HIF/HIF Prolyl-Hydroxylase Inhibitors (inhibitors, agonists and modulators)

Hypoxia-inducible factors (HIFs) are transcription factors that respond to decreases in available oxygen in the cellular environment, or hypoxia. HIF prolyl-hydroxylase is an enzyme involved in the HIF (Hypoxia-inducible factor) signalling pathways, and is the target for a set of therapeutic drugs called HIF prolyl-hydroxylase inhibitors.
Chlorogenic Acid - CAS 327-97-9

**Catalog Number:** B0084-066176  
**Price:** $288/100 g

**Molecular Weight:** 354.31  
**Molecular Formula:** C16H18O9

**Description:** Chlorogenic acid is a hydroxycinnamic acid and a member of a family of naturally occurring organic compounds. Chlorogenic acid exhibits an anti-inflammatory effect, and reduce blood pressure. Nutritional supplement in health care products.

Roxadustat (FG-4592) - CAS 808118-40-3

**Catalog Number:** B0084-438323  
**Price:** $198/500 mg

**Molecular Weight:** 352.34  
**Molecular Formula:** C19H16N2O5

**Description:** Roxadustat (FG-4592) is an HIF α prolyl hydroxylase inhibitor, stabilizes HIF-2 and induces EPO production.

Molidustat - CAS 1154028-82-6

**Catalog Number:** B0084-462731  
**Price:** $198/50 mg

**Molecular Weight:** 314.309  
**Molecular Formula:** C13H14N8O2

**Description:** Molidustat is a novel inhibitor of hypoxia-inducible factor (HIF) prolyl hydroxylase (PH) which stimulates erythropoietin (EPO) production and the formation of red blood cells. Phase I data have shown that inhibition of HIF-PH by Molidustat results in an increase in endogenous production of EPO. Molidustat is undergoing clinical trials at Bayer for the treatment of patients suffering from renal anemia due to chronic kidney disease.

MK-8617 - CAS 1187990-87-9

**Catalog Number:**

**Molecular Weight:** 443.45  
**Molecular Formula:** C24H21N5O4

**Description:** MK-8617 is a potent and selective pan-inhibitor of Hypoxia-inducible factor prolyl hydroxylase 1−3 (HIF PHD1−3) (PHD1: IC50 = 1.0 nM; PHD2: IC50 =1.0nM; PHD3: IC50 = 14nM) commonly used for the treatment of Anemia, a disease caused by inadequate red blood cells (RBCs) or hemoglobin (Hb).
Chetomin - CAS 1403-36-7

Catalog Number:
Molecular Weight: 710.87  Molecular Formula: C31H30N6O6S4

Description: Chetomin is a natural metabolite produced by several species of the genus chaetomium. It is an epidithiodioxopiperazine and is an inhibitor of hypoxia-inducible factor (HIF). It inhibits interaction of HIF1α and HIF2α with transcriptional co-activators p300 and cAMP response element binding (CREB) protein (CBP). It decreases tumor growth by attenuating hypoxia-inducible transcription and disrupting the ability of tumors to adapt to hypoxia. It also suppresses the proliferation of LPS-induced mouse spleen lymphocytes. It may be used as an antibacterial agent and is used in antitumor research. It also may be useful in radiotherapeutic.

HIF Phd Inhibitor 4 - CAS 1227946-51-1

Catalog Number:
Molecular Weight: 472.9  Molecular Formula: C21H17ClN4O5S

Description: An inhibitor of the Hypoxia Inducible Factor (HIF) Prolyl-Hydroxylases (PHD).

2-methoxyestradiol - CAS 362-07-2

Catalog Number: 362-07-2
Molecular Weight: 302.414  Molecular Formula: C19H26O3

Description: 2-methoxyestradiol, also known as 2-ME, is an orally bioavailable estradiol metabolite with potential antineoplastic activity. 2-Methoxyestradiol inhibits angiogenesis by reducing endothelial cell proliferation and inducing endothelial cell apoptosis. This agent also inhibits tumor cell growth by binding to tubulin, resulting in antimitotic activity, and by inducing caspase activation, resulting in cell cycle arrest in the G2 phase, DNA fragmentation, and apoptosis.

