Cassava and the Wang Lab: Seeing Through the Blind
Cassava & Wang claimed repeatedly to be conducting bioanalysis BLINDED

Statements describing Open-Label 6-Month study analysis in company SEC filings and presentations

The Wang lab is referred to as an outside lab conducting analysis of 6-Month OL samples blinded

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**INTERIM RESULTS – CSF Biomarkers**

Changes in CSF biomarkers were assessed in a subset of subjects (n=25) following 6 months of open-label simufilam treatment. CSF samples were analyzed in triplicate, blind to timepoint, by ELISA in an automated platereader. CSF P-tau\(^{181}\), total tau, A\(_{42}\),

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**July 29, 2021 Page 2 of 4**

**About Cerebrospinal Fluid (CSF) Biomarkers**

A key objective of this analysis was to measure changes in levels of biomarkers in patients before and after 6 months of treatment with open label simufilam. Biomarker data were analyzed from CSF collected from 25 patients with mild-to-moderate Alzheimer’s disease who are enrolled in an on-going open-label study and who agreed to undergo a lumbar puncture at baseline and again after 6 months of treatment. All bioanalyses were conducted blind by an outside lab. Simufilam robustly improved all measured CSF biomarkers (all p-values are baseline vs. 6-month levels by paired t-test):

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Simufilam robustly improved all measured CSF biomarkers in this cohort of 25 patients with mild-to-moderate Alzheimer’s disease.

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Emails reveal all parties had access to sensitive patient information

Participants inc members of Cassava and three academic collaborators; Drs Xu, Wang and Pei (Wang postdoc)

The email exchange discusses the shipping and labelling of clinical samples from a trial site
Emails show both Cassava & Wang were NOT BLINDED during the open-label study 1/2

Emails retrieved from a FOIL request to CUNY expose Cassava and the Wang Lab as being unblinded during sample analysis, prior to data presentation and while study is ongoing.

During April & May 2021, the shipment of samples individually labelled as **Day 1 or 6 Month** from Xu lab to Wang are discussed with multiple company members.

* Estimated study timeline
Emails show both Cassava & Wang were NOT BLINDED during the open-label study 2/2

Individual samples are labelled as either Day 1 or Month 6, and by site and patient ID. Hence, whether a patient is ON or OFF the drug is known to the person analyzing samples. This could allow Wang* to decide what sample measurements “should be”.

*Wang is currently under investigation for scientific misconduct.
Wang is UNBLINDED in Open Label Extension, Was he UNBLINDED for the entire P2b?

Similar claims of “blind to timepoint” were made about the 28-day P2b study. This CSF sample also served as our baseline for biomarkers that were measured again after just 28 days of treatment. **Biomarkers were measured by an outside lab, blind to treatment and timepoint.** We measured the core AD biomarkers as well as biomarkers of neurodegeneration, neuroinflammation and blood-brain barrier integrity. We saw significant improvements versus placebo.

RB, NF and LHB designed the clinical trial with guidance from JC. Biomarker analyses were conducted blind to treatment and time point by H-YW, ZP and K-CL. APOE genotyping was conducted by K-CL. CC

If Cassava is lying about blinded analysis now, were they lying about it the whole time?

“If unblinding is deliberate and/or not revealed, that greatly increases its seriousness, placing it in the research misconduct arena. FDA has a zero tolerance policy in this area.” – ex-FDA OSI member
Wang’s “Outside” lab has sensitive patient information including INITIALS

Alarmingly, Wang lab member Pei discusses labelling clinical sample vials with a patient’s initials.

Why would the Wang lab have access to this information?

Who provided them with this information?

Is the Wang/CUNY lab - as a third-party - authorised to hold patient-specific information?

We redacted per HIPAA Privacy Rule
Based on the obtained emails we conclude that:

There is risk to patient privacy and possible HIPAA violation

- It is entirely conceivable that an individual study participant can be identified simply via an online search
- No safeguards are in place to de-id patient samples or protect patient privacy
- Sensitive information has been shared with third-party, “outside”, “blinded” lab

There is a risk of biomarker data manipulation

- Lab personnel know subject ID and site PLUS dosing status (Day 1 vs 6 Month)
- Wang has clear COI as a Cassava SAB member, stockholder and lead Simufilam researcher
- Wang is under investigation for data manipulation

Previous assurances of data integrity are suspect

- Haphazard treatment of patient information observed in email makes “chain of custody” claim ridiculous
- Suspicious changes in the baseline of the cognitive scores become even more so

All relevant CUNY FOIA material can be found here
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