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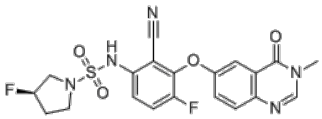
Data Sheet

Global Supplier of Chemical Probes, Inhibitors & Agonists.

Product Name	:	BRAF inhibitor Compound Ia
Cat. No.	:	PC-72243
CAS No.	:	2649372-20-1
Molecular Formula	:	$C_{20}H_{17}F_2N_5O_4S$
Molecular Weight	:	461.444
Target	:	Raf
Solubility	:	10 mM in DMSO



Biological Activity

BRAF inhibitor Compound Ia is a potent, selective, brain penetrant **BRAF** inhibitor with binding Kd of 0.6, 1.2, and 1.7 nM for BRAF WT, BRAF V600E, and c-RAF, presenting paradox breaker properties.
Compound Ia displays high selectivity profile conducted on 403 kinases with only one exception for the binding to the kinase BRK (Kd=156 nM).
Compound Ia demonstrated potent kinase inhibitory activity across all BRAF mutants with IC50 values of <1.77 nM, including the clinical relevant BRAF mutants V600E/K/A/D.
Compound Ia was designed to avoid paradoxical MAPK hyperactivation in non-BRAF V600E models, an undesired property of the three currently approved BRAFi.
Compound Ia exerted cytotoxic activity within a range of 5.2 to 30.2 nM in a collection of 94 cell lines representative of various histologic and genetic backgrounds.
Compound Ia drives prolonged MAPK inhibition, triggers superior antitumor activity in vivo in BRAF V600E models compared with dabrafenib and encorafenib.
Compound Ia is active in RAF dimer-mediated resistant tumors driven by the NRAS Q61K mutation, Compound Ia is highly brain penetrant and triggers potent antitumor activity in brain metastatic models of melanoma.

References

Wichmann J, et al. ***Clin Cancer Res.*** 2022 Feb 15;28(4):770-780.

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

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