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Two distinct late stage preclinical lead series of highly specific inhibitors of MAP4K4

A late-stage, pre-clinically validated inhibitor of MAP4K4 for a range of indications including anthracycline cardiotoxicity

Proposed use

Anthracycline chemotherapy leads to acute cardiotoxicity in up to 30% of patients. The MAP4K4 inhibitors can be commercialized to be used for protective agents against anthracycline therapy-induced cardiotoxicity.

Additionally, MAP4K4 is a pivotal mediator of a number of key pathways and a target in a range of clinical applications with significant unmet need. These targets include:

- Neurodegeneration
- Vascular disease
- Cancer (including glioblastoma)
- Anti-tumour and antiviral immunity
- Autoimmune disorders including diabetes

Technology overview

- Developed by Prof Schneider at Imperial
- Novel, potent, highly-selective, non-toxic inhibitors
- Protection against anthracycline therapy validated in human and rat cardiomyocytes.
- Good inhibitors of MAP4K4 with DMPK work undertaken
- Range of assays focused on developing highly-specific MAP4K4 inhibitor targeting ATP-binding pocket
- Multiple screen cascade/in vivo and in vitro validation of target and pre-lead candidates
- Encouraging safety profile with no adverse effect on cloned human channels
- Growing excitement in targeting MAP4K4 for other clinical applications

Benefits

- The compounds inhibit MAP4K4 in the low-mid nanomolar range
- Pre-clinically validated protection against anthracycline cardiotoxicity
- Demonstrated safety in murine and porcine models
- MAP4K4 an attractive target in other indications

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Intellectual property information

This technology is protected by a family of patents covering composition of matter and use of two distinct chemical series number WO2018035563A1 and number WO2019073253A1.

Link to published paper(s)

- https://www.nature.com/articles/s41598-020-68907-1
- https://www.sciencedirect.com/science/article/pii/S193459091930013X?via%3Dihub

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