[17] According to the Neuroscientist Defendants, "[t]he complex, multi-step cellular processes the authors claim to observe in tissue that has been dead for a decade are contrary to a basic understanding of neurobiology."[18] *Id*.

The CP points out another anomaly with the Western blot in the 2017 *Neurobiology of Aging* paper, in Figure 12. (ECF 30-5 at 25; *see* ECF 36-9 at 15, Fig. 12). According to the methods section of the paper, the same substrate gel was analyzed (probed) for six different proteins. (ECF 36-9 at 3–7). In order to assess the relative improvement (or not) in the levels of each of these proteins, they were compared with levels of NR1, NMDA receptor subunit 1, for each lane of the blot. (*See* ECF 36-9 at 15). Presumably, this comparison would normalize the effect of the number of receptors on the level of protein detected, because each lane represents brain tissue analyzed from a different individual. The problem, however, is that there are 12 NR1 bands to compare to 13 bands for all of the other protein bands. (ECF 30-5 at 25). The CP further identifies other anomalies in the NR1 and PLCy1 bands that the Neuroscientist Defendants suggest are the result of image manipulation. *Id*. at 26. The August 30 FDA letter also notes that there appear to be two "suspiciously similar" photos of brain tissue stained with reportedly

[17] "NMDA signaling was reported blocked by B-amyloid and in AD and rescued in both cases by the experimental drug." ECF 30-5 at 24.

[18] In particular, the CP lists four intermediate inferences that must be true in order for the authors' ultimate inference about the effect of simufilam to be true, any one of which would be revolutionary evidence that brain activity at the neuronal level could be restarted years after the brain and its owner had died. (*See* ECF 30-5 at 24) ("The suggestion is that post-mortem human brain tissue, frozen for a decade, thawed and chopped, (1) has intact NMDA receptor signaling, (2) is able to transmit that [electrical] signal to the cell body [of an intact, functioning neuron] . . .; (3) has the functioning cellular apparatus to rapidly produce the Arc protein and (4) enough intact neurons are present to mediate a >4 fold rise in Arc levels in this tissue."). *Id*. The November 17 FDA Letter notes that the 2021 *Journal of Neuroscience* erratum "does not address other concerns about the [2012] publication that we raised in our first petition, such as the methodology for the brain tissue 're-animation' experiments." (ECF 30-11 at 18).

different antibodies (to detect the presence of different proteins) used in the same figure. (*See* ECF 30-6 at 16).

iv. Appendix: Suspicious Claims

The appendix spends another 18 pages noting results that the Neuroscientist Defendants claim are not plausible, including pointing out numerous other instances of possible image manipulation in Western blots used to support the conclusions of Dr. Burns' and Wang's papers. (ECF 30-5 at 30–48). Each of these examples refers to one or more figures or summaries of data from papers used to support Cassava's research and scientific claims, and then explains why the Neuroscientist Defendants infer that the data and/or results are unreliable,[19] or do not support the conclusions that Drs. Burns and Wang draw in those papers.[20] *Id*.

v. November 17 FDA Letter

The cover letter summarizes the Neuroscientist Defendants' concerns about the integrity of the data presented in support of simufilam's clinical trials. (ECF 30-11 at 2). These concerns are no longer limited to integrity of the data, but identify several statements from Dr. Wang's and Dr. Burns's publications (apart from the Western blot concerns) that seem scientifically impossible or would suggest other error. *Id*. at 5–7. The letter challenges some of methodology, statistical analysis and results from the Stage 2b study as well. *Id*. at 7–8. The letter also lists

[19] By way of example, "Suspicious Claim #5" (ECF 30-5 at 34), challenges the mouse model of AD and simufilam's "purported improvements in memory." But both the wild type (non-AD) and transgenic mice showed atypical and similar behavior even before simufilam was administered. And after the transgenic (AD) mice were treated with simufilam, their measure of memory – the rate of spontaneous alternation in the Y maze – got *worse*, not better. *Id.*

[20] Notably, in "Suspicious Claim #4" (ECF 30-5 at 33), the Neuroscientist Defendants point out that Figure 2 of the 2021 AAIC poster, which purports to show that simufilam lowers plasma levels of altered FLNA, likely does not represent FLNA. The Dot.Com Defendants' presentation on SavaDX (*see* ECF 30-12), confirms that these blots represent, at best, a fragment of FLNA, and do not support the conclusions drawn by Cassava that simufilam can affect or detect levels of altered FLNA fragments in the blood.

several other "red flags" "discovered by the scientific community," citing to numerous publications by Drs. Wang and Burns. *Id*. at 9–17.

vi. Simufilam's Binding Affinity and the December 8 FDA Letter

The August 30 FDA Letter expands on the CP's "Suspicious Claim #1," which discusses the claim that PTI-125 (simufilam) has a *femtomolar* binding affinity for FLNA, which the Neuroscientist Defendants and other scientists assert is "suspiciously high and seemingly implausible." (ECF 30-6 at 15). The December 8 FDA Letter further explains "many major problems" with the methodology and binding affinity results published in the "foundational" 2017 *Neurobiology of Aging* paper. (ECF 30-13 at 4; *see also* ECF 36-9).

