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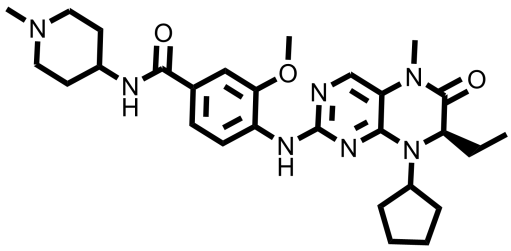
PLK1 and BRD4 Dual Inhibitor – BI-2536

Chemical Name: (R)-4-((8-cyclopentyl-7-ethyl-5-methyl-6-oxo-5,6,7,8-tetrahydropteridin-2-yl)amino)-3-methoxy-N-(1-methylpiperidin-4-yl)benzamide



Molecular Weight:	521.65
Formula:	$C_{28}H_{39}N_7O_3$
Purity:	≥98%
CAS#:	755038-02-9
Solubility:	DMSO up to 40 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

BI-2536 is a potent inhibitor of PLK1 (Polo-like kinase 1, IC_{50} ~0.83 nM) and BRD4 (IC_{50} ~37 nM). It also inhibits PLK2 and PLK3 with IC_{50} of 3.5 nM and 9.0 nM, respectively. BI-2536 treatment ranging from 10 nM to 100 nM leads to the blocking of the recruitment of γ-tubulin and phosphorylation of Apc6 at mitotic centrosomes, inhibition of cohesin release from chromosome arms, induction of monopolar spindles, and other Plk1 dependent processes. BI-2536 inhibits the growth of a panel of 32 human cancer cell lines with EC_{50} of 2-25 nM. It also displaces BRD4 from chromatin and suppresses c-Myc expression. The combination of inhibitory activities on independent kinase and bromodomain oncogenic pathways exemplifies a new strategy for rational single-agent polypharmacological targeting.

How to Use:

In vitro: BI-2536 was used at 0.1-1 μM in vitro.

In vivo: BI-2536 was dosed to mice by IV injection at 50 mg/kg once or twice a week in xenograft models. (Formulated in hydrochloric acid (0.1 N), and diluted with 0.9% NaCl)

Reference:

1. Steegmaier M, et al. BI 2536, a potent and selective inhibitor of polo-like kinase 1, inhibits tumor growth in vivo. (2007) Curr Biol. 17(4):316-22.
2. Nappi TC, et al. Identification of Polo-like kinase 1 as a potential therapeutic target in anaplastic thyroid carcinoma. (2009) Cancer Res. 69(5):1916-23.
3. Ciceri P, et al. Dual kinase-bromodomain inhibitors for rationally designed polypharmacology. (2014) Nat Chem Biol. In press.