Cassava Sciences is a U.S. clinical-stage biotechnology company with a market cap of nearly $1.5 billion USD. The company focuses on detecting and treating neurodegenerative diseases, such as Alzheimer’s.

Because the company is in a pre-revenue status, usual financial valuations like the DCF model or NPV used to derive the value of the company aren’t applicable. This pitch will heavily focus on the clinical and chemical inefficiencies.

The thesis of this work is based on the fact that $SAVA has only one potential drug candidate (Simufilam) in its pipeline, making the success of the company largely (if not completely) dependent on the clinical results of this drug. Unlike the overall positive analyst consensus and recent stock price hike (due to a new CEO), I remain extremely bearish (meaning I believe the company will fail) on the future of $SAVA.

About Simufilam: Simufilam targets the misfolding of the protein filamin A (FLNA). By correcting this misfolding, it is supposed to interrupt the toxic signaling of amyloid beta (AB42), a protein responsible for neurodegeneration (though it can also be found in healthy bodies but is typically cleared away). This mechanism of action could potentially reduce the degeneration of nerve cells. Research on Simufilam has shown major flaws in the drug's ability to block the a7nAChR receptor against AB42 (Wang HY et al. 2012), potentially leading to desensitization of one of the most important receptors for neurological interaction.

Problems: Even at the chemical stage, Simufilam faces major issues. To pass the Blood-Brain Barrier, it needs a logP of a maximum of 3, while Simufilam already shows a logP of 4.55, indicating that the molecule is lipophilic. This suggests potential problems crossing the BBB and difficulties with solubility (the company has had 29 failed medications and 0 approvals).

$SAVA has published recent Phase 2b data (with only 60 patients, which is too small for an Alzheimer's study, according to past FDA approvals) on the clinical trial (NCT04079803). The study's primary purpose was "treatment." The outcome measures showed poor performance (with important p-values >0.05 compared to placebo) and revealed that 42% of the treatment cases experienced major adverse events. The drug led to only approximately 4% of patients showing improvement while 42% experienced adverse effects, meaning the side effects may result in a sooner "death" than the drug could potentially cure.

Regarding the CEO change, it is crucial to understand that for $SAVA, the chemical side has much greater importance in the long run. Additionally, the former scientific advisor Hoau-Yan Wang is facing 31 allegations of research misconduct.

Catalyst: YE2024, when $SAVA will present its Phase III “RETHINK-ALZ” 52-week data (NCT04994483).

Strategy:

1. ATM options expiring in January 2025.

2. Short positioning through a margin account while hedging with long calls.