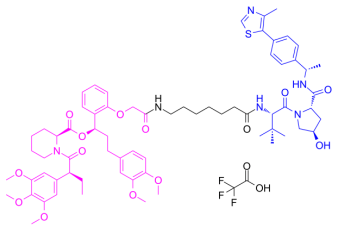
dTAGV-1 TFA

Cat. No.:	HY-145514
CAS No.:	2624313-15-9
Molecular Formula:	$C_{70}H_{91}F_3N_6O_{16}S$
Molecular Weight:	1361.56
Target:	PROTACs
Pathway:	PROTAC
Storage:	-20°C, sealed storage, away from moisture and light * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 37.5 mg/mL (27.54 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	0.7345 mL	3.6723 mL	7.3445 mL
	5 mM	0.1469 mL	0.7345 mL	1.4689 mL
	10 mM	0.0734 mL	0.3672 mL	0.7345 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 3.75 mg/mL (2.75 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 3.75 mg/mL (2.75 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

dTAGV-1 TFA is a potent and selective degrader of mutant $FKBP12^{F36V}$ fusion proteins. dTAGV-1 TFA can induce degradation of $FKBP12^{F36V}$-Nluc in vivo[1].

IC_{50} & Target

VHL

In Vitro

dTAGV-1 (0.1 nM-10 μM; 24 h) TFA induces potent degradation of $FKBP12^{F36V}$-Nluc with no effects on $FKBP12^{WT}$-Nluc in 293FT cells[1].

dTAGV-1 (125-2000 nM; 24 h) TFA co-treatment with THAL-SNS-032 leads to pronounced degradation of both LACZ-$FKBP12^{F36V}$ and CDK9[1].

dTAGV-1 (500 nM; 1-24 h) TFA leads to rapid $KRAS^{G12V}$ and pERK1/2 degradation[1].

dTAGV-1 (50-5000 nM; 24 h) TFA enables EWS/FLI degradation in Ewing sarcoma[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

dTAGV-1 (35 mg/kg; i.p. once daily for 4 days) TFA induces degradation of FKBP12^{F36V}-Nluc in mice[1].

dTAGV-1 (2-10 mg/kg; i.p.) TFA exhbits half-lives ($T_{1/2}$=3.64 and 4.4 h), C_{max} (595 and 2123 ng/mL) and great exposure (AUC_{inf} =3136 and 18517 h•ng/mL) in mice[1].

dTAGV-1 (2 mg/kg; i.v.) TFA exhbits half-life ($T_{1/2}$=3.02 h), C_{max} (7780 ng/mL) and great exposure (AUC_{inf} =3329 h•ng/mL) in mice[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	8-week-old immunocompromised female mice were transplanted with MV4;11 luc-FKBP12 ^{F36V} cells[1]
Dosage:	35 mg/kg
Administration:	I.p. once daily for 4 days
Result:	Observed striking loss of bioluminescent signal 4 h after the first and three administrations. Degradation evident 28 h after the final administration.

REFERENCES

[1]. Nabet B, et, al. Rapid and direct control of target protein levels with VHL-recruiting dTAG molecules. Nat Commun. 2020 Sep 18;11(1):4687.

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