

Catalog # 10-1560 ML323

CAS# 1571424-83-5

N-(4-(1H-1,2,3-Triazol-1-yl(benzyl)-5-methyl-2-(2-isopropylphenyl)pyrimidin-4-amine CID 60167849; NCGC00262306 Lot # X106413

Potent and reversible USP1-UAF1 deubiquitinase complex inhibitor with excellent selectivity against human DUBs, deSUMOylase, deneddylase and unrelated proteases, IC $_{50}$ =76 nm in a ubiquitin-rhodamine 110 assay. In H1299 non-small cell lung cancer cells treatment with ML323 dose dependently and robustly increased levels of monoubiquitinated PCNA compared to untreated cells at concentrations as low as 1 μ M. It potentiates cisplatin cytotoxicity in non-small cell lung cancer and osteosarcoma cells. ML323 inhibition of upregulated USP1 in BRCA1-deficient tumor cells results in replication fork destabilization and decreased viability.

- 1) Dexheimer et al. (2014), Synthesis and structure-activity relationship studies of N-benzyl-2-phenylpyrimidin-4-amine derivatives as potent USP1/UAF1 deubiquitinase inhibitors with anticancer activity against nonsmall cell lung cancer, J. Med. Chem., **57** 8099
- 2) Liang et al. (2014), A selective USP1-UAF1 inhibitor links deubiquitination to DNA damage responses; Nat. Chem. Biol., **10** 298
- 3) Lim et al. (2018) USP1 is required for replication fork protection in BRCA1-deficient tumors; Mol. Cell 72 925

PHYSICAL DATA

 $\begin{array}{lll} \mbox{Molecular Weight:} & 384.48 \\ \mbox{Molecular Formula:} & C_{23}H_{24}N_6 \\ \mbox{Purity:} & 98\% \ \mbox{by TLC} \end{array}$

NMR: (Conforms)

Solubility: Soluble in DMSO (up to 40 mg/ml) or in Ethanol (up to 20 mg/ml)

Physical Description: White solid

Storage and Stability: Store as supplied desiccated at -20°C for up to 1 year from the date of purchase.

Solutions in DMSO or ethanol may be stored at -20°C for up to 3 months.

Materials provided by Focus Biomolecules are for laboratory research use only and are not intended for human or veterinary applications.