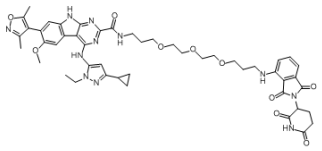
BETd-246

Cat. No.:	HY-115568
CAS No.:	2140289-17-2
Molecular Formula:	$C_{48}H_{55}N_{11}O_{10}$
Molecular Weight:	946.02
Target:	Epigenetic Reader Domain
Pathway:	Epigenetics
Storage:	Please store the product under the recommended conditions in the COA.



BIOLOGICAL ACTIVITY

Description	BETd-246 is a second-generation **BET bromodomain (BRD)** inhibitor, exhibiting superior selectivity, potency and antitumor activity[1].
IC_{50} & Target	BET BRD[1].

In Vitro

BETd-246 treatment (0-100 nM, 1-3 h) causes a dose-dependent depletion of BRD2, BRD3 and BRD4 in representative TNBC cell lines with 30-100 nM for 1 h or with 10-30 nM for 3 h incubation.
BETd-246 (100 nM, 24/48 hours) displays strong growth inhibition and apoptosis induction activity in MDA-MB-468 cell lines. BETd-246 induces a rapid and time-dependent downregulation of MCL1 protein in all the TNBC cell lines evaluated. BETd-246 induces much stronger apoptosis than BETi-211.
BETd-246 (100 nM, 24 hours) induces pronounced cell cycle arrest and apoptosis in TNBC cell lines[1].

Cell Proliferation Assay[1]

Cell Line:	MDA-MB-468 cells
Concentration:	100 nM
Incubation Time:	24 or 48 hours
Result:	Displayed strong growth inhibition and apoptosis induction activity in TNBC cell lines.

Cell Cycle Analysis[1]

Cell Line:	Human TNBC cells
Concentration:	100 nM
Incubation Time:	24 hours
Result:	Induced pronounced cell cycle arrest and apoptosis in TNBC cell lines.

Western Blot Analysis[1]

Cell Line:	Human TNBC cells

Concentration:	0-100 nM
Incubation Time:	1-3 hours
Result:	Caused a dose-dependent depletion of BRD2, BRD3 and BRD4.

In Vivo

BETd-246 (5 mg/kg, IV, 3 times per week for 3 weeks) treatment effectively inhibits WHIM24 tumor growth, similar to the antitumor activity of BETi-211 with higher dosage and more frequently administration. The treatment of 10 mg/kg induces partial tumor regression during treatment without apparent toxicity. BETd-246 has very limited drug exposure in the xenograft tumor tissue in MDA-M-231and MDA-MB-468 models[1].

Animal Model:	"Washington Human in Mouse (WHIM)" (PDX) model developed from a patient with treatment-resistant breast cancer (ESR^{E380Q}, PR- and HER2-))[1].
Dosage:	5, 10 mg/kg
Administration:	IV, 3 times per week for 3 weeks.
Result:	Effectively inhibited WHIM24 tumor growth.

REFERENCES

[1]. Bai L, et al. Targeted Degradation of BET Proteins in Triple-Negative Breast Cancer. Cancer Res. 2017 May 1;77(9):2476-2487.

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