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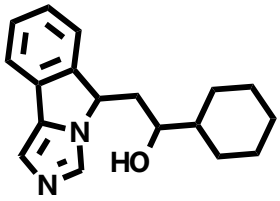
NLG919 (RG6078), IDO Inhibitor

Chemical Name: 1-cyclohexyl-2-(5H-imidazo[5,1-a]isoindol-5-yl)ethan-1-ol



Molecular Weight:	282.38
Formula:	$C_{18}H_{22}N_2O$
Purity:	≥98%
CAS#:	1402836-58-1
Solubility:	DMSO up to 50 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

NLG919 is a potent, selective and orally bioavailable IDO (indoleamine-(2,3)-dioxygenase) pathway inhibitor with Ki ~7 nM (EC_{50} ~75 nM) in vitro and in cell based assays. Oral administration of NLG919 reduces the [Kyn] in plasma and tissue by ~ 50%. Using human IDO+ pDCs in allogeneic MLR reactions, NLG919 potently blocked IDO- induced T cell suppression and restored robust T cell responses with an EC_{50} ~90 nM. NLG919 abrogated IDO-induced suppression of antigen-specific T cells (OT-I or pmel- 1) in vitro, (ED_{50} ~130 nM) using mouse IDO+ pDCs from tumor-draining lymph nodes. In mice bearing large established B16F10 tumors, administration of NLG919 markedly enhanced the antitumor responses of naïve, resting pmel-1 cells to vaccination with cognate hgp100 peptide plus CpG-1826 in IFA. Currently NLG919 is in phase I trial for the treatment of immunosuppression associated with cancer.

How to Use:

In vitro: NLG919 was used at 10 μM final concentration in various in vitro assays.

In vivo: NLG919 was dosed to mice orally or through IP injection with different dose and schedule.

Reference:

1. Li M, et al. The indoleamine 2,3-dioxygenase pathway controls complement-dependent enhancement of chemo-radiation therapy against murine glioblastoma. (2014) J Immunother Cancer. 2:21.
2. Mautino M, et al. NLG919, a novel indoleamine-2,3-dioxygenase (IDO)-pathway inhibitor drug candidate for cancer therapy. (2013) AACR poster 491.