Inflammasome Therapeutics to Enter Clinic with Treatment for Dry AMD

- *First-in-class clinical trial in dry AMD with new drug specifically designed to inhibit inflammasome activation in the eye and to be administered locally via a newly designed sustained release implant system.*
- *The investigator sponsored trial brings into the clinic a drug designed to halt the multiple processes that cause GA*

Newton, MA (November 13, 2023) – Inflammasome Therapeutics (https://inflam.com), a private company, developing a new class of inflammasome inhibitor drugs called Kamuvudines as therapies for prevalent, degenerative diseases, announced the FDA has granted approval for the opening of a Phase 1/2 clinical trial of the company's drug for the treatment of Geographic Atrophy (GA), the most severe form of dry AMD. This is the first clinical trial of an inflammasome inhibitor to treat GA. Paul Ashton, CEO of Inflammasome Therapeutics, said, "This is a very important milestone for the company, as it represents the initial clinical trial of several planned for our Kamuvudines in a number of other neuroinflammatory conditions, including Amyotrophic Lateral Sclerosis (ALS), Alzheimer's Disease (AD) and Multiple Sclerosis (MS).

In GA, the macula - the part of the retina responsible for central vision - slowly atrophies. The condition affects approximately one million people in the US and more than five million worldwide. The precise cause (or causes) of GA is unknown, but in the eyes of patients with GA (and brains and nervous systems of patients with ALS, AD, and MS) there are elevated levels of toxic substances such as complement, amyloid beta, retrotransposons, iron, and reactive oxygen species. This year, the first two treatments for GA were approved by the FDA (Syfovre and Izervay). These target different aspects of one of the toxic substances, complement. "While these drugs are much needed treatments in the arsenal for retinal specialists, they are not ideal. They only modestly slow the progression of the disease and increase the risk of developing wet AMD. Furthermore, the drugs need to be injected every 4-8 weeks," said Dr. Ashton. "While it's great that these complement inhibiting drugs are having an effect, we believe that targeting a single aspect of the disease may be suboptimal."

Dr Ashton continued: "Drug development for GA is similar to that for AD where researchers have been targeting one element of the disease. In AD, it's amyloid beta, and in 2023 a drug was approved in this area that modestly slows the progression of this disease. We are developing Kamuvudines for AD and other central nervous system (CNS) disorders as our drugs target multiple toxic pathways – complement, amyloid beta, iron overload, retrotransposons, etc. - via their common pathway to toxicity, inflammasome activation. We believe this approach will have a more profound effect." Dr. Ashton confirmed that the company is carrying out additional research on their Kamuvudines in the area of AD and intends to initiate clinical trials in this indication soon.

In the GA trial, patients will receive a tiny sustained release implant (*illustration is available)* that releases drug directly into the back of the eye for an initial period of three months after injection. The drug was specifically designed for retinal delivery, and the implants and injector system were crafted to deliver this particular drug. This combined drug and delivery strategy allows high, therapeutic doses to be maintained in the eye while the drug is undetectable in the systemic circulation.

The start of the trial represents the next step in a decade-long research effort led by Inflammasome Therapeutics' co-founder, Dr. Jayakrishna Ambati, initiated while he was at the University of Kentucky. In a series of publications in such journals as *Science* and *Nature*, he described the basic research on GA and pre-clinical development of Kamuvudines.:

https://www.science.org/doi/10.1126/science.1261754
https://www.nature.com/articles/nature09830
https://www.science.org/doi/10.1126/sciadv.abj3658
https://www.science.org/doi/10.1126/sciimmunol.abi4493

Dr. Ashton added that there is now a robust body of peer-reviewed science that demonstrates Kamuvudines and their precursors (nucleotide reverse transcriptase inhibitors) are powerful inhibitors of inflammasome activation and highly effective in pre-clinical models of GA. If replicated in human disease, the treatment would arrest the process that causes GA while most of the retina is still healthy. "It would be as close to a functional cure for GA as one could hope for in a condition where the only approved therapeutic treatments simply slow progression of the disease," said Dr. Ambati.

"The implications for treatments in other neuroinflammatory diseases like AD, ALS, and MS are extremely interesting," said Dr. Ashton "We have Kamuvudines that are specifically designed for neurological disease that penetrate into the brain and CNS from a simple oral tablet. We are looking forward to beginning clinical trials in some of these diseases as soon as possible."

Dr. Ashton will be discussing and showcasing the latest clinical updates from the company during the 4th Dry AMD Therapeutic Development Summit, being held in Boston November 14-16. Dr. Ashton's presentation is scheduled for 9 a.m. on Wednesday, November 15.

Inflammasome Therapeutics (https://www.inflam.com) was founded by Jayakrishna Ambati, M.D., and Paul Ashton, Ph.D., in 2016 to develop therapies for prevalent, degenerative diseases and to develop novel delivery technologies for the sustained release of therapeutic agents and compounds. The company combines scientific excellence with proven development expertise and works to develop products via a mixture of licensing agreements and internal development. Inflammasome has identified and licensed a series of molecules – Kamuvudines – that successfully inhibit inflammasome activation in cell cultures and animal models and is moving into the clinic for treatment of eye diseases and neurodegenerative diseases such as ALS, Alzheimer's disease, and MS.

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