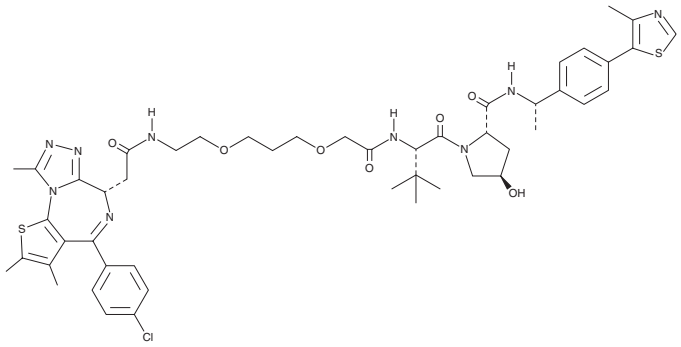
PRODUCT INFORMATION

ARV-771

Item No. 21299

CAS Registry No.: 1949837-12-0
Formal Name: (2S,4R)-1-((S)-2-(*tert*-butyl)-15-((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)-4,14-dioxo-6,10-dioxa-3,13-diazapentadecanoyl)-4-hydroxy-N-((S)-1-(4-(4-methylthiazol-5-yl)phenyl)ethyl)pyrrolidine-2-carboxamide
MF: $C_{49}H_{60}ClN_9O_7S_2$
FW: 986.6
Purity: ≥95%
UV/Vis.: λ_{max}: 257 nm
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

ARV-771 is supplied as a crystalline solid. A stock solution may be made by dissolving the ARV-771 in the solvent of choice, which should be purged with an inert gas. ARV-771 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of ARV-771 in these solvents is approximately 10, 15, and 20 mg/ml, respectively.

ARV-771 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, ARV-771 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. ARV-771 has a solubility of approximately 0.14 mg/ml in a 1:6 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

ARV-771 is a proteolysis-targeting chimera (PROTAC) that drives the degradation of bromodomain and extra terminal domain (BET) family proteins.[1] It is comprised of a BET-binding moiety conjugated *via* a linker to a von Hippel-Lindau (VHL) E3 ligase-binding moiety. ARV-771 induces degradation of bromodomain-containing protein 2 (BRD2), BRD3, and BRD4 in 22Rv1 castration-resistant prostate cancer (CRPC) cells with half-maximal degradation (DC_{50}) values of less than 5 nM for all. It inhibits proliferation of and increases poly(ADP-ribose) polymerase (PARP) cleavage in 22Rv1 cells in a concentration-dependent manner. ARV-771 reduces full-length androgen receptor protein levels and prevents increases in ERG induced by the synthetic androgen R1881 in VCaP cells in a concentration-dependent manner. ARV-771 (30 mg/kg per day, s.c.) induces tumor regression in a 22Rv1 mouse xenograft model.

Reference

1. Raina, K., Lu, J., Qian, Y., *et al.* PROTAC-induced BET protein degradation as a therapy for castration-resistant prostate cancer. *Proc. Natl. Acad. Sci. USA* **113(26)**, 7124-7129 (2016).

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