Product Data Sheet

Product Name: NK7-902 diTFA
Cat. No.: GC80891

Chemical Properties

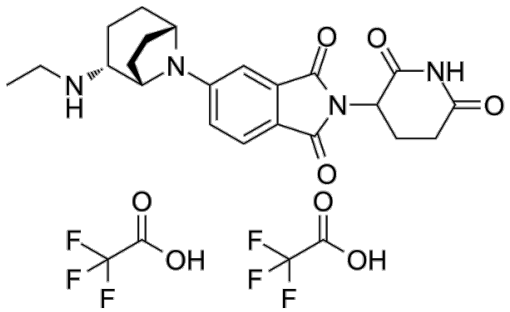
Cas. No.

Formula	$C_{26}H_{28}F_6N_4O_8$	M.Wt	638.51
Solubility	DMSO: 100 mg/mL (156.61 mM; Need ultrasonic)	Storage	Store at -20°C

General tips: For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.

Shipping Condition: Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



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Background

NK7-902 diTFA is a selective and orally active CRBN-dependent NEK7 molecular glue degrader with K d values of 1.5 and 2.6 μM for hNEK7 and mNEK7. NK7-902 diTFA fully degrades NEK7 in human primary monocytes and whole blood but only partially inhibits NLRP3 -dependent IL-1β production. NK7-902 diTFA shows activity in murine systems and induces a profound and long-lasting NEK7 degradation but only transiently blocks NLRP3 inflammasome activation. NK7-902 diTFA can be used for the research of inflammation, such as cryopyrin-associated periodic syndromes [1].

In Vivo, NK7-902 diTFA (30-300 mg/kg; p.o.; single dose; 6h/16h pre-LPS challenge) induces dose-dependent NEK7 degradation and corresponding inhibition of NLRP3 inflammasome-mediated IL-1β release in a mouse acute peritonitis model[1]. NK7-902 diTFA (300 mg/kg; p.o.; single dose; 16h pre-LPS challenge) induces robust NEK7 degradation and significant inhibition of NLRP3 inflammasome-mediated IL-1β release in a mouse CAPS model[1]. NK7-902 diTFA (0.2-2 mg/kg; p.o.; single dose) induces profound, long-lasting NEK7 degradation but only transient IL-1β inhibition in non-human primates[1].

In Vitro, NK7-902 diTFA (0.005-10000 nM; 18 h pre-treatment) potently and selectively degrades NEK7 (DC_{50} = 0.2 nM) in human primary monocytes, with partial, stimulus-dependent inhibition of NLRP3 inflammasome-mediated IL-1β secretion[1]. NK7-902 diTFA (0.009-10000 nM; 18 h) potently degrades NEK7 (DC_{50} = 1.6 nM) in human PBMCs, with full NLRP3 inflammasome inhibition in most CAPS mutations but partial inhibition in the NEK7T348M mutation[1]. NK7-902 diTFA (0.001-10000 nM; 18 h) potently degrades NEK7 in human whole blood (DC_{50} = 8.7 nM) and neutrophils, with partial IL-1β inhibition in whole blood but full inhibition in isolated neutrophils[1]. NK7-902 diTFA (1-10000 nM; 18 h) potently degrades NEK7 (DC_{50} = 54.2 nM) in mouse primary splenocytes in a CRBN-dependent manner[1]. NK7-902 diTFA (0.1-10000 nM; 18 h) potently degrades NEK7 (DC_{50} = 4.1 nM) in NHP blood in vitro[1]. NK7-902 diTFA (20-411 μg/mL; 96 h) degrades NEK7 in human primary blood lymphocytes without inducing significant chromosomal damage or cell cycle delay[1].

References:

[1]. Sylvain A, et, al. A cereblon (CRBN) molecular glue degrader of NIMA-related kinase 7 (NEK7)

reveals a context-dependent role in NLRP3 inflammasome activation. bioRxiv. 2024.11.06.622079.