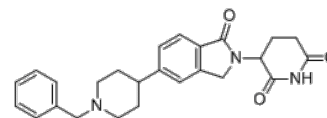


Product Name : NVP-DKY709
Cat. No. : PC-20145
CAS No. : 2291360-73-9
Molecular Formula : C₂₅H₂₇N₃O₃
Molecular Weight : 417.51
Target : PROTAC
Solubility : 10 mM in DMSO



Biological Activity

NVP-DKY709 (DKY709) is a first-in-class, selective CRBN glue degrader of **IKZF2** with DC50 of 4 nM in cellular assays, completely spares degradation of IKZF1/3.

NVP-DKY709 (DKY709) recruited IKZF1 to CRBN (Amax 550%, 400% recruitment at 0.28 μM) but had no effect on IKZF1 degradation in the cellular assay up to 50 μM.

NVP-DKY709 (DKY709) dose-dependently and selectively degrades IKZF2 (Dmax 69%, DC50 11 nM) with no effect on IKZF1 up to 10 μM, in the Jurkat human T cell cancer cell line, which expresses both IKZF2 and IKZF1.

DKY709 also degrades IKZF4 (DC50 13 nM, Dmax 21%), whose zinc finger 2 β-hairpin sequence is identical to that of IKZF2.

DKY709 degrades the SALL4 zinc finger transcription factor (Dmax 55%, DC50 2 nM [ProLabel], Dmax 88%, DC50 13 nM [HiBit]), which has been linked to IMiD-induced teratogenicity.

DKY709 does not degrade translation termination factor GSPT1 up to 50 μM.

DKY709 shows high affinity of for CRBN with Kd of 18 nM.

DKY709 dose-dependently increases the IL-2 concentration in Jurkat T cells stimulated with phytohemagglutinin (PHA).

DKY709 dose-dependently degrades IKZF2, but not IKZF1, in human primary CD25-enriched T cells with DC50 of 11 nM, Dmax 89%.

DKY709 reduces the suppressive activity of human Treg cells and rescues cytokine production in exhausted T-effector cells.

NVP-DKY709 (100 mg/kg once daily) reduced tumor growth in MDA-MB-231 (breast cancer) xenografts comparable with treatment with the anti-PD1 antibody PDR001 as a single agent, with robust IKZF2 degradation in both tumor and peripheral blood Treg cells.

References

Bonazzi S, et al. *Cell Chem Biol.* 2023 Feb 25:S2451-9456(23)00054-5.

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

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