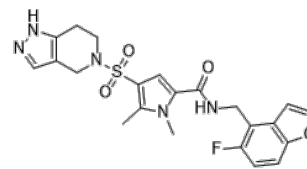


Product Name : TDI-015051
Cat. No. : PC-23632
CAS No. : 3052313-73-9
Molecular Formula : C₂₂H₂₂FN₅O₄S
Molecular Weight : 471.51
Target : SARS-CoV-2 Inhibitors
Solubility : 10 mM in DMSO



CAS: 3052313-73-9

Biological Activity

TDI-015051 is a highly potent, specific inhibitor of SARS-CoV-2 **NSP14 RNA cap methyltransferase** with K_d of 61 pM and IC₅₀ of <0.15 nM, inhibits viral mRNA translation.

TDI-015051 occupies the SAH-stabilized cap-binding pocket of NSP14, forming additional stabilizing interactions.

TDI-015051 inhibits SARS-CoV-2 infection with an EC₅₀ of 11.4 nM in Huh-7.5 cells, with no cytotoxicity up to 3 μM, co-treatment of Huh-7.5 cells with 5 μM DZNeP further potentiated TDI-015051 antiviral activity (EC₅₀ = 0.8 nM).

TDI-015051 potently inhibits viral infection in the adenocarcinoma-derived alveolar basal epithelial cell line A549 expressing ACE2 and TMPRSS2 (EC₅₀ = 64.7 nM), TDI-015051 (>4 nM) also prevented SARS-CoV-2 viral replication in human primary small airway epithelial cells grown at the air-liquid interface.

NSP14(V290A), NSP14(N306K), NSP14(P335S) and NSP14(H424R) plaque-purified viruses showed resistance to TDI-015051 with EC₅₀ values elevated 40-fold or more relative to wild type.

TDI-015051 inhibits NSP14 of other hCoVs with IC₅₀ of 1.7 nM, 2.6 nM or 3.6 nM for NSP14 of alphacoronaviruses α-hCoV-NL63, α-hCoV-229E, and betacoronavirus β-hCoV-MERS, respectively.

TDI-015051 inhibits hCoV-NL63 and hCoV-229E infection in Huh-7.5 cells with EC₅₀ of 0.12 μM and 3.7 μM, respectively.

TDI-015051 does not inhibit the human RNA guanine-7 methyltransferase (RNMT) in complex with its protein cofactor RAM29 nor NS5 MTase from Zika virus.

TDI-015051 (150-500 mg/kg, orally) reduces SARS-CoV-2 viral lung burden in a K18-hACE2 transgenic mouse model.

References

Meyer C, et al. *Nature*. 2024 Dec 11. doi: 10.1038/s41586-024-08320-0.

Caution: Product has not been fully validated for medical applications. Lab Use Only!

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