Product Data Sheet

Product Name: RN486
Cat. No.: GC11230

Chemical Properties

Cas. No.	1242156-23-5		
Chemical Name	6-cyclopropyl-8-fluoro-2-[2-(hydroxymethyl)-3-[1-methyl-5-[[5-(4-methylpiperazin-1-yl)pyridin-2-yl]amino]-6-oxopyridin-3-yl]phenyl]isoquinolin-1-one		
SMILES	CN1CCN(CC1)C2=CN=C(C=C2)NC3=CC(=CN(C3=O)C)C4=C(C(=CC=C4)N5C=CC6=CC(=CC(=C6C5=O)F)C7CC7)CO		
Formula	$C_{35}H_{35}FN_6O_3$	M.Wt	606.69
Solubility	≥ 30.35mg/mL in DMSO with gentle warming	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

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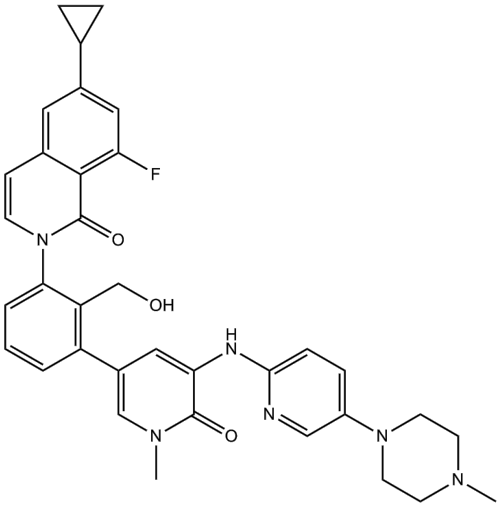
Structure



Background

RN486 is a reversible inhibitor of Btk with IC50 value of 4.0 nM [1].
Bruton's tyrosine kinase (Btk) is a type of kinase protein which is expressed by immune system-related cells (B-lymphocyte, monocytes, macrophages, neutrophils and mast cells) and plays a pivotal role in cell differentiation and proliferation at the transition from pre-B to later B cell stages as well as in the process of both BCR and FcR signaling [2]. It has been reported that aberrant BCR signaling is associated with autoimmune diseases, for example, rheumatoid arthritis (RA) [3].
RN486 is a selective Btk inhibitor. When tested with human Ramos B cells or whole blood, RN486 treatment reduced the expression of CD69/B cells proliferation and IgG production by blocking BCR and FcR Signaling [1].
In NZB × NZW mouse model with systemic lupus erythematosus (SLE), compared with control group, RN486 treatment completely stopped disease progression by inhibiting BTK signaling and targeting

other autoantibody-producing and effector cells [4]. In a PCA (type I hypersensitivity) mouse model or rPCA (type III hypersensitivity) mouse model, RN486 treatment significantly inhibited inflammatory response. In mouse model of RA, administration of RN486 orally could reduce both paw swelling and inflammatory markers in the blood by inhibiting both joint and systemic inflammation alone or in combination with methotrexate [1].

RN486 may also play a pivotal role in reducing immune complex-mediated activation of human monocytes and down-regulating the expression of macrophage-related and interferon-inducible genes [4].

References:

[1]. Xu, D., et al., RN486, a selective Bruton's tyrosine kinase inhibitor, abrogates immune hypersensitivity responses and arthritis in rodents. J Pharmacol Exp Ther, 2012. 341(1): p. 90-103.

[2]. Kil, L.P., et al., Btk levels set the threshold for B-cell activation and negative selection of autoreactive B cells in mice. Blood, 2012. 119(16): p. 3744-56.

[3]. Hartkamp, L.M., et al., Btk inhibition suppresses agonist-induced human macrophage activation and inflammatory gene expression in RA synovial tissue explants. Ann Rheum Dis, 2014.

[4]. Mina-Osorio, P., et al., Suppression of glomerulonephritis in lupus-prone NZB x NZW mice by RN486, a selective inhibitor of Bruton's tyrosine kinase. Arthritis Rheum, 2013. 65(9): p. 2380-91.