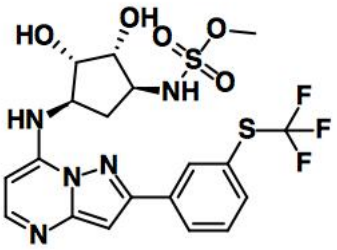
Xcess Biosciences Inc.
7144 N Harlem Ave #169
Chicago, IL 60631 USA

http://www.xcessbio.com
Toll free: 1-866-706-2330
Fax: 1-619- 810-0718
Email: info@xcessbio.com

Ubiquitin Activating Enzyme (UAE) Inhibitor – TAK-243 (MLN7243)

Chemical Name: methyl ((1S,2R,3S,4R)-2,3-dihydroxy-4-((2-(3-((trifluoromethyl)thio)phenyl)pyrazolo[1,5-a]pyrimidin-7-yl)amino)cyclopentyl)sulfamate



Molecular Weight:	519.51
Formula:	$C_{19}H_{20}F_3N_5O_5S_2$
Purity:	≥98%
CAS#:	1450833-55-2
Solubility:	DMSO up to 100 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

TAK-243 (MLN7243) is a potent, selective and cell permeable small molecule inhibitor of the ubiquitin activating enzyme (UAE) at nM range. The ubiquitin-activating enzymes, found more active in cancer cells than in normal healthy cells, catalyze the first step in ubiquitination reaction, targeting a protein for degradation via proteasome. TAK-243 treatment caused depletion of cellular ubiquitin conjugates, resulting in disruption of signaling events, induction of proteotoxic stress, and impairment of cell cycle progression and DNA damage repair pathways. TAK-243 treatment caused death of cancer cells and, in primary human xenograftstudies, demonstrated antitumor activity at tolerated doses. Due to its specificity and potency, TAK-243 allows for interrogation of ubiquitin biology and for assessment of UAE inhibition as a new approach for cancer treatment. TAK-243 is now in phase I clinical trials for adult patients with advanced solid tumors.

How to Use:

In vitro: TAK-243 was suggested to be used at 1-10 μM final concentration in vitro and in cellular assays.

In vivo: TAK-243 was administered intravenously at 12.5-25 mg/Kg to a panel of human-patient-derived and cell-line-derived xenograft (PDX and CDX, respectively) tumor models on a twice-per-week schedule.

Reference:

1. Hyer ML, et al. A small-molecule inhibitor of the ubiquitin activating enzyme for cancer treatment. (2018) Nat Med. In press.