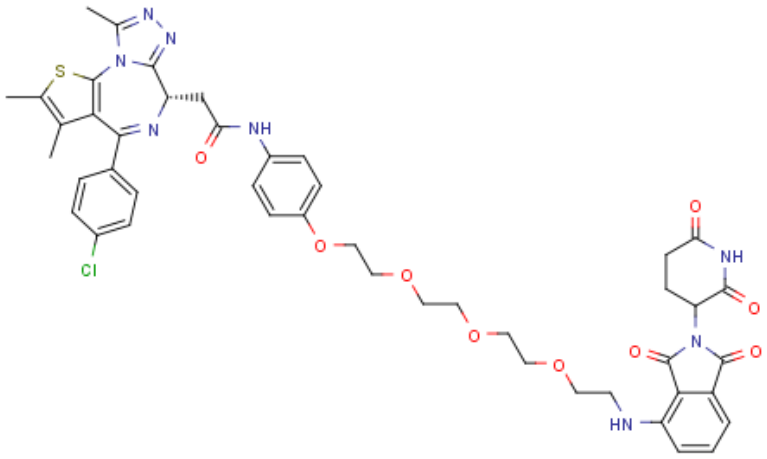
Name: ARV-825

Cat#: EX-A2379

Target: PROTACs/Epigenetic Reader Domain
Pathway: Epigenetics/Others Pathway

Chemical Structure:



Chemical Name	2-((S)-4-(4-chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)-N-(4-(2-(2-(2-(2-((2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)amino)ethoxy)ethoxy)ethoxy)ethoxy)phenyl)acetamide

Molecular Weight	923.432	Storage	Powder 3 years -20°C; 2 years 4°C 6 months -80°C in solvent Away from light
Formula	C46H47ClN8O9S		
CAS No.	1818885-28-7	Synonyms	

Solubility (25°C) *	In vitro	DMSO	>=50mg/mL
		Ethanol	N/A
		Water	N/A
	In vivo (should be freshly prepared each time)	In Vivo Add each solvent one by one: 1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% Saline Solubility: ≥ 2.5 mg/mL (2.71 mM); Clear solution	

		2. 10% DMSO >> 90% Corn Oil Solubility: 2.5 mg/mL (4.28 mM); Solubility: ⩾ 2.5 mg/mL (2.71 mM); Clear solution

* <1 mg/ml means slightly soluble or insoluble.
* Please note that Selleck tests the solubility of all compounds in-house, and the actual solubility may differ slightly from published values. This is normal and is due to slight batch-to-batch variations.

Preparing Stock Solutions:

Mass / Volume / Concentration	1 mg	5 mg	10 mg
1 mM	1.0829 mL	5.4146 mL	10.8292 mL
5 mM	0.2166 mL	1.0829 mL	2.1658 mL
10 mM	0.1083 mL	0.5415 mL	1.0829 mL

DMSO :

*The above data is based on the product molecular weight 923.43.

Biological Activities:

Description	ARV-825 is a PROTAC connected by ligands for Cereblon and BRD4. ARV-825 binds to BD1 and BD2 of BRD4 with Kds of 90 and 28 nM, respectively.
IC_{50} & Target	Kd: 90 nM (Bromodomain 1 of BRD4), 28 nM (Bromodomain 2 of BRD4) [1]
In Vitro	ARV-825 is a hetero-bifunctional proteolysis-targeting chimera (PROTAC) that recruits BRD4 to the E3 ubiquitin ligase cereblon. ARV-825 actively recruits BRD4 to cereblon, resulting in the rapid and efficient degradation of the former via the proteasome. Given that BRD4 and cereblon binding moieties in ARV-825 have Kds of 28-90 nM and ~3 μM to their respective targets, this suggests that ARV-825 acts in a substoichiometric way in mediating BRD4 degradation. ARV-825 treatment results in prolonged BRD4 down-regulation and downstream signaling suppression compared to BRD4 inhibitors[1].

References	[1]. Lu J, et al. Hijacking the E3 Ubiquitin Ligase Cereblon to Efficiently Target BRD4. Chem Biol. 2015 Jun 18;22(6):755-63.