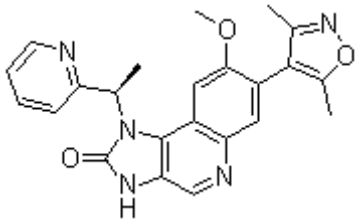
Product Introduction

I-BET151 (GSK1210151A)

I-BET151 (GSK1210151A) is a novel selective BET inhibitor for **BRD2**, **BRD3** and **BRD4** with **IC50** of 0.5 μM, 0.25 μM, and 0.79 μM, respectively.

Technical Data:

Molecular Weight (MW):	415.44	
Formula:	$C_{23}H_{21}N_5O_3$	
Solubility (25℃) * <1 mg/ml means slightly soluble or insoluble:	DMSO 83 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃ Powder	
	6 months-80℃ in DMSO	
CAS No.:	1300031-49-5	

Biological Activity

I-BET151 exhibits potent selectivity over an extensive range of diverse protein types such as COX-2, P450, Aurora B, GSK3β, PI3K-γ, GPCR, ion channels, and transporters. Similar to I-BET762 (GSK525762A), I-BET151 displays potent binding affinity to BRD2, BRD3 and BRD4 with K_D of 0.02-0.1 μM, and significantly inhibits lipopolysaccharide-stimulated IL-6 cytokine production in human peripheral blood mononuclear cells (PBMC) and whole blood (WB) as well as rat WB with IC50 of 0.16 μM, 1.26 μM, and 1.26 μM, respectively. I-BET151 (0.5 or 5 μM) inhibits the binding of BETs (BRD2, BRD3, BRD4, and

BRD9) but not the binding of 23 other bromodomain proteins in HL60 nuclear extract to acetylated histone peptides. I-BET151 has potent efficacy against cell lines harboring different MLL-fusions such as MV4;11, RS4;11, MOLM13, and NOMO1 cells with IC50 of 15-192 nM. Consistently, I-BET151 completely ablates the colony-forming potential of MLL-fusion-driven leukaemias (MOLM13) but not leukaemias driven by tyrosine kinase activation (K562). I-BET151 also displays potent efficacy in both liquid culture and clonogenic assays using primary murine progenitors transformed with either MLL-ENL or MLL-AF9. I-BET151 treatment significantly induces apoptosis and prominent G0/G1 arrest in MLL-fusion cell lines driven by distinct MLL fusions (MOLM13 and MV4;11 containing MLL-AF9 and MLL-AF4, respectively) but not the K562 cells, probably due to the inhibition of transcription of BCL2, C-MYC and CDK6 by blocking the recruitment of BRD3/4, PAFc and SEC components into transcriptional start site (TSS). [1]

Administration of I-BET151 at 30 mg/kg/day significantly inhibits tumor growth of murine MLL-AF9 and human MLL-AF4 leukaemia in mice, and provides marked survival benefit. [1]

Optimized to retain excellent BET target potency and selectivity while enhancing the in vivo pharmacokinetics and terminal half-life to enable prolonged in vivo studies.

References

[1] Dawson MA, et al. Nature, 2011, 478(7370), 529-533.