Syk Inhibitors
(inhibitors, agonists and modulators)

Spleen tyrosine kinase (Syk) is a cytoplasmic protein tyrosine kinase well known for its ability to couple immune cell receptors to intracellular signaling pathways that regulate cellular responses to extracellular antigens and antigen–immunoglobulin (Ig) complexes of particular importance to the initiation of inflammatory responses. Thus, Syk is an attractive target for therapeutic kinase inhibitors designed to ameliorate the symptoms and consequences of acute and chronic inflammation.
**R406 - CAS 841290-80-0**

**Catalog Number:** B0084-051786  
**Price:** $198/25 mg

**Molecular Weight:** 470.45  
**Molecular Formula:** C22H23FN6O5

**Description:** R406 is a potent inhibitor of immunoglobulin E (IgE)- and IgG-mediated activation of Fc receptor signaling (EC50 for degranulation=56-64 nM). The primary target for R406 is the spleen tyrosine kinase (Syk). R406 inhibited phosphorylation of Syk substrate linker for activation of T cells in mast cells and B-cell linker protein/SLP65 in B cells. R406 bound to the ATP binding pocket of Syk and inhibited its kinase activity as an ATP-competitive inhibitor (K(i)=30 nM). Furthermore, R406 blocked Syk-dependent FcR-mediated activation of monocytes/macrophages and neutrophils and BCR-mediated activation of B lymphocytes. R406 is orally bioavailable, achieving exposures capable of inhibiting Syk-dependent IgE-mediated basophil activation. Collectively, the results show R406 potential for modulating Syk activity in human disease.

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**FF-10102-01**

**Catalog Number:**

**Molecular Weight:**

**Molecular Formula:**

**Description:** FF-10102-01 is a novel and selective inhibitor of spleen tyrosine kinase (Syk). Syk plays a role in downstream pathways in signaling from B-cell receptor (BCR) in B cells and Fc-gamma receptors in macrophages. FF-10102-01 exhibits an inhibitory effect on the phosphorylation of SLP76 and ERK1/2 in THP-1 cells, and on inflammation as well as thrombocytopenia. FF-10102-01 is promisingly to be a drug used for the treatment of autoimmune disease.

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**R-932348 - CAS 916742-11-5**

**Catalog Number:**

**Molecular Weight:** 483.52  
**Molecular Formula:** C23H22FN5O4S

**Description:** A dual JAK/SYK inhibitor that can be used to treat diseases and disorders of the eye.
**TAK-659 hydrochloride - CAS 1952251-28-3**

Catalog Number:  
Molecular Weight: 380.85  
Molecular Formula: C17H22ClFN6O  
Description: TAK-659 hydrochloride is a hydrochloride salt of TAK-659 which is a potent spleen tyrosine kinase (syk) inhibitor (IC50= 3.2 nM) under the development of Takeda Oncology, with potential anti-inflammatory, immunomodulating, and antineoplastic activities.

**OXSI 2 - CAS 622387-85-3**

Catalog Number:  
Molecular Weight: 353.39  
Molecular Formula: C18H15N3O3S  
Description: OXSI 2 is a Syk kinase inhibitor with IC50 value of 14 nM. OXSI-2 can inhibit inflammasome assembly, caspase-1 activation, IL-1β processing and release, mitochondrial ROS generation, and pyroptotic cell death.

**ER 27319 maleate - CAS 1204480-26-1**

Catalog Number:  
Molecular Weight: 396.17  
Molecular Formula: C18H20N2O.C4H4O4  
Description: ER 27319 maleate is a selective Syk kinase inhibitor. It suppresses tyrosine phosphorylation of Syk initiated by the engagement of FcεRI in rat and human mast cells, causing the abrogation of degranulation, TNF-α production (IC50 = 10 μM) and other related signaling events.

**Piceatannol - CAS 10083-24-6**

Catalog Number: 10083-24-6  
Molecular Weight: 244.24  
Molecular Formula: C14H12O4  
Description: Piceatannol, a natural stilbene, is a selective Syk inhibitor and ~10-fold selectivity versus Lyn.
**R788 disodium hexahydrate - CAS 914295-16-2**

**Catalog Number:** 914295-16-2  
**Molecular Weight:** 624.42  
**Molecular Formula:** C23H24FN6Na2O9P  
**Description:** R788 sodium salt hydrate, a methylene phosphate prodrug of the active metabolite R406, is a potent Syk inhibitor. It can be rapidly converted to R406 in vivo. It effectively inhibits BCR signaling in vivo, resulting in reduced proliferation and survival of the malignant B cells and significantly prolonged survival of the treated animals.

