## ARC1905 inhibits C5 - Dry/Wet AMD Intravitreal

ARC 1905 (Ophthotech Corp. Princeton, NJ) is a PEGylated, stabilized aptamer targeting complement factor C5.

ARC1905 inhibits activation of the downstream proinflammatory complement cascade (including generation of C5a and the membrane attack complex).

"Ophthotech's anti-C5 aptamer, ARC1905, is a potent and selective inhibitor of factor C5 of the complement cascade.

Inhibition of the complement cascade at the level of C5 prevents the formation of the key terminal fragments responsible for tissue pathology, C5a and the membrane attack complex (MAC: C5b-9).

The C5a fragment is pro-inflammatory, while the membrane attack complex initiates cell lysis and releases proangiogenic molecules (eg. PDGF and VEGF).

Histopathologic specimens of human dry AMD lesions strongly stain for C5 and MAC at the key sites of pathology.

ARC1905 spares the formation of upstream complement components such as C3b, which are important in host defense mechanisms.

By inhibiting C5-mediated inflammatory and MAC activities, therapeutic benefit may be achieved in both dry and wet AMD while sparing the immunoprotective functions of the complement system.

A phase I open-label, multicenter study of ARC1905, in combination with an anti-VEGF agent (Lucentis $^{\$}$ ), in patients with wet AMD is ongoing.

In addition, a study investigating ARC1905 in patients with dry AMD will be initiated in O2 2009."(56)

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