Oltipraz - CAS 64224-21-1

Catalog Number: 64224-21-1
Molecular Weight: 226.33  Molecular Formula: C8H6N2S3

Description: Oltipraz, a promising cancer chemopreventive agent, is a bifunctional inducer, modulating both phase I and II drug-metabolizing enzymes to enhance carcinogen detoxification.
**DMOG - CAS 89464-63-1**

**Catalog Number:** 89464-63-1  
**Molecular Weight:** 175.14  
**Molecular Formula:** C₆H₉NO₅  
**Description:** DMOG is an antagonist of α-ketoglutarate cofactor and inhibitor for HIF prolyl hydroxylase.

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**Adaptaquin - CAS 385786-48-1**

**Catalog Number:**  
**Molecular Weight:** 377.82  
**Molecular Formula:** C₂₁H₁₆ClN₃O₂  
**Description:** Adaptaquin is an inhibitor of hypoxia-inducible factor (HIF) prolyl hydroxylase 2 (PHD2) with IC₅₀ value of 2 μM in a reporter assay using SH-SY5Y-ODD-Luc cells. It displays neuroprotective effects and enhances functional recovery in rodent intracerebral hemorrhage models by inhibition of ATF4 dependent genes. It reduces neuronal death and behavioral deficits after intracerebral hemorrhage (ICH) in several rodent models. It blocks glutamate induced ROS production in HT-22 cells, independent of MnSOD. It stabilizes HIF-1α protein and induces expression of the HIF1-regulated genes EPO and VEGF in SH-SYSY human neuroblastoma cells. It is used in ischemic injury research, renal anemia, and used as an antioxidant. It is also used in pyruvate dehydrogenase (PDH) related research.

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**TAT-cyclo-CLLFVY - CAS 1446322-66-2**

**Catalog Number:**  
**Molecular Weight:** 2559.10  
**Molecular Formula:** C₁₁₁H₁₈₈N₄₂O₂₄S₂  
**Description:** TAT-cyclo-CLLFVY has been found to be a HIF-1 dimerization inhibitor and could block protein-protein interaction of recombinant HIF-1α.

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**TC-S 7009 - CAS 1422955-31-4**

**Catalog Number:**  
**Molecular Weight:** 308.65  
**Molecular Formula:** C₁₂H₆ClFN₄O₃  
**Description:** TC-S 7009 is a high affinity and selective HIF-2α inhibitor (Kᵋ = 81 nM) that displays ≈60-fold selectivity for HIF-2α over HIF-1α. TC-S 7009 binds to the HIF-2α PAS-B domain to disrupt HIF-2α-ARNT heterodimerization, decrease HIF-2α DNA-binding and suppress expression of HIF-2α target genes in vitro.
## PX-478 - CAS 685898-44-6

**Catalog Number:** 685898-44-6  
**Molecular Weight:** 394.114  
**Molecular Formula:** C13H20Cl4N2O3  
**Description:** PX-478 is HIF-1alpha inhibitor, is also an orally active small molecule with potential antineoplastic activity. Although its mechanism of action has yet to be fully elucidated, HIF1-alpha inhibitor PX-478 appears to inhibit hypoxia-inducible factor 1-alpha (HIF1A) expression, which may result in decreased expression of HIF1A downstream target genes important to tumor growth and survival, a reduction in tumor cell proliferation, and the induction of tumor cell apoptosis. The inhibitory effect of this agent is independent of the tumor suppressor genes VHL and p53 and may be related to derangements in glucose uptake and metabolism due to inhibition of glucose transporter-1 (Glut-1). PX-478 has excellent activity against established human tumor xenografts, providing tumor regressions with prolonged growth delays which correlate positively with HIF-1 levels. PX-478 is a highly water soluble molecule, with good i.v., i.p. and p.o. antitumor activity. It is rapidly absorbed following oral and i.p. administration and gives excellent Cmax and AUC via these routes.

