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**Prolonged Intraocular Residence of a Fourth Generation Compstatin Complement C3 Inhibitor Supports Its Clinical Development for Geographic Atrophy**

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**Purpose:**

Complement component 3 (C3) has become a key therapeutic target for the geographic atrophy of age-related macular degeneration. A derivative of a 2nd generation compstatin C3 inhibitor (pegcetacoplan, Apellis Pharmaceuticals) is currently in phase III clinical trials for geographic atrophy. Our purpose was to determine the pharmacokinetics and tissue distribution after intravitreal injection of a 4th generation compstatin C3 inhibitor that is non-pegylated and has improved affinity and solubility.

**Methods:**

The C3 inhibitor AMY-106 (also known as Cp40-KKK, Amyndas Pharmaceuticals) was injected (500 micrograms) into the vitreous cavity of cynomolgus monkey eyes. For the pharmacokinetics study protocol, the vitreous concentration was determined over 3 months by periodic vitreous taps. For the tissue distribution protocol, monkeys were euthanized and eyes were harvested 1 month after intravitreal injection of AMY-106 (500 micrograms). Control eyes were from monkeys that did not receive an AMY-106 injection. Immunohistochemistry was then performed to determine the tissue location of C3 and AMY-106.

**Results:**

After a single intravitreal injection, AMY-106 was detected in the vitreous at C3-saturating concentrations for over 3 months. Using immunohistochemistry, both C3 and AMY-106 were detected within the retina with predominant co-localization to Bruch’s membrane and the choriocapillaris.

**Conclusions:**

After a single intravitreal injection, AMY-106 has a prolonged intraocular residence of more than 3 months at C3 inhibiting concentrations, supporting a potential injection frequency of once every 3 months. This therapeutic follows a target driven distribution and primarily localizes to Bruch’s membrane and the choriocapillaris. This data supports the clinical development of AMY-106 as a treatment for geographic atrophy.