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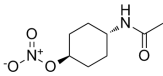
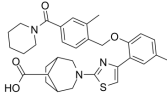
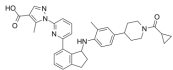
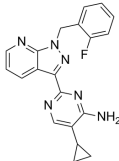
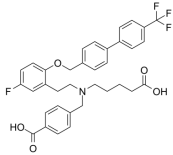
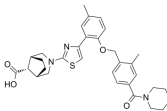
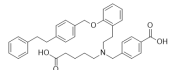
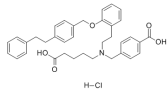
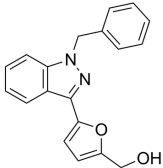
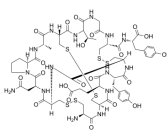
Inhibitors, Agonists, Screening Libraries

# Guanylate Cyclase

Guanylatecyclase (guanylylcyclase, GC) is a lyase enzyme. Guanylylcyclase is often part of the G protein signaling cascade that is activated by low intracellular calcium levels and inhibited by high intracellular calcium levels. In response to calcium levels, guanylylcyclase synthesizes cGMP from GTP. cGMP keeps cGMP-gated channels open, allowing for the entry of calcium into the cell. The guanylylcyclase activity is modulated by the calcium-binding guanylylcyclase activating proteins (GCAP1 and GCAP2). A key mechanism by which  $\text{Ca}^{2+}$  modulates phototransduction in rods involves the synthesis of cGMP by guanylylcyclase (GC), regulated by a pair of  $\text{Ca}^{2+}$ -binding GuanylylCyclase Activating Proteins (GCAP1 and GCAP2).

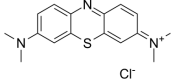
The second messenger cyclic guanosine monophosphate (cGMP) is generated by the heterodimeric  $\alpha/\beta$ -heme protein soluble guanylatecyclase (sGC) upon activation by its endogenous ligand nitric oxide (NO). NO binds to the reduced prosthetic heme group bound to the  $\beta$  subunit. cGMP is a key mediator of the cardiovascular system and its effects lead to vasodilation, inhibition of smooth muscle proliferation, blockade of leukocyte infiltration and inhibition of platelet aggregation. Impairment of the cytoprotective NO/sGC/cGMP-signalling pathway is associated with the development of serious cardiovascular diseases such as hypertension or heart failure.

## Guanylate Cyclase Inhibitors, Agonists & Activators

<p><b>(4-Acetamidocyclohexyl) nitrate</b> (BM121307)</p> <p>Cat. No.: HY-100295</p>	<p><b>(Rac)-BI 703704</b></p> <p>Cat. No.: HY-117962</p>
<p>(4-Acetamidocyclohexyl) nitrate (BM121307) is a <b>guanylate cyclase</b> activator.</p>  <p><b>Purity:</b> &gt;98% <b>Clinical Data:</b> No Development Reported <b>Size:</b> 1 mg, 5 mg</p>	<p>(Rac)-BI 703704 is a potent <b>soluble guanylyl cyclase (sGC)</b> activator. (Rac)-BI 703704 reduces progression of renal damage in the ZSF1 rat, and highlight the potential of sGC activation as an effective therapy for diabetic nephropathy.</p>  <p><b>Purity:</b> &gt;98% <b>Clinical Data:</b> No Development Reported <b>Size:</b> 1 mg, 5 mg</p>
<p><b>(Rac)-MGV354</b></p> <p>Cat. No.: HY-117917</p>	<p><b>BAY 41-2272</b></p> <p>Cat. No.: HY-12376</p>
<p>(Rac)-MGV354 is the racemate of MGV354. MGV354 is a soluble guanylate cyclase (sGC) activator with EC<sub>50</sub>s of &lt;0.5 nM, and 5 nM in CHO and GTM-3 E cells, respectively.</p>  <p><b>Purity:</b> &gt;98% <b>Clinical Data:</b> No Development Reported <b>Size:</b> 1 mg, 5 mg</p>	<p>BAY 41-2272 is a soluble guanylate cyclases (sGC) activator.</p>  <p><b>Purity:</b> 99.97% <b>Clinical Data:</b> No Development Reported <b>Size:</b> 10 mM × 1 mL, 5 mg, 10 mg, 25 mg, 50 mg, 100 mg</p>
<p><b>BAY 60-2770</b></p> <p>Cat. No.: HY-113926</p>	<p><b>BI 703704</b></p> <p>Cat. No.: HY-117962A</p>
<p>BAY 60-2770 is a potent, selective, and orally active <b>soluble guanylyl cyclase (sGC)</b> activator. BAY 60-2770 increases the activity of sGC in a nitric oxide-independent manner. BAY 60-2770 shows antifibrotic effect.</p>  <p><b>Purity:</b> &gt;98% <b>Clinical Data:</b> No Development Reported <b>Size:</b> 1 mg, 5 mg</p>	<p>BI 703704 is a potent <b>soluble guanylate cyclase (sGC)</b> activator. BI 703704 inhibits the progression of diabetic nephropathy in the ZSF1 rat.</p>  <p><b>Purity:</b> &gt;98% <b>Clinical Data:</b> No Development Reported <b>Size:</b> 1 mg, 5 mg</p>
<p><b>Cinaciguat</b> (BAY 58-2667)</p> <p>Cat. No.: HY-14181</p>	<p><b>Cinaciguat hydrochloride</b> (BAY 58-2667 hydrochloride)</p> <p>Cat. No.: HY-14181A</p>
<p>Cinaciguat is an activator of <b>guanylate cyclase (sGC)</b>, and used for acute decompensated heart failure.</p>  <p><b>Purity:</b> 99.40% <b>Clinical Data:</b> Phase 2 <b>Size:</b> 10 mM × 1 mL, 2 mg, 5 mg, 10 mg, 50 mg</p>	<p>Cinaciguat hydrochloride is a potent soluble <b>guanylate cyclase (GC)</b> activator with EC<sub>50</sub> of 15 nM in platelets.</p>  <p><b>Purity:</b> 99.64% <b>Clinical Data:</b> Phase 2 <b>Size:</b> 10 mM × 1 mL, 2 mg, 5 mg, 10 mg, 50 mg</p>
<p><b>Lifiguat</b> (YC-1)</p> <p>Cat. No.: HY-14927</p>	<p><b>Linaclotide</b></p> <p>Cat. No.: HY-17584</p>
<p>Lifiguat binds to the β subunit of <b>soluble guanylyl cyclase (sGC)</b> with K<sub>d</sub> of 0.6-1.1 μM in the presence of CO.</p>  <p><b>Purity:</b> 99.83% <b>Clinical Data:</b> No Development Reported <b>Size:</b> 10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg, 200 mg</p>	<p>Linaclotide is a potent and selective <b>guanylate cyclase C</b> agonist; developed for the treatment of constipation-predominant irritable bowel syndrome (IBS-C) and chronic constipation.</p>  <p><b>Purity:</b> 98.18% <b>Clinical Data:</b> Launched <b>Size:</b> 10 mM × 1 mL, 5 mg, 10 mg</p>

