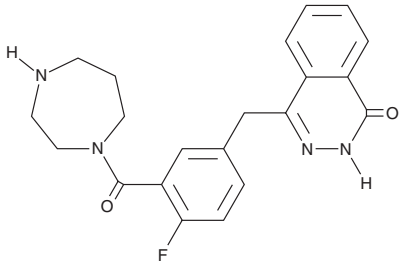
PRODUCT INFORMATION

KU-0058948

Item No. 42098

CAS Registry No.:	763111-49-5
Formal Name:	4-[[4-fluoro-3-[(hexahydro-1H-1,4-diazepin-1-yl)carbonyl]phenyl]methyl]-1(2H)-phthalazinone
MF:	$C_{21}H_{21}FN_4O_2$
FW:	380.4
Purity:	≥95%
Supplied as:	A solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

KU-0058948 is supplied as a solid. A stock solution may be made by dissolving the KU-0058948 in the solvent of choice, which should be purged with an inert gas. KU-0058948 is sparingly soluble (1-10 mg/ml) in DMSO and slightly soluble (0.1-1 mg/ml) in acetonitrile.

Description

KU-0058948 is an inhibitor of poly(ADP-ribose) polymerase 1 (PARP1) and PARP2 (IC_{50}s = 3.4 and 1.5 nM, respectively).[1] It is selective for PARP1 over PARP3, PARP4, and tankyrase (IC_{50}s = 40, 1,200, and >10,000 nM, respectively). It also selectively inhibits the survival of mouse embryonic stem cells lacking Brca1 or Brca2 over mouse embryonic stem cells expressing wild-type Brca1 or Brca2. KU-0058948 (1 µM) induces apoptosis in P39 and MUTZ-3 acute myeloid leukemia (AML) cells.[2] It decreases the survival of P39 and MUTZ-3 cells but not a variety of other AML and non-AML cells, including ME-1, U937, HL-60, and K562 cells. KU-0058948 (5 nM) potentiates cytotoxicity induced by MS-275 (Item No. 13284) in patient-derived AML cells. It reduces survival of HCT116 cells deficient in phosphatase and tensin homolog (PTEN) but not those expressing wild-type PTEN or containing a PTEN construct ($HCT116^{+/neo}$).[3]

References

1. Farmer, H., McCabe, N., Lord, C.J., *et al.* Targeting the DNA repair defect in *BRCA* mutant cells as a therapeutic strategy. *Nature* **434(7035)**, 917-921 (2005).
2. Gaymes, T.J., Shall, S., Macpherson, L.J., *et al.* Inhibitors of poly ADP-ribose polymerase (PARP) induce apoptosis of myeloid leukemic cells: Potential for therapy of myeloid leukemia and myelodysplastic syndromes. *Haematologica* **94(5)**, 638-646 (2009).
3. Mendes-Pereira, A.M., Martin, S.A., Brough, R., *et al.* Synthetic lethal targeting of *PTEN* mutant cells with PARP inhibitors. *EMBO Mol. Med.* **1(6-7)**, 315-322 (2009).

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