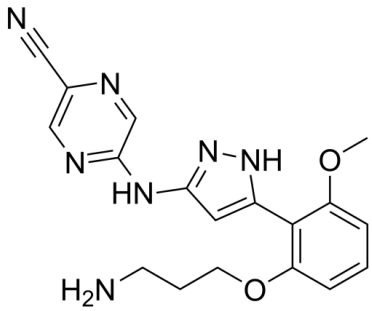
Data Sheet

Product Name:	Prexasertib
Cat. No.:	CS-2198
CAS No.:	1234015-52-1
Molecular Formula:	$C_{18}H_{19}N_7O_2$
Molecular Weight:	365.39
Target:	Apoptosis; Checkpoint Kinase (Chk)
Pathway:	Apoptosis; Cell Cycle/DNA Damage
Solubility:	DMSO : 16.67 mg/mL (45.62 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

Prexasertib (LY2606368) is a selective, ATP-competitive second-generation **checkpoint kinase 1 (CHK1)** inhibitor with a **K_i** of 0.9 nM and an **IC_{50}** of <1 nM. Prexasertib inhibits CHK2 (IC_{50}=8 nM) and RSK1 (IC_{50}=9 nM). Prexasertib causes double-stranded DNA breakage and replication catastrophe resulting in **apoptosis**. Prexasertib shows potent anti-tumor activity[1][2]. **In Vitro:** Prexasertib (LY2606368) inhibits MELK (IC_{50}=38 nM), SIK (IC_{50}=42 nM), BRSK2 (IC_{50}=48 nM), ARK5 (IC_{50}=64 nM). LY2606368 requires CDC25A and CDK2 to cause DNA damage[1].

Prexasertib (33, 100 nM; for 7 hours) results in DNA damage during S-phase in HeLa cells[1].

Prexasertib (8-250 nM; pre-treated for 15 minutes) inhibits CHK1 autophosphorylation (S296) and CHK2 autophosphorylation (S516) in HT-29 cells[1].

Prexasertib (4 nM; 24 hours) results in a large shift in cell-cycle populations from G1 and G2-M to S-phase with an accompanied induction of H2AX phosphorylation in U-2 OS cells[1].

Prexasertib (33 nM; for 12 hours) causes chromosomal fragmentation in HeLa cells. Prexasertib (100 nM; 0.5 to 9 hours) induces replication stress and depletes the pool of available RPA2 for binding to DNA[1].

In Vivo: Prexasertib (LY2606368; 1-10 mg/kg; SC; twice daily for 3 days, rest 4 days; for three cycles) causes growth inhibition in tumor xenografts[1].

Prexasertib (15 mg/kg; SC) causes CHK1 inhibition in the blood and the phosphorylation of both H2AX (S139) and RPA2 (S4/S8)[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [2]Proliferation inhibition effect of Chk1 ablation, IR sensitivity, anticancer effect of BMN673 and Prexasertib are detected by MTS Cell Proliferation Colorimetric Assay Kit. Cells are seeded into 96 wells cell culture plate, then treated with indicated experiment conditions, then added 20 μL MTS reagent to each well subsequently, after incubated for 2 hours, cell viability of each well is detected on microplate reader at a wavelength of 490 nM[2]. **Animal Administration:** LY2606368 is formulated in vehicle consisting of 20% Captisol[1].[1]Female CD-1 nu-/nu- mice (26-28 g) are used for this study. Tumor growth is initiated by subcutaneous injection of 1×10^6 Calu-6 cells in a 1:1 mixture of serum-free growth medium and Matrigel in the rear flank of each subject animal. When tumor volumes reach approximately 150 mm^3 in size, the animals are randomized by tumor size and body weight, and placed into their respective treatment groups. Vehicle consisting of 20% Captisol pH4 or Prexasertib is administered by subcutaneous injection in a volume of 200 μL. Four, eight, 12, 24, and 48 hours after drug administration, blood for plasma drug exposure is extracted. The xenograft tissue is promptly removed and prepared. Lysates are analyzed by immunoblot analysis for protein phosphorylation levels. Group means, SEs and P values are calculated using Kronos.

References:

[1]. King C, et al. LY2606368 Causes Replication Catastrophe and Antitumor Effects through CHK1-Dependent Mechanisms. Mol Cancer Ther. 2015 Sep;14(9):2004-1

[2]. Yin Y, et al. Chk1 inhibition potentiates the therapeutic efficacy of PARP inhibitor BMN673 in gastric cancer. Am J Cancer Res. 2017 Mar 1;7(3):473-483.

CAIndexNames:

2-Pyrazinecarbonitrile, 5-[[5-[2-(3-aminopropoxy)-6-methoxyphenyl]-1H-pyrazol-3-yl]amino]-

SMILES:

NCCCOC(C=CC=C1OC)=C1C2=CC(NC3=NC=C(C#N)N=C3)=NN2

Tel: 610-426-3128 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA