21. Apelin receptor antagonist

(CRUK)

Asset Overview

Product Type	Peptide
Diseases Area	Oncology
Indication	GBM or Apelin dependent tumor
Current Stage	Lead Optimization
Target	Apelin receptor
MoA	selective Apelin(GPCR) receptor antagonist
Brief Description	• Apelin is an endogenous peptide identified as a ligand of the G protein-coupled receptor APJ. Extensive tissue distribution of Apelin and its receptor suggests involvement in many physiological processes, and it has also been shown to participate in pathological processes such as heart failure and cancer. Apelin receptor is over-expressed in a number of cancers including glioblastoma (GBM), cervical, renal, lung and liver cancer. • We have developed a lead compound, MM315, which is a potent competitive antagonist of the Apelin receptor, demonstrating a binding affinity of 2.4 nM (pA2=9.55 for β-Arrestin, pA2=8.48 for cAMP). MM315 shows in vivo efficacy in GBM models, significantly extending survival in intracranial orthotopically implanted mice, and it has potential for synergy with temozolomide and radiation therapy.
Intellectual Property	filed
Publication	-
Inventors	-

Highlights

- Potent (β-Arrestin KB = 0.28nM) and selective Apelin receptor antagonist, water soluble, excellent PK (mouse)
- Structurally-enabled and extensively-elaborated, with well-understood SAR
- Demonstrated therapeutic potential in orthotopic models of glioblastoma
- Well tolerated in vivo (mouse)
- In vitro and in vivo data packages available
- Biochemical and cell-based assays fully developed
- Patents covering MM315 and a diverse series of linear analogs have been filed in CRUK's name and are at national/regional phase

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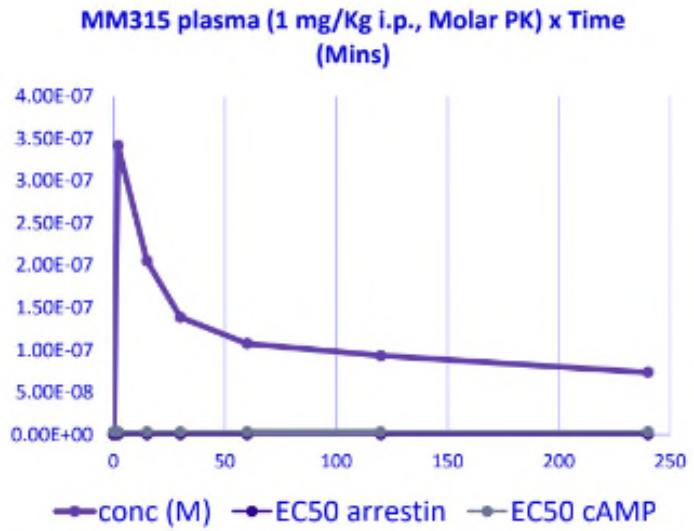
Key Data

MM315 ANTAGONIST OVERVIEW



APELIN EXPRESSION & MM315 IN-VIVO EFFICACY: GBM