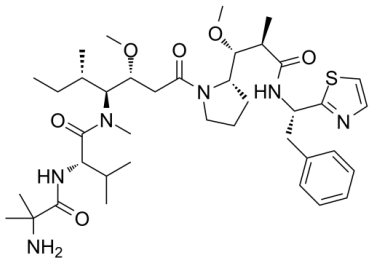
Data Sheet

Product Name:	PF-06380101
Cat. No.:	CS-3706
CAS No.:	1436391-86-4
Molecular Formula:	$C_{39}H_{62}N_6O_6S$
Molecular Weight:	743.01
Target:	ADC Cytotoxin; Microtubule/Tubulin
Pathway:	Antibody-drug Conjugate/ADC Related; Cell Cycle/DNA Damage; Cytoskeleton
Solubility:	DMSO : ≥ 65 mg/mL (87.48 mM)



BIOLOGICAL ACTIVITY:

PF-06380101 (Aur0101), an auristatin **microtubule** inhibitor, is a cytotoxic Dolastatin 10 analogue. PF-06380101 (Aur0101) shows excellent potencies in tumor cell proliferation assays and differential ADME properties when compared to other synthetic auristatin analogues that are used in the preparation of ADCs. **In Vivo:** After an IV dose of 20a at 20 μg/kg to Wistar Han rats, PF-06380101 exhibited a mean systemic clearance (Cl) of 70 mL/min/kg and a volume of distribution (Vss) of 14.70 L/kg, resulting in a terminal elimination half-life (t1/2) of approximately 6 h. PF-06380101 preferentially distributes into human plasma relative to whole blood and that PF-06380101 is a P-glycoprotein (P-gp) substrate. PF-06380101 is anticipated to be of low risk to perpetrate pharmacokinetic drug interactions with compounds for which CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, and/or CYP3A4/5-mediated metabolism constitutes the primary mechanism of clearance. The utility of the new auristatin analogues as ADC payloads including the development of the lead analogue 20a (PF-06380101) will be reported in due course.

PROTOCOL (Extracted from published papers and Only for reference)

Cytotoxicity Assay [1]: N87 cells were obtained from ATCC and were originally derived from a liver metastasis of gastric carcinoma. BT474 cells (ATCC) were derived from a breast carcinoma. MDA-MB-361-DYT2 cells were derived from breast carcinoma and were generously provided by Dr. Dajun Yang of Georgetown University. Cells were seeded in 96-well plates at low density, then treated the following day with compounds in 3-fold serial dilutions at 10 concentrations in duplicate. Cells were incubated for 4 days in a humidified 37 °C/5% CO2 incubator. The plates were harvested by incubating with CellTiter 96 AQueous One MTS solution for 1.5 h and absorbance measured on a Victor plate reader at wavelength 490 nm.

References:

[1]. Maderna A, et al. Discovery of cytotoxic dolastatin 10 analogues with N-terminal modifications. J Med Chem. 2014 Dec 26;57(24):10527-43.

CAIndexNames:

L-Valinamide, 2-methylalanyl-N-[(1S,2R)-2-methoxy-4-[(2S)-2-[(1R,2R)-1-methoxy-2-methyl-3-oxo-3-[[(1S)-2-phenyl-1-(2-thiazolyl)ethyl]amino]propyl]-1-pyrrolidinyl]-1-[(1S)-1-methylpropyl]-4-oxobutyl]-N-methyl-

SMILES:

CC[C@H](C)[C@@H]([C@@H](CC(N1[C@@H](CCC1)[C@@H]([C@@H](C)C(N[C@H](C2=NC=CS2)CC3=CC=CC=C3)=O)OC)=O)OC)N(C([C@H](C(C

)C)NC(C(C)(C)N)=O)=O)C

Caution: Product has not been fully validated for medical applications. For research use only.

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