![PX-478 molecular structure]

## IOX2 - CAS 931398-72-0

**Catalog Number:** 931398-72-0  
**Molecular Weight:** 352.346  
**Molecular Formula:** C19H16N2O5  
**Description:** IOX2 is a specific prolyl hydroxylase-2 (PHD2) inhibitor with IC50 of 22 nM.

![IOX2 molecular structure]

## ML228 - CAS 1357171-62-0

**Catalog Number:** 1357171-62-0  
**Molecular Weight:** 415.49  
**Molecular Formula:** C27H21N5  
**Description:** HIF pathway activator (EC50 values are 1.23 and 1.4 μM for HRE gene reporter assay and HIF-1α nuclear translocation assay respectively); acts via chelation of iron, independently of PHD. Also exhibits > 80% inhibition of the human A3 receptor, dopamine transporter, μ receptor, hERG and 5-HT2B receptor, and rat sodium channel site 2, at a concentration of 10 μM.

![ML228 molecular structure]
**BAY 87-2243 - CAS 1227158-85-1**

**Catalog Number:** 1227158-85-1  
**Molecular Weight:** 525.53  
**Molecular Formula:** C26H26F3N7O2  
**Description:** BAY 87-2243 inhibits HIF-1 reporter gene activity and CA9 protein expression with IC50 of 0.7 nM and 2 nM, respectively.

**JNJ-42041935 - CAS 1193383-09-3**

**Catalog Number:** 1193383-09-3  
**Molecular Weight:** 346.65  
**Molecular Formula:** C12H6ClF3N4O3  
**Description:** JNJ-42041935 is a potent (pK(I) = 7.3-7.9), 2-oxoglutarate competitive, reversible, and selective inhibitor of PHD enzymes. JNJ-42041935 is a new pharmacological tool, which can investigate PHD inhibition and demonstrate that PHD inhibitors offer great promise for the treatment of inflammation-induced anemia.

**DASA-58 - CAS 1203494-49-8**

**Catalog Number:** 1203494-49-8  
**Molecular Weight:** 453.53  
**Molecular Formula:** C19H23N3O6S2  
**Description:** DASA-58 is a specific and potent Pyruvate kinase M2 (PKM2) activator.

**FG-2216 - CAS 223387-75-5**

**Catalog Number:** 223387-75-5  
**Molecular Weight:** 280.66  
**Molecular Formula:** C12H9ClN2O4  
**Description:** FG-2216, also known as YM311, is orally bioavailable HIF-prolyl hydroxylase inhibitor. FG-2216 induced significant and reversible Epo induction in vivo.

**KC7F2 - CAS 927822-86-4**

**Catalog Number:** 927822-86-4  
**Molecular Weight:** 570.38  
**Molecular Formula:** C16H16Cl4N2O4S4  
**Description:** KC7F2 is a selective HIF-1α transcription inhibitor with IC50 of 20 μM in a cell-based assay.
**Daprodustat - CAS 960539-70-2**

**Catalog Number:** 960539-70-2  
**Molecular Weight:** 393.44  
**Molecular Formula:** C19H27N3O6  
**Description:** Daprodustat, also known as GSK1278863, is a novel HIF-prolyl hydroxylase inhibitor. Hypoxia inducible factor (HIF) stabilization by HIF-prolyl hydroxylase (PHD) inhibitors may improve ischemic conditions such as peripheral artery disease (PAD).

**THS-044 - CAS 62054-67-5**

**Catalog Number:** 62054-67-5  
**Molecular Weight:** 291.23  
**Molecular Formula:** C11H12F3N3O3  
**Description:** THS-044 binding stabilizes the HIF2α PAS-B folded state, for regulating HIF2 activity in endogenous and clinical settings.

**PT-2385 - CAS 1672665-49-4**

**Catalog Number:** 1672665-49-4  
**Molecular Weight:** 383.34  
**Molecular Formula:** C17H12F3NO4S  
**Description:** PT-2385 is a small molecule inhibitor with oral activity that inhibits hypoxia inducible factor (HIF)-2alpha heterodimerization and its subsequent binding to DNA by binding to HIF-2alpha.