产品名称：OTX-015
产品别名：Birabresib

生物活性：

Description	Birabresib (OTX-015) is a potent bromodomain (BRD2/3/4) inhibitor with IC_{50}s ranging from 92 to 112 nM.
IC_{50} & Target	IC50: 92-112 nM (BRD2, BRD3, BRD4)[1]
In Vitro	Birabresib (OTX-015) (500 nM) exposure induces a strong decrease of BRD2, BRD4 and c-MYC and increase of HEXIM1 proteins, while BRD3 expression is unchanged. c-MYC, BRD2, BRD3, BRD4 and HEXIM1 mRNA levels do correlate however with viability following exposure to Birabresib (OTX-015)[2]. Birabresib (OTX-015) (0.1, 1, 5 μM) treatment induces HIV-1 full-length transcripts and viral outgrowth in resting CD4+ T cells from infected individuals receiving suppressive antiretroviral therapy (ART), while exerting minimal toxicity and effects on T cell activation. Birabresib-mediated activation of HIV-1 involves an increase in CDK9 occupancy and RNAP II C-terminal domain (CTD) phosphorylation[3].
In Vivo	In MDA-MB-231 murine xenografts, tumor mass is significantly ($p < 0.05$) reduced by Birabresib (OTX-015) (50 mg/kg) with respect to vehicle-treated animals. Birabresib (OTX-015) in combination with 2 mg/kg RAD001 shows more effective activity than Birabresib alone[4].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 49 mg/mL (99.60 mM)** **H2O : < 0.1 mg/mL (insoluble)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0326 mL	10.1628 mL	20.3256 mL
	5 mM	0.4065 mL	2.0326 mL	4.0651 mL
	10 mM	0.2033 mL	1.0163 mL	2.0326 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (5.08 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.08 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)

Solubility: 2.5 mg/mL (5.08 mM); Suspended solution; Need ultrasonic

	此方案可获得 2.5 mg/mL (5.08 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.08 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.08 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. J. Kay Noel, et al. Abstract C244: Development of the BET bromodomain inhibitor OTX015. Mol Cancer Ther November 2013 12; C244. [2]. Marie-Magdelaine Coudé, et al. BET inhibitor OTX015 targets BRD2 and BRD4 and decreases c-MYC in acute leukemia cells. Oncotarget. 2015 Jul 10; 6(19): 17698–17712. [3]. Lu P, et al. The BET inhibitor OTX015 reactivates latent HIV-1 through P-TEFb. Sci Rep. 2016 Apr 12;6:24100 [4]. Vázquez R, et al. The bromodomain inhibitor OTX015 (MK-8628) exerts anti-tumor activity in triple-negative breast cancer models as single agent and in combination with RAD001. Oncotarget. 2017 Jan 31;8(5):7598-7613.

实验参考：

Cell Assay	For the MTT assay, cells are seeded in 24-well plates at 1×10^6 per well and treated with Birabresib (OTX-015) (0.01 nM-10 μM) for 72 h. Cells are transferred to 96-well plates and incubated with 0.5 mg/mL 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) in the dark at 37°C for 4 h. Cells are then lysed with 25% sodium dodecyl sulfate (SDS) lysis buffer and absorbance is read at 570 nm using a Microplate Reader. Three independent experiments are run for each cell line and untreated cells are used as negative controls.［2］
Animal Administration	Mice are subcutaneously injected in the right flank with 10×10^6 MDA-MB-231 cells. When average tumor weight is appr 130 mg, mice are randomized (nine animals/group) to one of the following experimental groups: vehicle (for Birabresib (OTX-015), water, twice daily, oral; for RAD001 vehicle, 5% Tween-80/5% polyethylene glycol 400, thrice weekly, intraperitoneal); 50 mg/kg Birabresib (OTX-015), twice daily, oral; 2 mg/kg RAD001, thrice weekly, intraperitoneal; 50 mg/kg Birabresib (OTX-015) + 2 mg/kg RAD001, according to the single agent dosing schedules.［4］
References	[1]. J. Kay Noel, et al. Abstract C244: Development of the BET bromodomain inhibitor OTX015. Mol Cancer Ther November 2013 12; C244. [2]. Marie-Magdelaine Coudé, et al. BET inhibitor OTX015 targets BRD2 and BRD4 and decreases c-MYC in acute leukemia cells. Oncotarget. 2015 Jul 10; 6(19): 17698–17712. [3]. Lu P, et al. The BET inhibitor OTX015 reactivates latent HIV-1 through P-TEFb. Sci Rep. 2016 Apr 12;6:24100 [4]. Vázquez R, et al. The bromodomain inhibitor OTX015 (MK-8628) exerts anti-tumor activity in triple-negative breast cancer models as single agent and in combination with RAD001. Oncotarget. 2017 Jan 31;8(5):7598-7613.