Small Molecules

AZ628

MEK/ERK pathway inhibitor; Inhibits B-RAF, B-RAFV600E, and C-RAF-1

Catalog #	72982	1 mg
	72984	10 mg

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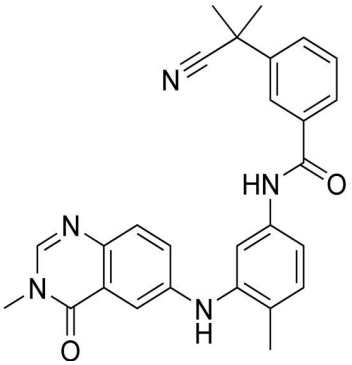
Product Description

AZ628 is a quinazolinone that inhibits several rapidly accelerated fibrosarcoma (RAF) kinases, including B-RAF, B-RAF V600E, and C-RAF-1 (in vitro kinase assay IC_{50} values of 105, 34, and 29 nM respectively; Khazak et al.). It strongly promotes B-RAF dimerization as a tight-binding inhibitor with a very slow off rate (Hatzivassiliou et al.; Lavoie et al.). From specificity profiling it is known to prevent activation of several other tyrosine kinases, including vascular endothelial growth factor receptor 2 (VEGFR2), discoidin domain receptor 2 (DDR2), Lck/Yes Novel (LYN), feline McDonough sarcoma (FMS), and FMS-like tyrosine kinase 1 (FLT1) (Khazak et al.).

Molecular Name:	AZ628
Alternative Names:	Not applicable
CAS Number:	878739-06-1
Chemical Formula:	$C_{27}H_{25}N_5O_2$
Molecular Weight:	451.5 g/mol
Purity:	≥ 98%
Chemical Name:	3-(2-cyanopropan-2-yl)-N-[4-methyl-3-[(3-methyl-4-oxoquinazolin-6-yl)amino]phenyl]benzamide
Structure:	

Properties

Physical Appearance:	A crystalline solid
Storage:	Product stable at -20°C as supplied. Protect from prolonged exposure to light. Stable as supplied for 12 months from date of receipt.
Solubility:	· DMSO ≤ 65 mM · Absolute ethanol ≤ 0.5 mM For example, to prepare a 10 mM stock solution in DMSO, resuspend 1 mg in 221 µL of DMSO. Prepare stock solution fresh before use. Information regarding stability of small molecules in solution has rarely been reported, however, as a general guide we recommend storage in DMSO at -20°C. Aliquot into working volumes to avoid repeated freeze-thaw cycles. The effect of storage of stock solution on compound performance should be tested for each application. Compound has low solubility in aqueous media. For use as a cell culture supplement, stock solution should be diluted into culture medium immediately before use. Avoid final DMSO concentration above 0.1% due to potential cell toxicity.

Published Applications

CANCER RESEARCH
· Inhibits tumor growth, induces cell cycle arrest, and causes apoptosis in a variety of cancer cell lines, especially in lines with the B-RAF V600E mutation (McDermott et al.; Khazak et al.).

References

Hatzivassiliou G et al. (2010) RAF inhibitors prime wild-type RAF to activate the MAPK pathway and enhance growth. Nature 464(7287): 431–5.
Khazak V et al. (2007) Selective Raf inhibition in cancer therapy. Expert Opin Ther Targets 11(12): 1587–609.
Lavoie H et al. (2013) Inhibitors that stabilize a closed RAF kinase domain conformation induce dimerization. Nat Chem Biol 9(7): 428–36.
McDermott U et al. (2007) Identification of genotype-correlated sensitivity to selective kinase inhibitors by using high-throughput tumor cell line profiling. Proc Natl Acad Sci USA 104(50): 19936–41.

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This product is hazardous. Please refer to the Safety Data Sheet (SDS).