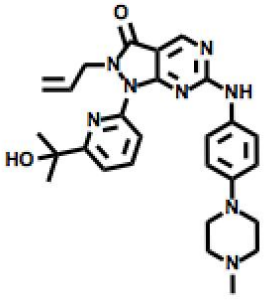
Xcess Biosciences Inc.
7144 N Harlem Ave #169
Chicago, IL 60631 USA

http://www.xcessbio.com
Toll free: 1-866-706-2330
Fax: 1-619- 810-0718
Email: info@xcessbio.com

WEE1 Inhibitor – MK-1775 (AZD1775)

Chemical Name: 2-allyl-1-(6-(2-hydroxypropan-2-yl)pyridin-2-yl)-6-((4-(4-methylpiperazin-1-yl)phenyl)amino)-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one



Molecular Weight:	500.61
Formula:	$C_{27}H_{32}N_8O_2$
Purity:	≥98%
CAS#:	955365-80-7
Solubility:	DMSO up to 100 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

MK-1775 (AZD1775) is a highly potent, selective and orally bioavailable Wee1 kinase inhibitor with IC_{50} of 5.2 nM. It abrogated DNA damaged checkpoints induced by gemcitabine, carboplatin, and cisplatin etc. and enhanced the anti-tumor efficacy of these agents selectively in p53-deficient tumor cells. At tolerated doses, MK-1775 treatment leads to xenograft tumor growth inhibition or regression. It inhibits Wee1 in H3K36me3-deficient cells results in RRM2 reduction, critical dNTP depletion, S-phase arrest, and apoptosis. MK-1775 can regresse H3K36me3-deficient tumor xenografts too. Right now MK-1775 is in phase I/II clinical trials for various cancers.

How to Use:

In vitro: MK-1775 was used at 1 μM in vitro and cellular assays.

In vivo: MK-1775 was orally dosed to mice at 20 mg/Kg once per day.

Reference:

1. Hirai H, et al. Small-molecule inhibition of Wee1 kinase by MK-1775 selectively sensitizes p53-deficient tumor cells to DNA-damaging agents. (2009) Mol Cancer Ther. 8(11):2992-3000.
2. Rajeshkumar NV, et al. MK-1775, a potent Wee1 inhibitor, synergizes with gemcitabine to achieve tumor regressions, selectively in p53-deficient pancreatic cancer xenografts. (2011) Clin Cancer Res. 17(9):2799-806.
3. Guertin AD, et al. Preclinical evaluation of the WEE1 inhibitor MK-1775 as single-agent anticancer therapy. (2013) Mol Cancer Ther. 12(8):1442-52.
4. Pfister SX, et al. Inhibiting WEE1 Selectively Kills Histone H3K36me3-Deficient Cancers by dNTP Starvation. (2015) Cancer Cell. 28(5):557-68.