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产品名称：CALICHEAMICIN GAMMA(1)I
产品别名：卡奇霉素；Calicheamicin

生物活性：

Description	Calicheamicin, an antitumor antibiotic, is a cytotoxic agent that causes double-strand DNA breaks. Calicheamicin is a DNA synthesis inhibitor.
IC_{50} & Target	Calicheamicins
In Vitro	PF-06647263 (anti-EFNA4-ADC) is generated via conjugation of hE22 lysine residues to the AcButDMH-N-Ac-calicheamicin-γ1 linker-payload with an average drug-to-antibody ratio (DAR) of 4.6. PF-06647263 elicits antigen- and concentration-dependent cytotoxicity, as exposure to PF-06647263 for 96 hours results in cell death (EC50= appr 1 ng/mL)[1]. CMC-544, consisting of a humanized CD22 Ab linked to calicheamicin, is effective in pediatric primary B-cell precursor acute lymphoblastic leukemia (BCP-ALL) cells in vitro. CMC-544 induces cell death in various ALL cell lines in a dose- and time-dependent way, with IC50 values ranging from 0.15 to 4.9 ng/mL. CMC-544 (10 ng/mL) is effective and specific in primary BCP-ALL cells[2]. In CMC-544-treated cells, the level of CD22 has decreased relative to that on G5/44-treated cells and continued to decrease[3].
In Vivo	An ADC comprising a humanized anti-EFNA4 monoclonal antibody conjugated to the DNA-damaging agent calicheamicin achieves sustained tumor regressions in both TNBC and ovarian cancer PDX in vivo. PF-06647263 (0.27, 0.36 mg/kg) results in significant tumor regressions in TNBC xenografts[1].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 100 mg/mL (73.08 mM)** **H_2O : < 0.1 mg/mL** (insoluble) * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	0.7308 mL	3.6540 mL	7.3081 mL
	5 mM	0.1462 mL	0.7308 mL	1.4616 mL
	10 mM	0.0731 mL	0.3654 mL	0.7308 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: ≥ 3 mg/mL (2.19 mM); Clear solution 此方案可获得 ≥ 3 mg/mL (2.19 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 30.0 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% corn oil Solubility: ≥ 3 mg/mL (2.19 mM); Clear solution 此方案可获得 ≥ 3 mg/mL (2.19 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 30.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Damelin M, et al. Anti-EFNA4 Calicheamicin Conjugates Effectively Target Triple-Negative Breast and Ovarian Tumor-Initiating Cells to Result in Sustained Tumor Regressions. Clin Cancer Res. 2015 Sep 15;21(18):4165-73 [2]. de Vries JF, et al. The novel calicheamicin-conjugated CD22 antibody inotuzumab ozogamicin (CMC-544) effectively kills primary pediatric acute lymphoblastic leukemia cells. Leukemia. 2012 Feb;26(2):255-64 [3]. Takeshita A, et al. CMC-544 (inotuzumab ozogamicin), an anti-CD22 immuno-conjugate of calicheamicin, alters the levels of target molecules of malignant B-cells. Leukemia. 2009 Jul;23(7):1329-36.

实验参考：

Cell Assay	The enhancement of the CDC effect is studied in a similar way in the presence of CMC-544 or G5/44. Specifically, after cells are incubated with or without CMC-544 (5 ng/mL calichemicin DMH) or G5/44 at 37°C for 2 h, they are washed three times to remove unbound antibodies. The viability of cells before incubation with CMC-544 is 99.8%. After the cells are re-incubated in CMC-544- and rituximab-free medium at 37°C for 0-48 h, CDC is analyzed. [3]
Animal Administration	Cohorts of tumor-bearing mice (140-180 mm^3) are randomized into study groups of 6 to 10 based on the number of available mice. The IDBS electronic notebook statistical package, Biobook, is used for automated animal randomization. Animals are dosed by intraperitoneal injection (or intravenously for 144580) twice a week for 4 cycles with ADC, or once a week for 2 cycles with 1.5 mg/kg doxorubicin for breast PDX tumors or 5 mg/kg Cisplatin for ovarian PDX. Study groups are followed until either individual mice or entire cohort measurements reach 1,200 mm^3, at which point sacrifice is indicated. Tumor regression is defined as a reduction in mean tumor volume after dosing. In cases where tumors regress, time to progression (TTP) is determined to be the number of days between the first dose and the time at which mean tumor volume significantly increase (regrow) after regression. [1]
References	[1]. Damelin M, et al. Anti-EFNA4 Calicheamicin Conjugates Effectively Target Triple-Negative Breast and Ovarian Tumor-Initiating Cells to Result in Sustained Tumor Regressions. Clin Cancer Res. 2015 Sep 15;21(18):4165-73 [2]. de Vries JF, et al. The novel calicheamicin-conjugated CD22 antibody inotuzumab ozogamicin (CMC-544) effectively kills primary pediatric acute lymphoblastic leukemia cells. Leukemia. 2012 Feb;26(2):255-64

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