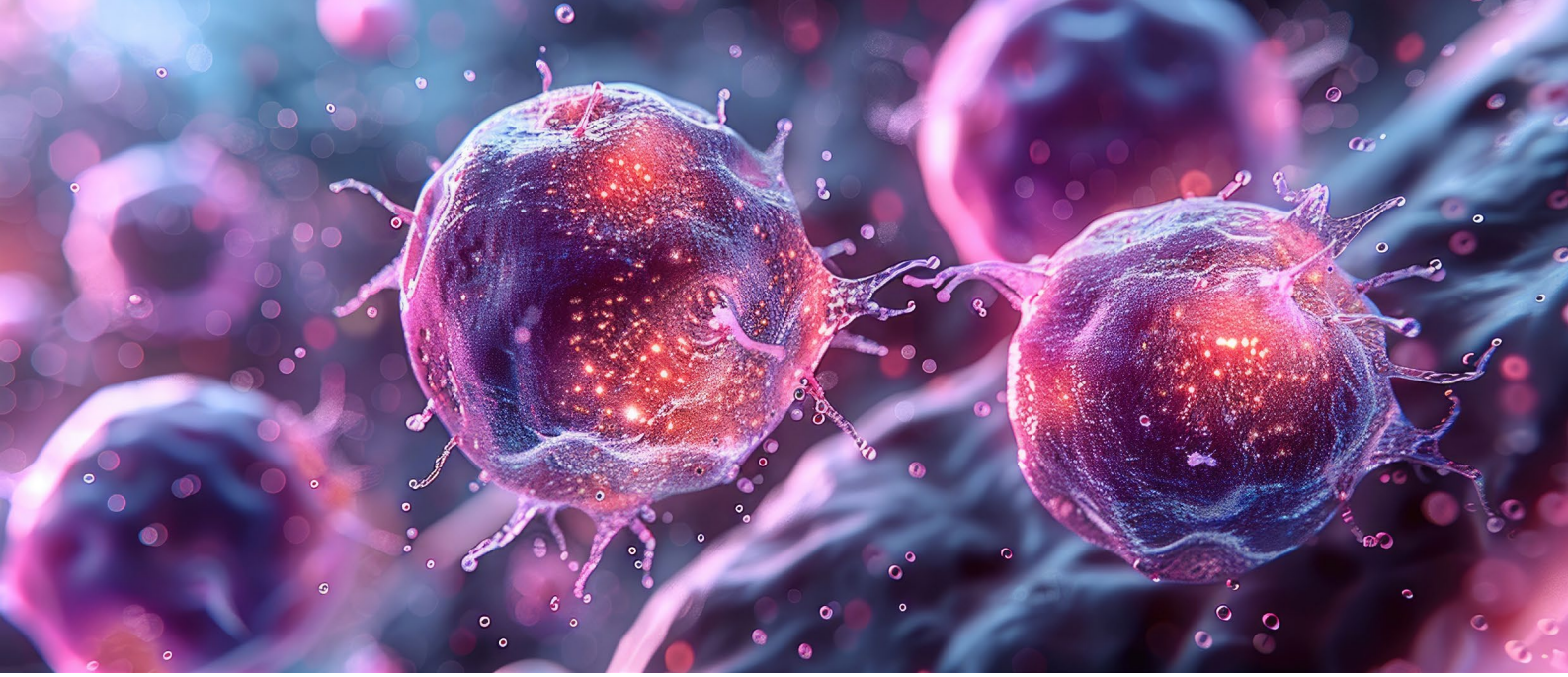


Please note: header image is purely illustrative. Source: Ummeya via Adobe Stock.

Superpotent, superselective mTOR inhibitors

Small molecule inhibitors of mTOR kinase featuring sub-nanomolar potency and a high level of selectivity over the rest of the kinome. The novel drug candidates display excellent PK properties and highly potent antiproliferative activity in a range of cell lines representing different cancer types.

APPLICATION	DEVELOPMENT STATUS	IP STATUS	COMMERCIAL OFFERING
Treatment of solid and blood cancers, metabolic disorders, fibrosis, ageing, neurodegenerative disorders and other immune-related diseases	Undergoing preclinical development in state-of-the-art cancer models	PCT/GB2025/052680 filed December 2025	Licence opportunity

THE UNIVERSITY of EDINBURGH

EDINBURGH INNOVATIONS

OPPORTUNITY

Mechanistic Target Of Rapamycin (mTOR), a Serine/Threonine kinase, is a master regulator of key oncogenic processes central to cancer, including cell migration (responsible for metastases), protein synthesis and cell proliferation. mTOR exerts its effects as a core unit of two multimeric protein complexes, mTORC1 and mTORC2, which are both highly implicated in haematological, solid cancers and many other therapeutic indications. In addition, the role of mTOR is well established in other pathologies such as ageing, fibrosis, neurodegenerative disorders and immune-related diseases, opening up opportunities for therapeutic intervention in these indications.