First, Cassava incorrectly notes in the paper that the specific activity[21] of carbon-14 ("[C14]"), the radioisotope purportedly used in radioassays to detect the presence of simufilam, is "57.7 Ci/mmol." (ECF 30-13 at 3–4). It is not. It is 62.5 **milli**Curies per millimole, or 62.5 **m**Ci/mmol, or 0.0625 Ci/mmol. *Id*. In other words, the specific activity of [C14] as reported in the paper is off by a factor of approximately 1000. *Id*.

The December 8 FDA Letter then goes on to calculate the volumes of solutions containing [C14] that would have been necessary to yield the results reported in the paper, based on the actual specific activity of [C14]. *Id*. at 5. Using an assumption that only one carbon atom in simufilam was substituted with [C14], the Neuroscientist Defendants show, if their calculations are correct, how it would have been impossible to obtain the number of "counts"

[21] The specific activity of a radioactive isotope is a number that is intrinsic to the isotope and is a measure of the rate at which the isotope releases energy in the form of radiation that can then be measured and visualized in a radioassay. The Neuroscientist Defendants note that [C14]'s decay rate is too slow to be useful for the radioassays done here.

(radiation measured as a sign of binding) reported in the paper using the volumes that are normally used in such experiments or that were used in the paper (5ml). *Id*.; *see also* ECF 36-9.

III. ANALYSIS

A. Standard of Review

For the purpose of deciding a motion to dismiss pursuant to Federal Rule of Civil Procedure 12(b)(6), the Court must accept all allegations in the complaint as true, and draw all reasonable inferences in the plaintiff's favor. *McCarthy v. Dun & Bradstreet Corp.*, 482 F.3d 184, 191 (2d Cir. 2007). The Court's function on a motion to dismiss is "not to weigh the evidence that might be presented at a trial but merely to determine whether the complaint itself is legally sufficient." *Goldman v. Belden*, 754 F.2d 1059, 1067 (2d Cir. 1985). If the plaintiff has stated "enough facts to state a claim to relief that is plausible on its face," the complaint should not be dismissed. *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 570 (2007). "A claim has facial plausibility when the plaintiff pleads factual content that allows the court to draw the reasonable inference that the defendant[s] [are] liable for the misconduct alleged." *Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009). For a claim to sufficiently "raise a right to relief above the speculative level," it must be grounded on factual allegations. *Twombly*, 550 U.S. at 555. A claim grounded on mere suspicion is not enough to meet this standard. *Id*. "'[L]abels and conclusions' or 'a formulaic recitation of the elements of a cause of action will not do.' Nor does a complaint suffice if it tenders 'naked assertion[s]' devoid of 'further factual enhancement.'" *Iqbal*, 556 U.S. at 678 (quoting *Twombly*, 550 U.S. at 555, 557) (internal citation omitted, alteration in original).

Generally, "[w]hen considering a motion to dismiss, the Court's review is confined to the pleadings themselves," because "[t]o go beyond the allegations in the [c]omplaint would

convert the Rule 12(b)(6) motion to dismiss into one for summary judgment pursuant to [Rule] 56." *Thomas v. Westchester Cnty. Health Care Corp.*, 232 F. Supp. 2d 273, 275 (S.D.N.Y. 2002) (citation omitted). However, "the Court's consideration of documents attached to, or incorporated by reference in the [c]omplaint, and matters of which judicial notice may be taken, would not convert the motion to dismiss into one for summary judgment." *Id.* (citations omitted); *Maroney v. Woodstream Corp.*, No. 19-CV-8294 (KMK), 2023 WL 6318226, at *1 (S.D.N.Y. Sept. 28, 2023). The Court can take judicial notice of public disclosures such as those filed with the SEC or FDA. *See, e.g.*, *In re Restasis (Cyclosporine Ophthalmic Emulsion) Antitrust Litig.*, 333 F. Supp. 3d 135, 152 (E.D.N.Y. 2018) (taking judicial notice of three citizen petitions to the FDA).

