

Product Data Sheet

Product Name: TH-Z827 diTFA

Cat. No.: GC81859

Chemical Properties

Cas. No.

Formula $C_{34}H_{40}F_6N_6O_5$ M.Wt 726.71

Solubility DMSO: 100 mg/mL (137.61 mM; Storage Store at -20°C
Need ultrasonic)

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



Caution: Product has not been fully validated for medical applications. For research use only.

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Background

TH-Z827 diTFA is a selective KRAS G12D inhibitor that exhibits activity against GDP-bound and GMPPNP-bound KRAS G12D, but shows no activity against KRAS (WT) and KRAS G12C. TH-Z827 diTFA blocks the KRAS G12D -CRAF interaction with a IC_{50} value of 42 μ M. TH-Z827 diTFA can be used for the research of pancreatic cancer [1] [2].

In Vivo, TH-Z827 (10-30 mg/kg; i.p.; Days 38, 41, 44, 47, 50, 53, 56, 59, 62) diTFA reduces pancreatic tumor volumes in a dose-dependent manner in BALB/c nude mice, with the 30 mg/kg intraperitoneal dose achieving greater tumor volume reduction than the 10 mg/kg dose^[1]. TH-Z827 (10 mg/kg; i.p.) diTFA reduces pancreatic tumor volumes in C57BL/6 mice, and exhibits synergistic antitumor activity when combined with anti-PD-1 antibody^[1]. TH-Z827 diTFA synergizes with an anti-PD-1 antibody to reduce tumor volume in C57BL/6 mice bearing KPC pancreatic cancer xenografts^[2].

In Vitro, TH-Z827 (10 min) diTFA potently inhibits SOS-catalyzed nucleotide exchange of GDP-bound KRASG12D with an IC_{50} of 3.1 μ M, and displays nearly 10-fold selectivity for KRASG12D over KRASG12C^[1]. TH-Z827 (800 μ M) diTFA binds to both GDP-bound and GMPPNP-bound KRASG12D with similar affinities (K_d of 6.52 μ M and 7.01 μ M, respectively), and does not bind to KRASWT or KRASG12C^[1]. TH-Z827 diTFA blocks the KRASG12D-CRAF interaction with an IC_{50} of 42 μ M, without affecting interactions involving KRAS(WT) or KRASG12C^[1]. TH-Z827 diTFA potently inhibits SOS-catalyzed GDP/GDP exchange of purified GDP-bound KRASG12D protein with an IC_{50} of 3.1 μ M^[2]. TH-Z827 diTFA exhibits selective binding and inhibition for purified KRASG12D protein over KRAS WT and KRASG12C proteins, with no measurable binding to the latter two variants^[2]. TH-Z827 (24 h) diTFA inhibits proliferation of KRASG12D-mutant PANC-1 and Panc 04.03 pancreatic cancer cells with IC_{50} values of 4.4 μ M and 4.7 μ M, respectively^[1]. TH-Z827 (1-20 μ M; 3 h) diTFA inhibits MAPK and PI3K/mTOR signaling in KRASG12D-mutant PANC-1 and Panc 04.03 pancreatic cancer cells by reducing pERK and pAKT levels following 3 h of treatment^[1].

References:

[1]. Mao Z, et al. KRAS(G12D) can be targeted by potent inhibitors via formation of salt bridge. Cell

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discovery. 2022 Jan 25;8(1):5.

[2]. Mao Z, et al. KRAS G12D can be targeted by potent salt-bridge forming inhibitors[J]. bioRxiv, 2021: 2021.12. 13.472365.

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