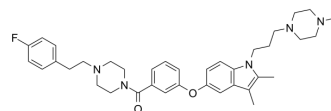


## ATM-3507

Cat. No.:	HY-100948
CAS No.:	1861449-70-8
Molecular Formula:	C <sub>37</sub> H <sub>46</sub> FN <sub>5</sub> O <sub>2</sub>
Molecular Weight:	611.79
Target:	Myosin
Pathway:	Cytoskeleton
Storage:	4°C, protect from light * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



### SOLVENT & SOLUBILITY

In Vitro	DMSO : 33.33 mg/mL (54.48 mM; Need ultrasonic)						
	Preparing Stock Solutions	Solvent Concentration	Mass	1 mg	5 mg	10 mg	
				1 mM	1.6345 mL	8.1727 mL	16.3455 mL
				5 mM	0.3269 mL	1.6345 mL	3.2691 mL
				10 mM	0.1635 mL	0.8173 mL	1.6345 mL
Please refer to the solubility information to select the appropriate solvent.							

### BIOLOGICAL ACTIVITY

Description	ATM-3507 is a potent tropomyosin inhibitor with IC <sub>50</sub> s from 3.83-6.84 μM in human melanoma cell lines.
IC <sub>50</sub> & Target	IC <sub>50</sub> : 3.83-6.84 μM (tropomyosin, in human melanoma celllines) <sup>[1]</sup> .
In Vitro	<p>The cell lines differ in their relative expression of Tpm3.1 as well as in the expression of other isoforms. After determining the IC<sub>50</sub> concentrations for TR100 and ATM-3507 (CHLA-20: 4.99±0.45 μM, CHP-134: 3.83±0.67 μM, CHLA-90: 6.84±2.37 μM, SK-N-BE(2): 5.00±0.42 μM) in each of the neuroblastoma cell lines, combinations of tropomyosin inhibitors plus Vincristine are tested at levels of each drug alone that kill less than 50% of the neuroblastoma cells. The combinations of both tropomyosin inhibitors plus Vincristine are completely cytotoxic in CHLA-20 cells. All 4 cell lines show some degree of synergy as determined by the Chou–Talalay method. The effect is not limited to the vinca alkaloids as a similar combination efficacy using paclitaxel plus TR100 or ATM-3507<sup>[1]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
In Vivo	<p>The maximal tolerance dose (MTD) for TR100 and ATM-3507 is 60 and 150 mg/kg, respectively. It is found that a significant inhibition of tumor growth and prolongation of animal survival using either combination compared with each monotherapy. The median survival of mice increased from 18 days for mice treated with ATM-3507 to more than 49 days for mice treated with the combination. It is also found that twice weekly intravenous administration of ATM-3507 also show combination</p>

efficacy. The impact of each treatment or the combination on body weight is minimal. Drug levels are measured following the intravenous administration of ATM-3507 at 30 mg/kg in Balb/c mice (n=3 per time point). The mean half-life of ATM-3507 is 5.01 hrs for the terminal elimination phase. The mean AUC<sub>0-t</sub> in the plasma is 14,548 ng/h/mL. The C<sub>max</sub> of ATM-3507 is 5,758 ng/mL and the t<sub>1/2</sub> is 5.01 h. The observed plasma clearance and volume of distribution at steady state of ATM-3507 is 33.8 mL/min/kg and 7.23 L/kg, respectively<sup>[1]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

### Cell Assay <sup>[1]</sup>

The 4 melanoma cell lines CHLA-20, CHLA-90, SK-N-BE(2) and CHP-134 are cultured at 37°C in a humidified incubator at 5% CO<sub>2</sub> and supplemented 100 U/mL penicillin and 100 mg/mL streptomycin. Cells are plated in 96-well plates at 2000-4000 cells per well, incubated at 37°C overnight and then treated with various concentrations of TR100/ATM-3507 (0.1-2.5 μM) alone, TR100 and ATM-3507 plus various chemotherapy drugs. The cell viability is performed on day 3-5. For the dosing schedule optimization experiment, TR100 or Vincristine is added at day 1 with the other being added at day 2 or both TR100 and Vincristine are added on day 1 and plates are read at day 5. Results are presented as percentage of survival cells compared with controls. All cell viability assays are run in quadruplicate and the data shown are representative of at least 2 independent experiments<sup>[1]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

### Animal Administration <sup>[1]</sup>

Mice<sup>[1]</sup>  
Female athymic nude mice (age 4-6 weeks) are used. Mice are subcutaneously injected with 5.0×10<sup>6</sup> CHLA-20 cells in a 150 mL mix of PBS and Matrigel (2:1). ATM-3507 and TR100 are formulated at 15 mg/mL in 30% sulfobutyl-ether-β-cyclodextrin sodium salt (SBECD). Vincristine is dissolved in H<sub>2</sub>O at 0.125 mg/kg. When the tumors reached volumes of 200-400 mm<sup>3</sup>, mice are randomized into the study groups. Animals are followed until the animal reached endpoint criteria. Tumor size is measured using digital calipers twice per week and tumor volume is calculated. Mice are also weighed and observed twice per week for signs of endpoint condition. Mice that demonstrate signs of toxicity or reach endpoint criteria are humanely euthanized by CO<sub>2</sub> asphyxiation and subjected to cervical dislocation as the secondary method of euthanasia<sup>[1]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## REFERENCES

[1]. Currier MA, et al. Identification of Cancer-Targeted Tropomyosin Inhibitors and Their Synergy with Microtubule Drugs. *Mol Cancer Ther.* 2017 Aug;16(8):1555-1565.

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

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