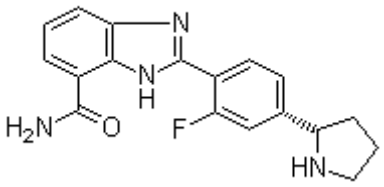
Product Introduction

A-966492

A-966492 is a novel and potent inhibitor of **PARP1** and **PARP2** with K_i of 1 nM and 1.5 nM, respectively.

Technical Data:

Molecular Weight (MW):	324.35	
Formula:	$C_{18}H_{17}FN_4O$	
Solubility (25℃) * <1 mg/ml means slightly soluble or insoluble:	DMSO 65 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃ Powder	
	6 months-80℃ in DMSO	
CAS No.:	934162-61-5	

Biological Activity

A-966492 is one of the most potent PARP inhibitors. A-966492 displays excellent potency against the PARP-1 enzyme with a Kiof 1 nM and an EC50 of 1 nM in a whole cell assay. A-966492 significantly enhances the efficacy of TMZ in a dose-dependent manner. In addition, A-966492 is orally bioavailable across multiple species, crosses the blood–brain barrier, and appears to distribute into tumor tissue. A-966492 represents a promising, structurally diverse benzimidazole analogue and is being further characterized preclinically. [1]

A-966492 also demonstrates good in vivo efficacy in a B16F10 subcutaneous murine melanoma model in combination with temozolomide and in an MX-1 breast cancer xenograft model both as a single agent and in combination with carboplatin. In addition, A-966492 has excellent pharmaceutical properties and has demonstrated in vivo efficacy in preclinical mouse tumor models in combination with TMZ and carboplatin, as well as single agent activity in a BRCA1-deficient MX-1 tumor model. A-966492 is further characterized in Sprague−Dawley rats, beagle dogs, and cynomolgus monkeys, with A-966492 demonstrating oral bioavailabilities of 34−72% and half-lives of 1.7−1.9 hours. In vivo, A-966492 demonstrates significant enhancement of the efficacy of TMZ in a murine B16F10 syngeneic melanoma model, with the A-966492 combination groups showing superior efficacy. [1]

A promising, structurally diverse benzimidazole analogue that is being further characterized preclinically.

References

[1] Penning TD, et al. J Med Chem, 2010, 53(8), 3142-53.