B. The Neuroscientist Defendants' Statements are Protected by the First Amendment

Under New York law, a complaint asserting defamation must plausibly allege five elements: "(1) a written defamatory statement of and concerning the plaintiff, (2) publication to a third party, (3) fault, (4) falsity of the defamatory statement, and (5) special damages or per se actionability." *Palin v. N.Y. Times Co.*, 940 F.3d 804, 809 (2d Cir. 2019). When a defamation claim is brought by a public figure,[22] the First Amendment independently requires a showing that the defendant acted with actual malice. *N.Y. Times Co. v. Sullivan*, 376 U.S. 254, 283 (1964).

In *Milkovich v. Lorain Journal*, 497 U.S. 1, 11–14 (1990), the Supreme Court examined the tension between defamation claims and the First Amendment and issues of public concern. *Id*. (citing cases). Merely prefacing a statement with, "In my opinion," or using the word

[22] Cassava does not deny that it is a public figure. (*See* ECF 81 at 5, 9: "Cassava does not and cannot deny that it is a public company that made public filings in pursuit of a drug it hopes to test on and sell to the public.").

"opinion" does not protect an allegedly defamatory statement under the First Amendment. *Id*. at 19. In distinguishing the following statements, "In my opinion Mayor Jones is a liar," and, "In my opinion Mayor Jones shows his abysmal ignorance by accepting the teachings of Marx and Lenin," as actionable and non-actionable, respectively, Justice Rehnquist explained that "a statement of opinion relating to matters of public concern which does not contain a provably false factual connotation will receive full constitutional protection." *Id*. at 20.[23]

Four factors are considered to ascertain whether, under the "totality of circumstances," a statement is fact or opinion. These factors are: (1) "the specific language used"; (2) "whether the statement is verifiable"; (3) "the general context of the statement"; and (4) "the broader context in which the statement appeared." *Milkovich*, 497 U.S. at 9. In *ONY, Inc. v. Cornerstone Therapeutics, Inc*, 720 F.3d 490 (2d Cir. 2013), the Second Circuit considered these four factors in the context of statements arising from scientific research, when they affirmed the dismissal of Lanham Act claims. *Id*. There, claims arose from a dispute concerning different inferences to be drawn from data concerning the efficacy of competing surfactants that are used to treat respiratory distress in prematurely born infants. *Id*. In its decision, the Second Circuit first acknowledged that "[s]cientific academic discourse poses several problems for the fact-opinion paradigm of First Amendment jurisprudence." *Id*. at 496. The "very premise of the scientific enterprise" is that it "engages with empirically verifiable facts about the universe," but "it is [also] the essence of the scientific method that the conclusions of empirical research are tentative and subject to revision, because they represent inferences about the nature of reality

[23] Even in dissent, Justices Brennan and Marshall used the same analysis but arrived at a different result. *Id*. at 26–27.

based on the results of experimentation and observation." *Id*. Where findings among and between scientists are challenged and articles in peer-reviewed journals reach different conclusions, the typical continuing discourse would include attempts to replicate the experiments, conducting their own experiments, and challenging the experimental design and inferences to be drawn from the results. *Id*. at 497.

Plaintiff asserts that because the Neuroscientist Defendants claim that Cassava's underlying data and research is fraudulent, *ONY* is inapplicable. (ECF 80 at n.7). In so doing, Plaintiff ignores the reasoned analysis in *ONY* and attempts to equate the Neuroscientist Defendants' actual statements concerning the integrity of Cassava's data to the Supreme Court's example in *Milkovich*, that the statement "'in my opinion John Jones is a liar' is no different from merely asserting that John Jones is a liar." *ONY*, 720 F.3d at 496 (citing *Milkovich*, 497 U.S. at 19–20).[24] There are two problems with Plaintiff's argument, however. First, the Neuroscientist Defendants made many different statements in the CP that examined Cassava's published data, and which challenged both the data and the inferences to be drawn from the data. Plaintiff collects and collapses all of these statements into an assertion of "fact" that "Cassava is a fraud," which was not in fact made by the Neuroscientist Defendants. (*See* ECF 80-1). Second, Plaintiff oversimplifies the analysis in *ONY* and does not consider the reasoning in *Milkovich*, in both the majority opinion and the dissent. The inference the Neuroscientist Defendants draw after examining the data and empirical research is not that "Cassava is a