The patented set of drug candidates displays superb inhibition of mTOR kinase activity. Thus, unlike rapalogs which only inhibit the mTORC1 complex, the novel drugs disrupt both mTORC1 and mTORC2. These molecules are currently in pre-clinical development with efficacy obtained in cancer models. The University of Edinburgh is looking for a partner with the experience and capital to progress this IP towards IND-enabling studies and clinical trials.

TECHNOLOGY OVERVIEW

The novel inhibitors display **sub-nanomolar IC_{50} values** both in biochemical assays and in cell culture (**Fig 1**). Notably, at 1 µM, full kinome profiling (364 kinases) shows that the compounds inhibit 50 % of the enzymatic activity of less than 10 kinases (**Fig 2**). The lead compound, eALM1396 is >50-fold less potent against the second-most inhibited kinase (the PIKK family member DNA-PK) in the panel and features optimal PK properties in murine models, including excellent oral bioavailability (>70 %).

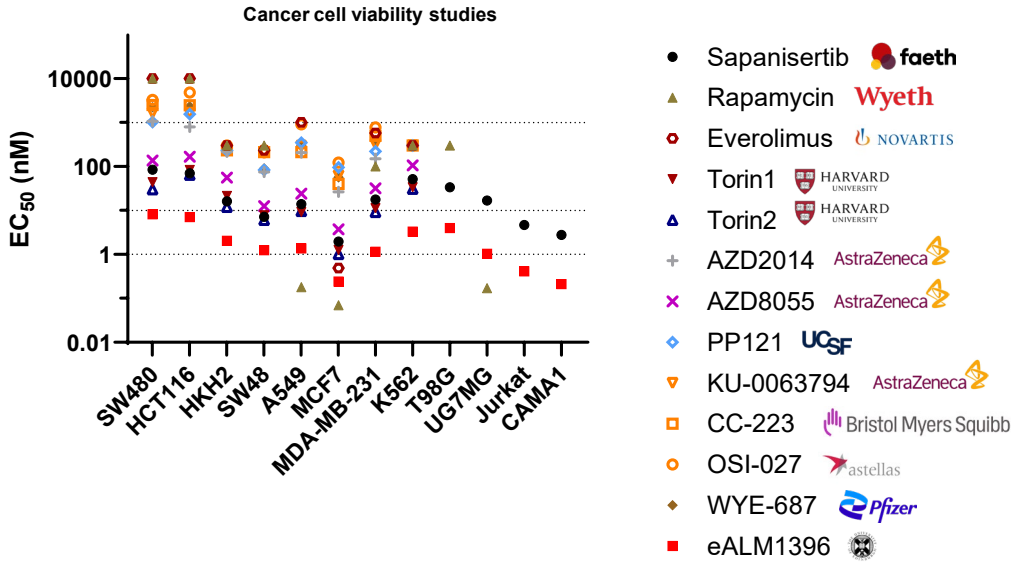


Fig 1, eALM1396 comparison with other mTOR inhibitors (Pre-clinical, Clinical and approved) against a panel of Cancer cell lines

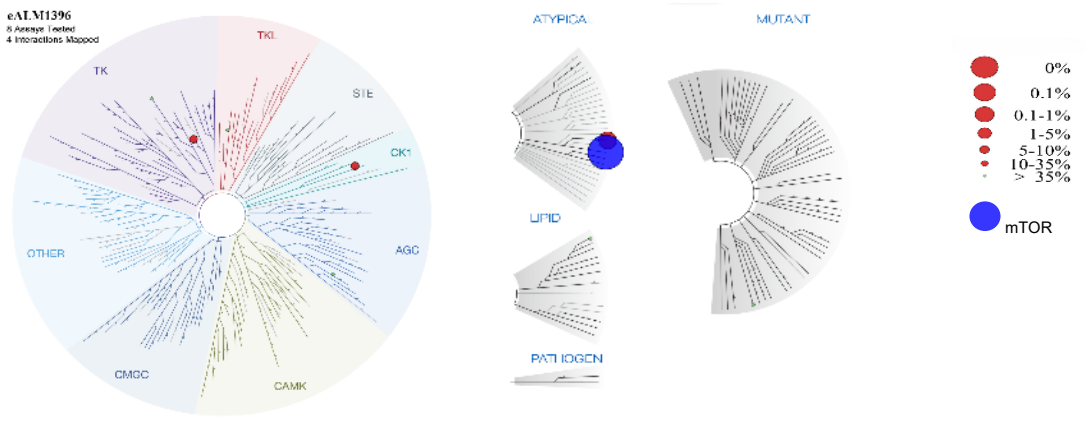
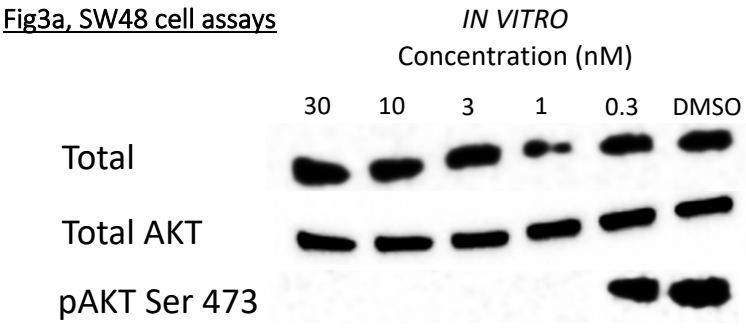


Fig 2, Kinome screening shows that eALM1396 displays high selectivity and affinity against mTOR kinase.

