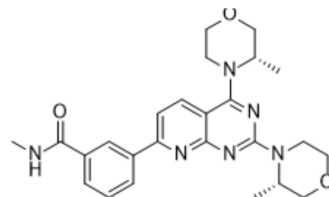


## Vistusertib

<b>Cat. No.:</b>	HY-15247		
<b>CAS No.:</b>	1009298-59-2		
<b>Molecular Formula:</b>	C <sub>25</sub> H <sub>30</sub> N <sub>6</sub> O <sub>3</sub>		
<b>Molecular Weight:</b>	462.54		
<b>Target:</b>	mTOR; Autophagy; Apoptosis		
<b>Pathway:</b>	PI3K/Akt/mTOR; Autophagy; Apoptosis		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	1 year
		-20°C	6 months



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : ≥ 50 mg/mL (108.10 mM)  
 \* "≥" means soluble, but saturation unknown.

	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.1620 mL	10.8099 mL	21.6198 mL
	5 mM	0.4324 mL	2.1620 mL	4.3240 mL
	10 mM	0.2162 mL	1.0810 mL	2.1620 mL

Please refer to the solubility information to select the appropriate solvent.

#### In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility: ≥ 2.5 mg/mL (5.40 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: 2.5 mg/mL (5.40 mM); Suspended solution; Need ultrasonic and warming
- Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline  
Solubility: 2.5 mg/mL (5.40 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)  
Solubility: 2.5 mg/mL (5.40 mM); Suspended solution; Need ultrasonic

### BIOLOGICAL ACTIVITY

#### Description

Vistusertib (AZD2014) is an ATP competitive mTOR inhibitor with an IC<sub>50</sub> of 2.81 nM. AZD2014 inhibits both mTORC1 and mTORC2 complexes.

#### IC<sub>50</sub> & Target

mTOR	mTORC1	mTORC2	PI3Kα
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	2.81 nM (IC <sub>50</sub> )		3.766 μM (IC <sub>50</sub> )
	Autophagy		
<b>In Vitro</b>	<p>The inhibitory effects of Vistusertib (AZD2014) are measured against isolated recombinant mTOR enzyme (IC<sub>50</sub> of 2.81 nM) as well as in cellular assays measuring both mTORC1 and mTORC2 activities. In MDAMB468 cells, Vistusertib (AZD2014) decreases the phosphorylation of the mTORC1 substrate ribosomal protein S6 (Ser235/236) with a mean IC<sub>50</sub> value of 210 nM and the mTORC2 substrate AKT (Ser473) with a mean IC<sub>50</sub> value of 78 nM<sup>[1]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>		
<b>In Vivo</b>	<p>Vistusertib (AZD2014) induces dose-dependent tumor growth inhibition in several xenograft and primary explant models. The antitumor activity of Vistusertib (AZD2014) is associated with modulation of both mTORC1 and mTORC2 substrates, consistent with its mechanism of action. The pharmacokinetics of Vistusertib (AZD2014) in mice is tested upon administration of doses between 7.5 and 15 mg/kg. A dose-dependent increase in C<sub>max</sub> and AUC is observed following single dose and repeat dosing of AZD2014: C<sub>max</sub> range from 1 to 16 μM and AUC range from 220 to 5,042 μM·h across this dose range. The pharmacodynamic effect of Vistusertib (AZD2014) against an mTORC1 biomarker (phosphorylation of S6) and an mTORC2 biomarker (phosphorylation of AKT) is assessed in SCID mice bearing MCF7 xenografts following administration of 3.75, 7.5, and 15 mg/kg AZD2014. There is a good relationship between the drug plasma concentrations and biomarker levels (estimated p-AKT IC<sub>50</sub> of 0.119 μM total, 53% SE, and estimated p-S6 IC<sub>50</sub> 0.392 μM, 28.8% SE)<sup>[1]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>		

## PROTOCOL

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

Mice<sup>[1]</sup>

MCF7 experiments: 5×10<sup>6</sup> MCF7 cells are injected s.c. in a volume of 0.1 mL in male SCID mice and are randomized into control and treatment groups when tumor size reach 0.2 cm<sup>3</sup>. Vistusertib (AZD2014) is dissolved in captisol, and diluted to a final captisol concentration of 30% (w/v). Vistusertib (AZD2014) is administered by oral gavage (0.1 mL/10 g body weight). The control group receive vehicle only. Tumor volumes (measured by calliper), animal body weight and condition are recorded twice weekly for the duration of the study. The tumor volume is calculated (taking length to be the longest diameter across and width to be the corresponding perpendicular diameter) using the formula: (length×width)×√(length×width)×(π/6).

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Science. 2017 Dec 1;358(6367):eaan4368.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Nat Commun. 2019 Jul 1;10(1):2901.
- Nat Commun. 2017 Jun 8;8:15617.
- Autophagy. 2021 Jun;17(6):1349-1366.

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## REFERENCES

[1]. Guichard SM, et al. AZD2014, an inhibitor of mTORC1 and mTORC2, is highly effective in ER+ breast cancer when administered using intermittent or continuous

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

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