

# Small Molecules

## Tivantinib

HGF pathway inhibitor; Inhibits MET

Catalog # 73482  
73484

1 mg  
10 mg



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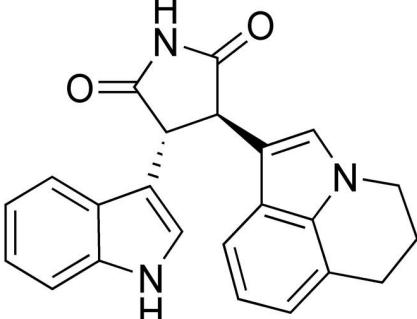
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## Product Description

Tivantinib is a staurosporine derivative which binds to inactive, dephosphorylated c-MET receptor tyrosine kinase, in a manner that is not competitive with ATP (Munshi et al.; Eathiraj et al.). It is selective for c-MET ( $K_i \approx 355$  nM) in a screen of 230 kinases (Munshi et al.). It also shows cytotoxic activity, which is distinct from its inhibition of c-MET (Basilico et al.; Katayama et al.). It has also been shown to bind directly to the colchicine binding pocket of tubulin, thereby reducing tubulin polymerization (Aoyama et al.).

Molecular Name:	Tivantinib
Alternative Names:	ARQ 197
CAS Number:	905854-02-6
Chemical Formula:	$C_{23}H_{19}N_3O_2$
Molecular Weight:	369.4 g/mol
Purity:	$\geq 98\%$
Chemical Name:	(3R,4R)-3-(5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1-yl)-4-(1H-indol-3-yl)-2,5-pyrrolidinedione
Structure:	 The chemical structure of Tivantinib is a complex molecule. It features a central carbon atom bonded to a 5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1-yl group, an indol-3-yl group, and two 2,5-pyrrolidinedione groups. One 2,5-pyrrolidinedione group is attached to the central carbon, and the other is attached to the indol-3-yl group. The molecule also contains a tryptamine-like side chain.

## Properties

Physical Appearance:	A crystalline solid
Storage:	Product stable at -20°C as supplied. Protect from prolonged exposure to light. Stable as supplied for 12 months from date of receipt.
Solubility:	<ul style="list-style-type: none"><li>DMSO <math>\leq 50</math> mM</li><li>Absolute ethanol <math>\leq 13</math> mM</li></ul> For example, to prepare a 10 mM stock solution in DMSO, resuspend 1 mg in 271 $\mu$ L of DMSO.

Prepare stock solution fresh before use. Information regarding stability of small molecules in solution has rarely been reported, however, as a general guide we recommend storage in DMSO at -20°C. Aliquot into working volumes to avoid repeated freeze-thaw cycles. The effect of storage of stock solution on compound performance should be tested for each application.

Compound has low solubility in aqueous media. For use as a cell culture supplement, stock solution should be diluted into culture medium immediately before use. Avoid final DMSO concentration above 0.1% due to potential cell toxicity.

## Published Applications

### CANCER RESEARCH

- Induces apoptosis of human myeloma CD138+ plasma cells in vitro, and demonstrates efficacy in a mouse xenograft model of myeloma (Zaman et al.).
- Inhibits metastatic growth of breast cancer cells in bone and reduces tumor-induced osteolysis, in a mouse xenograft model (Previdi et al.).
- Perturbs microtubule dynamics, induces G2/M arrest, and promotes apoptosis independently of c-MET inhibition in a variety of cancer cell lines (Basilico et al.).

## References

Aoyama A et al. (2014) Tivantinib (ARQ 197) exhibits antitumor activity by directly interacting with tubulin and overcomes ABC transporter-mediated drug resistance. *Mol Cancer Ther* 13(12): 2978–90.

Basilico C et al. (2013) Tivantinib (ARQ197) displays cytotoxic activity that is independent of its ability to bind MET. *Clin Cancer Res* 19(9): 2381–92.

Eathiraj S et al. (2011) Discovery of a novel mode of protein kinase inhibition characterized by the mechanism of inhibition of human mesenchymal–epithelial transition factor (c-Met) protein autophosphorylation by ARQ 197. *J Biol Chem* 286(23): 20666–76.

Katayama R et al. (2013) Cytotoxic activity of tivantinib (ARQ 197) is not due solely to c-MET inhibition. *Cancer Res* 73(10): 3087–96.

Munshi N et al. (2010) ARQ 197, a novel and selective inhibitor of the human c-Met receptor tyrosine kinase with antitumor activity. *Mol Cancer Ther* 9(6): 1544–53.

Previdi S et al. (2012) Breast cancer-derived bone metastasis can be effectively reduced through specific c-MET inhibitor tivantinib (ARQ 197) and shRNA c-MET knockdown. *Mol Cancer Ther* 11(1): 214–23.

Zaman S et al. (2015) Targeting the pro-survival protein MET with tivantinib (ARQ 197) inhibits growth of multiple myeloma cells. *Neoplasia* 17(3): 289–300.

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