Once daily administration of eALM1396 (2.5, 5, and 10mg/kg) to mice bearing SW48 xenografts resulted in total inhibition of mTOR activity. pAKT Ser473 was used as readout for mTORC2 activity inhibition in these models (**Fig3b**). Similar results were obtained using the SW48 cell line in culture where the phosphorylation of AKT on Ser473 was fully inhibited at concentrations above 1nM (**Fig3a**).



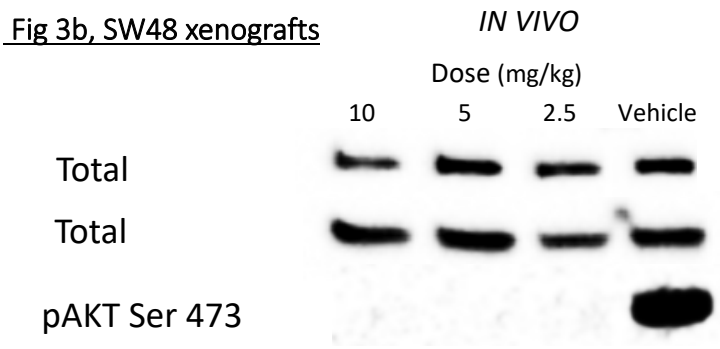


*Fig 3, Inhibition of the **mTORC2** pathway in vitro and in vivo.*

In vivo, eALM1396 induced a dose dependent reduction of tumour growth in an SW48 Xenograft model achieving >70% TGI at day 14 of treatment by once daily oral dosing (**Fig 4**). The results correlated with the reduced cell proliferation observed *in vitro* for this model

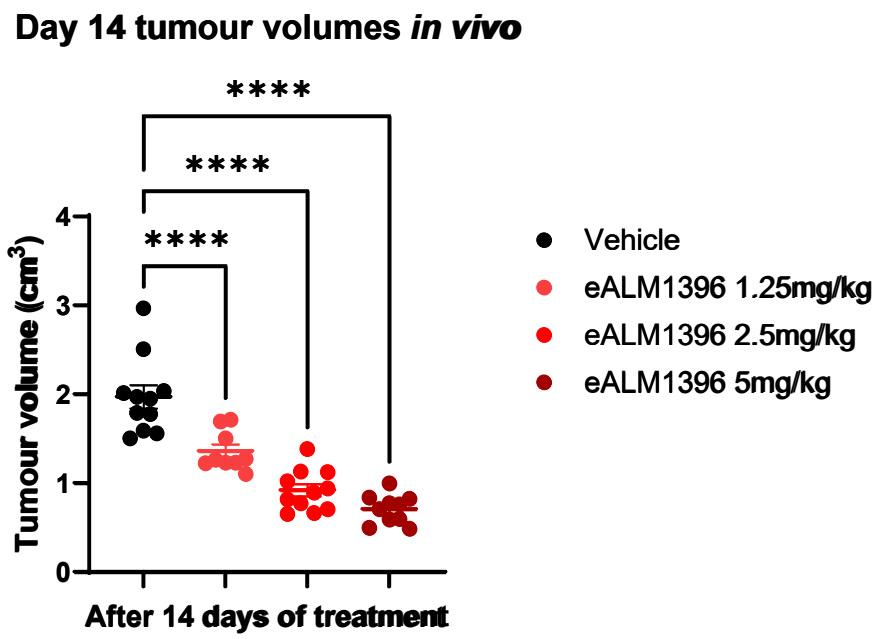


Fig 4, Tumour growth inhibition in SW48 xenograft mouse model, analysis of tumours at day 14 of treatment

BENEFITS

- Highly potent mTOR kinase inhibition
- Inhibition of both mTORC1 and mTORC2 complexes, circumventing the limitations of rapalogs
- Superselectivity over the rest of the kinome, offering potential superior tolerability for medical treatment than current less selective kinase inhibitors that inhibit mTOR
- Excellent *in vivo* PK properties

PUBLICATIONS

Over 20 analogues, which are more potent and selective than Sapanisertib, have been discovered and patented. Examples include the tool compound eALM1137, which was shown to strongly suppress Glioblastoma Multiform Cell growth recently published in J Med Chem.

Álvaro Lorente-Macias, Jonathon Mok, John C. Dawson, Ana Juan-Albuquerque, Neil O. Carragher, Margaret C. Frame, and Asier Unciti-Broceta. Discovery of a Highly Potent and Selective mTOR Inhibitor that Strongly Suppresses Glioblastoma Multiforme Cell Growth. *Journal of Medicinal Chemistry* 2026, 69, 8, 9680-9712

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