[24] See also *Milkovich*, 497 U.S. at 16–17 ("Rejecting a contention that liability could be premised on the notion that the word "blackmail" implied the developer had committed the actual crime of blackmail, we held that "the imposition of liability on such a basis was constitutionally impermissible—that as a matter of constitutional law, the word 'blackmail' in these circumstances was not slander when spoken, and not libel when reported in the Greenbelt News Review.").

fraud" or even that "simufilam is not effective," which would have been analogous to the statements in *ONY*. Rather, the Neuroscientist Defendants drew a more measured and nuanced series of inferences from Cassava's own underlying research, on which Cassava relies to support clinical testing of simufilam in humans: namely, that the research may be unreliable,[25] based on certain irregularities in the reporting of data in the research. Numerous press releases and basic science papers are attached and incorporated into the FAC (*see, e.g.*, ECF Nos. 30-19, 30-20, 31-3 through 31-10), as if all of these statements, taken together, could be sufficient to "prove" Cassava's scientific conclusions to be true (or not). This is part of the "ongoing discourse" referenced in *ONY* that courts should avoid. *ONY*, 720 F.3d at 497. Indeed, the parties' repeated filings concerning CUNY's subsequent investigation (and its results) are irrelevant to this analysis. Rather, the fact of the investigation, conducted well after the Neuroscientist Defendants raised their concerns, shows that these statements are also not yet verifiable.

Applying the factors to the Neuroscientist Defendants' statements, they are non-actionable opinion. "[A] statement of opinion that is accompanied by a recitation of the facts on which it is based or one that does not imply the existence of undisclosed underlying facts" is not actionable. *Gross v. New York Times Co.*, 82 N.Y.2d 146, 153–54 (N.Y. 1993) (citing Justice Brennan's dissent in *Milkovich*, reasoning "a proffered hypothesis that is offered after a full recitation on which it is based is readily understood by the audience as conjecture.").

[25] Plaintiff's reference to "nonfraudulent data" in *ONY* is also not enough to distinguish the case. To be sure, Neuroscientist Defendants' statements challenge the reliability and integrity of the reported data, but the "data" relied on by the Neuroscientist Defendants are the published figures, data and methodology that were published by Drs. Wang and Burns themselves in numerous papers. *ONY*, 720 F.3d at 497–98.

That is what happened here. The Neuroscientist Defendants' statements arise from – and refer to – Cassava's own published research, and call for further investigation after drawing inferences about Dr. Wang's and Dr. Burns's research and reported results. The resulting investigations and discourse among the scientists is aimed first at verifying the results of Cassava's scientists, after which different inferences may be drawn.[26] (*See* ECF 74-1 at 8).[27] The general and broader context also support a finding that these defendants' statements are protected by the First Amendment as non-actionable opinion. Scientific discourse — even when it challenges the integrity of a fellow scientist's research — belongs first among the scientists, who are best suited to assess the underlying research, and the inferences to be drawn from it. *See Underwager v. Salter*, 22 F.3d 730, 736 (7th Cir. 1994) ("Scientific controversies must be settled by the methods of science rather than by the methods of litigation. More papers, more discussion, better data, and more satisfactory models—not larger awards of damages—mark the path toward superior understanding of the world around us.") (internal citation omitted). Alzheimer's Disease and other dementias are terrible afflictions, and an effective cure or treatment would significantly benefit the lives of millions of people. But it is also important to ensure that funding is directed toward reliable, replicable research.

Because I find that the statements are statements of opinion,[28] specifically, inferences drawn from facts and data presented by Cassava, they are not actionable. I respectfully

[26] The Court has not reviewed the results of or relied on the CUNY investigation in its recommendation of dismissal. (*See* ECF Nos. 101-103).

[27] "In fact, Cassava admits that "independent scientists" found "problems," "obvious errors," and "tweaks" in the data. The CP laid out admittedly accurate facts, and Cassava's challenge to opinions derived from those true facts states no claim." (ECF 74-1 at 8) (quoting FAC ¶¶ 362–63).

