Inflammasome Therapeutics Announces Topline 3-month Data from a Clinical Trial of its First-in-Class Dual Inflammasome Inhibitor, K8, in Geographic Atrophy, Demonstrating Rapid, Substantial and Significant Efficacy and Safety

- *In a U.S. clinical trial of 5 patients with bilateral GA, sustained-release intravitreous implants of K8 were well tolerated, with no drug-related ocular or systemic serious adverse events.*
- *In each of the 5 patients, eyes treated with the K8 implant displayed rapid and substantial reduction of GA lesion growth compared to their contralateral untreated eyes.*
- *The mean lesion growth in K8-treated eyes was 66% less than that of untreated contralateral eyes at 3 months after a single implant injection (p value=0.029), as assessed by an independent masked reading center.*
- *K8 is a first-in-class dual inflammasome inhibitor that targets multiple GA disease pathways via a novel mechanism of action.*
- *An expanded 30-patient trial is underway.*

Newton, MA (January 15, 2025) – Inflammasome Therapeutics (https://www.inflam.com/), a clinical-stage biotech company developing novel, first-in-class dual inflammasome inhibitors for prevalent ophthalmic and neurodegenerative diseases, today announced positive topline 3-month data from a clinical trial of its K8 implant in patients with geographic atrophy (GA), the most serious form of dry age-related macular degeneration (AMD). Positive efficacy and safety data were observed at 3 months after a single injection of K8 in this study conducted at the University of Kentucky (NCT06164587).

In the 5 patients with bilateral GA who received a K8 implant in one eye, there was a mean reduction in GA lesion growth of 66% at 3 months compared to the untreated contralateral eyes with GA (p = 0.029, mixed effects model), as measured by fundus autofluorescence (FAF) imaging by an independent masked reading center. Also, in all 5 patients, the GA lesions progressed at a much slower rate in the K8-treated eyes compared to the contralateral eyes. No drug-related intraocular or systemic safety issues were identified, and patients will receive a second K8 injection at month 3 of this 6-month trial. Given the extremely positive efficacy and safety data, the trial has now been expanded to 30 patients (60 eyes).

“We are excited to see such rapid and dramatic reduction of GA lesion growth within only 3 months following a single injection,” said **Jayakrishna Ambati, M.D.**, co-founder of Inflammasome Therapeutics. “Natural history studies have shown that in bilateral GA patients the lesion growth rates in the two eyes are almost identical, with less than 5% difference between eyes. Therefore, a 66% reduction in K8-treated eyes compared to contralateral eyes of the same patients provides strong evidence of efficacy. K8 has a

unique mechanism of action whereby it blocks the effects of complement activation as well as numerous other inflammatory pathways in GA, a multifactorial disease. The rapid, profound, and uniform clinical efficacy seen in all 5 patients in this trial is consistent with the extensive preclinical data showing this multipronged protective action of K8. Remarkably, lesion growth was reduced irrespective of the FAF pattern, whether the lesions were fast- or slow-growing, location or duration of disease, or type of AMD drusen, demonstrating the broad-based action of K8," continued Dr. Ambati.

"These initial clinical trial results are extremely encouraging, and we look forward to follow-up data from additional patients," said **Paul Ashton, Ph.D.,** CEO and co-founder of Inflammasome Therapeutics. "We are delighted that a single injection of K8 delivered via our unique drug-delivery technology achieved substantial and rapid efficacy that is much greater and faster than the approximate 20% reduction reported for the two FDA-approved drugs with monthly injections after 12 months. Furthermore, we believe that the statistical significance of the 66% reduction in lesion growth ($p=0.029$) compared to the untreated eyes seen with only 5 patients is indicative of the drug's robust effect. Thus, K8 may present an opportunity to break through the efficacy ceiling observed with the approved anti-complement drugs in GA," continued Dr. Ashton.

The next phase of this 6-month trial will further evaluate safety and efficacy of K8 injected every 3 months in up to 30 participants with GA. The primary endpoints are safety and the difference in GA lesion growth in treated eyes versus contralateral untreated eyes.

About Inflammasome Therapeutics and Kamuvudines

Inflammasome Therapeutics (https://www.inflam.com/) is a private, clinical-stage, biotech company developing novel, first-in-class, dual inflammasome inhibitors known as Kamuvudines for multiple ocular and neurological diseases. K8, delivered via a sustained-release intravitreous implant, is the Company's lead product for retinal diseases such as GA. K8 has a unique, differentiated mechanism of action that enables it to block multiple toxic pathways that drive GA.

GA affects approximately one million individuals in the US and more than eight million worldwide. In GA, multiple toxic substances including complement, retrotransposons, amyloid β, iron, and reactive oxygen species accumulate in the eye and trigger inflammasome activation as a final common pathway, which then causes cells in the macula to slowly die (atrophy). Over time, the area of atrophy grows in size and can lead to vision loss. The two currently FDA-approved drugs each target just a single toxic substance in the complement pathway but not the many other toxic substances seen in GA. They only modestly slow progression of GA, do not appear to slow down the rate of vision loss, and are associated with increased risk of developing wet AMD.

The global annual market for GA has been estimated by Precision Business Insights to exceed $30 billion, and there is tremendous interest in developing new GA therapies. There are 40 interventional clinical trials for GA registered in ClinicalTrials.gov, almost all of which target individual toxic substances. In contrast, K8 blocks inflammasome activation caused by multiple toxic substances that accumulate in GA. Inflammasome Therapeutics believes this differentiated mechanism of action targeting the final common pathway could lead to improved, best-in-disease efficacy.

Kamuvudines could also have application in a wide variety of neuro-inflammatory diseases such as ALS, Parkinson's disease, Alzheimer's disease, and Multiple Sclerosis. "Preclinical data show impressive efficacy of Kamuvudine K9 in multiple neurodegeneration models," said Dr, Ambati. Oral K9 is currently being tested in a clinical trial in subjects with Thyroid Eye Disease (NCT06467435). "We have Kamuvudines specifically designed for neurological diseases that penetrate into the brain and central nervous system from a simple oral tablet. Inflammasome Therapeutics expects to begin clinical trials in some neurodegenerative diseases soon as well," Dr. Ashton said.

Dr. Ambati has spent more than a decade developing Kamuvudines and identifying their role in the inhibition of inflammasome activity that is now recognized to be the critical driving force of many chronic diseases. In a series of publications in journals such as *Science* and *Nature*, his group has described the basic research on GA and preclinical 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

Please visit www.inflam.com to learn more.

Contact: Beverly Jedynak, Bevlyn Consulting, blj@bevlynconsulting.com, 312-943-1123; 773-350-5793 (cell)