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**Fostamatinib sodium - CAS 1025687-58-4**

**Catalog Number:** 1025687-58-4  
**Molecular Weight:** 624.42  
**Molecular Formula:** C23H24FN6O9P.2Na  
**Description:** R788 (Fostamatinib) disodium, a prodrug of the active metabolite R406, is a Syk inhibitor with IC50 of 41 nM, strongly inhibits Syk but not Lyn, 5-fold less potent to Flt3. Phase 3.

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**R406 - CAS 841290-81-1**

**Catalog Number:** 841290-81-1  
**Molecular Weight:** 628.63  
**Molecular Formula:** C28H29FN6O8S  
**Description:** R406 is a potent Syk inhibitor with IC50 of 41 nM, strongly inhibits Syk but not Lyn, 5-fold less potent to Flt3.

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**BAY 61-3606 - CAS 732983-37-8**

**Catalog Number:** 732983-37-8  
**Molecular Weight:** 390.4  
**Molecular Formula:** C20H18N6O3  
**Description:** BAY 61-3606 is a potent, ATP-competitive, reversible, and highly selective inhibitor of Syk tyrosine kinase activity with no inhibitory effect against Btk, Fyn, Itk, Lyn, and Src.
Fostamatinib - CAS 901119-35-5

Catalog Number: 901119-35-5

Molecular Weight: 580.46  Molecular Formula: C23H26FN6O9P

Description: Fostamatinib, a prodrug of the active metabolite R406, is a Syk inhibitor with IC50 of 41 nM, strongly inhibiting Syk but not Lyn, and 5-fold less potent to Flt3.

PRT062607 - CAS 1370261-96-3

Catalog Number: 1370261-96-3

Molecular Weight: 393.45  Molecular Formula: C19H23N9O

Description: Highly specific and potent inhibitor of spleen tyrosine kinase (Syk) (IC50: 1-2 nM)

P505-15 - CAS 1370261-97-4

Catalog Number: 1370261-97-4

Molecular Weight: 429.913  Molecular Formula: C19H23N9O.HCl

Description: P505-15, also known as PRT2607, PRT062607, and BiliB057, is a novel, highly selective, and orally bioavailable small molecule SYK inhibitor (SYK IC(50) = 1 nM) with anti-SYK activity that is at least 80-fold greater than its affinity for other kinases. P505-15 successfully inhibited SYK-mediated B-cell receptor signaling and decreased cell viability in NHL and CLL. Oral dosing in mice prevented BCR-mediated splenomegaly and significantly inhibited NHL tumor growth in a xenograft model. In addition, combination treatment of primary CLL cells with P505-15 plus fludarabine produced synergistic enhancement of activity at nanomolar concentrations. P505-15 may be a therapeutic agent for B-cell malignancies. A dose finding study in healthy volunteers has been completed.
**R112 - CAS 575474-82-7**

**Catalog Number:** 575474-82-7  
**Molecular Weight:** 312.3  
**Molecular Formula:** C16H13FN4O2  
**Description:** R112 is a Syk inhibitor. R112 inhibited degranulation induced by anti-IgE cross-linking in mast cells (tryptase release, effective concentration for 50% inhibition [EC(50)] = 353 nmol/L) or basophils (histamine release, EC(50) = 280 nmol/L), and by allergen (dust mite) in basophils (histamine release, EC(50) = 490 nmol/L). R112 also blocked leukotriene C4 production and all proinflammatory cytokines tested. Subsequent molecular characterization indicated that R112 is an ATP-competitive spleen tyrosine kinase (Syk) inhibitor (inhibitory constant [K(i)] = 96 nmol/L). R112 was able to completely inhibit all three IgE-induced mast cell functions: degranulation, lipid mediator production, and cytokine production. R112 and its analogues offer a new modality in the treatment of allergic rhinitis.

**BAY 61-3606 dihydrochloride - CAS 648903-57-5**

**Catalog Number:** 648903-57-5  
**Molecular Weight:** 463.32  
**Molecular Formula:** C20H18N6O3.2HCl  
**Description:** BAY 61-3606 is a potent, ATP-competitive, reversible, and highly selective inhibitor of Syk tyrosine kinase activity with no inhibitory effect against Btk, Fyn, Itk, Lyn, and Src.

**Entospletinib - CAS 1229208-44-9**

**Catalog Number:** 1229208-44-9  
**Molecular Weight:** 411.46  
**Molecular Formula:** C23H21N7O  
**Description:** Entospletinib (GS-9973) is an orally bioavailable, selective Syk inhibitor with IC50 of 7.7 nM. Phase 2.