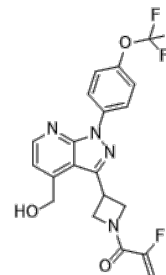


Product Name : GNE-2181
Cat. No. : PC-27127
CAS No. : 2933893-78-6
Molecular Formula : C₂₀H₁₆F₄N₄O₃
Molecular Weight : 436.37
Target : YAP-TEAD
Solubility : 10 mM in DMSO



CAS: 2933893-78-6

Biological Activity

GNE-2181 is a potent, selective, covalent, orally bioavailable and brain-penetrant pan-**TEAD** inhibitor, disrupts **YAP-TEAD** interaction with biochemical IC₅₀s of 2/4/8/6 nM for TEAD1/2/3/4 in TR-FRET assays.

GNE-2181 bind potently and covalently to the lipid pocket of TEAD proteins, form a covalent linkage with the lipid pocket cysteine (C380) of TEAD2 through the acrylamide warhead.

GNE-2181 exhibits strong activity against all four isoforms of TEAD.

GNE-2181 potently inhibits cell proliferation of Hippo-driven cell lines NCI-H226 and MSTO-211H with EC₅₀ of 3 nM and 7 nM, but not Hippo-independent VMRC-LCD cells with >2500-fold higher EC₅₀ values.

GNE-2181 shows superior efficacy in both NCI-H226 and MSTO-211H cells versus GNE-6915 and GNE-7883, downregulates YAP/TAZ-TEAD-dependent gene programs to exert anti-proliferative effects.

GNE-2181 enhances the efficacy of targeted cancer therapies, particularly when combined with inhibitors of RTKs and the RAS/MAPK pathway.

GNE-2181 (10 or 50 mg/kg) effectively inhibited brain tumor growth in brain metastasis with advanced stage lung cancer NCI-H226, with a concomitant reduction of the YAP/TAZ target score and proliferation marker (Ki67).

References

Hagenbeek TJ, et al. *Nat Commun.* 2026 Jun 27. doi: 10.1038/s41467-026-74722-5.

Caution: Product has not been fully validated for medical applications. Lab Use Only!

E-mail: tech@probechem.com