[28] The SAC also fails to plead facts supporting actual malice and causation. Pleading that the Neuroscientist Defendants are short sellers is insufficient to plead that the Neuroscientist Defendants knew that the CP and its follow up letters were false or made with reckless disregard for their falsity. Similarly, the SAC's conclusory

recommend that the Neuroscientist Defendants' motion to dismiss the defamation claim be **GRANTED**.[29] [30]

C. The FAC Does not Satisfy Rule 8

Rule 8(a) requires a short and plain statement sufficient to put a defendant "on notice of the claim against him." Fed. R. Civ. P. 8(a). Plaintiff asserts that the Neuroscientist Defendants' arguments for dismissal "are predicated on a misrepresentation of the facts alleged" and "**nearly everything** Bredt and Pitt said in their petitions and **everything** that they republished was factually inaccurate." (ECF 80 at 25) (emphases added). This conclusory statement, based on a FAC that attaches and incorporates more than 100 exhibits (many of which contain multiple links) and spans nearly 1600 pages,[31] is tantamount to dropping all of the scientific discourse – spanning years of research – in the lap of a randomly selected federal judge. That the parties happened to be referred to a randomly selected federal judge with a Ph.D. in science made the review of this motion only marginally more efficient. In any event, I have reviewed all of the Neuroscientist Defendants' statements and find that their factual statements are accurate

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assertions of causation are also insufficient. Therefore, as an alternative ground, I also find that Cassava has not sufficiently pleaded causation or malice.

[29] The Court has considered, but not addressed Defendants' allegations that claims based on the CP are barred by the one-year statute of limitations for defamation claims under New York law, because it is clear that there were allegedly defamatory statements made during the one-year period, many of which build off of and reference the CP. (ECF 74-1 at 16–17).

[30] It is well-settled that New York does not recognize an independent cause of action for civil conspiracy, which may only be asserted "to connect the actions" of separate defendants to an underlying tort. *Eze v. Mangal*, No. 521409/2019, 2020 WL 13469845, at *3 (N.Y. Sup. Ct. Nov. 13, 2020); *see Reich v. Lopez*, 38 F. Supp. 3d 436, 460 (S.D.N.Y. 2014), *aff'd*, 858 F.3d 55 (2d Cir. 2017). I have already recommended dismissal of the underlying defamation claim, and if this recommendation is accepted, it is fatal to Plaintiff's civil conspiracy claim against Defendants Bredt and Pitt, because there is no underlying tort perpetrated on Plaintiff by the Neuroscientist Defendants,[30] nor is there any more than a conclusory allegation of conspiracy with the remaining defendants.

[31] It is not clear whether Plaintiff has even cited every exhibit they have attached, but even if they had, alleging that "nearly everything Bredt and Pitt said [is false]" is probably not sufficient under Rule 8. *See United States v. Int'l Longshoremen's Ass'n*, 518 F. Supp. 2d 422, 463, n.74 (E.D.N.Y 2007) (in RICO case, simply pointing to complaint and attached documents "without identification of which allegations . . . apply to which person and for what reason does not provide the type of notice required" fails to provide fair notice for defendants to respond).

restatements of representations made and data presented by Cassava or its scientists in press releases and peer-reviewed scientific papers, but the inferences and opinions drawn therefrom are in sharp dispute, and thus not actionable. Moreover, the level of debate and scrutiny among scientists suggests that the scientific discourse is ongoing and nonjusticiable. *See, e.g.*, *Georgia High School Ass'n v. Waddell*, 248 Ga. 542, 542 (Ga. 1981) ("We now go further and hold that courts of equity in this state are without authority to review decisions of football referees because those decisions do not present judicial controversies.").

IV. CONCLUSION

For the reasons above, I respectfully recommend that the Neuroscientist Defendants' motion be **GRANTED** in its entirety.

V. OBJECTIONS

In accordance with 28 U.S.C. §636(b)(1) and Fed. R. Civ. P. 72(b), the parties shall have fourteen (14) days (including weekends and holidays) from receipt of this Report to file written objections. *See also* FED. R. CIV. P. 6 (allowing three (3) additional days for service by mail). A party may respond to any objections within fourteen (14) days after being served. Such objections, and any responses to objections, shall be addressed to the Honorable Gregory H. Woods, United States District Judge. Any requests for an extension of time for filing objections must be directed to Judge Woods.

FAILURE TO FILE OBJECTIONS WITHIN FOURTEEN (14) DAYS WILL RESULT IN A WAIVER OF OBJECTIONS AND WILL PRECLUDE APPELLATE REVIEW. *See Thomas v. Arn*, 474 U.S. 140, 155 (1985); *IUE AFL-CIO Pension Fund v. Herrmann*, 9 F.3d 1049, 1054 (2d Cir. 1993); *Frank v. Johnson*, 968 F.2d 298, 300 (2d Cir. 1992); *Wesolek v. Canadair Ltd.*, 838 F.2d 55, 58 (2d Cir.

1988); *McCarthy v. Manson*, 714 F.2d 234, 237–38 (2d Cir. 1983).

Respectfully submitted,

/s/ Ona T. Wang

Dated: January 3, 2024
New York, New York

Ona T. Wang
United States Magistrate Judge