**Methylene Blue**  
(Basic Blue 9; Methylthionium chloride; CI-52015) Cat. No.: HY-14536

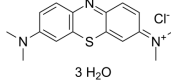
Methylene blue (Basic Blue 9) is a **guanylyl cyclase (sGC), monoamine oxidase A (MAO-A) and NO synthase (NOS) inhibitor**. Methylene blue is a vasopressor and is often used as a dye in several medical procedures.



**Purity:** >98.0%  
**Clinical Data:** Launched  
**Size:** 100 mg, 500 mg

**Methylene blue trihydrate**  
(C.I. Basic Blue 9 trihydrate) Cat. No.: HY-B1359

Methylene blue trihydrate (C.I. Basic Blue 9 trihydrate) is a **guanylyl cyclase (sGC), monoamine oxidase A (MAO-A) and NO synthase (NOS) inhibitor**. Methylene blue trihydrate is a vasopressor and is often used as a dye in several medical procedures.



**Purity:** >97.0%  
**Clinical Data:** Launched  
**Size:** 10 mM × 1 mL, 500 mg, 1 g

**MGV354** Cat. No.: HY-111516

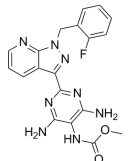
MGV354 is a **soluble guanylate cyclase (sGC) activator** with  $EC_{50}$ s of <0.5 nM, and 5 nM in CHO and GTM-3 E cells, respectively.



**Purity:** >98%  
**Clinical Data:** No Development Reported  
**Size:** 1 mg, 5 mg

**Nelociguat**  
(BAY60-4552) Cat. No.: HY-78237

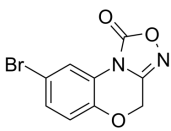
Nelociguat (BAY60-4552) is a nitric oxide sensitive soluble guanylate cyclase stimulator.



**Purity:** 99.73%  
**Clinical Data:** Phase 2  
**Size:** 10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg, 200 mg

**NS-2028** Cat. No.: HY-12379

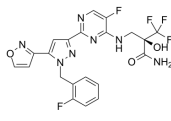
NS-2028 is a highly selective soluble Guanylyl Cyclase (sGC) inhibitor with  $IC_{50}$  values of 30 nM and 200 nM for basal and NO-stimulated enzyme activity.



**Purity:** 99.91%  
**Clinical Data:** No Development Reported  
**Size:** 10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg

**Olinciguat**  
(IW-1701) Cat. No.: HY-109066

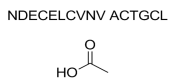
Olinciguat (IW-1701) is an oral **guanylate cyclase (sGC) stimulator** with concentration-dependent stimulation of sGC in purified rat and human enzyme assays and a whole cell assay.



**Purity:** 98.44%  
**Clinical Data:** No Development Reported  
**Size:** 10 mM × 1 mL, 5 mg, 20 mg

**Plecanatide acetate** Cat. No.: HY-108741A

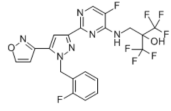
Plecanatide acetate is a **guanylate cyclase-C (GC-C) receptor agonist**, with an  $EC_{50}$  of 190 nM in T84 cells. Plecanatide acetate shows anti-inflammatory activity in models of murine colitis.



**Purity:** 99.26%  
**Clinical Data:** No Development Reported  
**Size:** 10 mM × 1 mL, 5 mg, 10 mg

**Pralinciguat**  
(IW-1973) Cat. No.: HY-109039

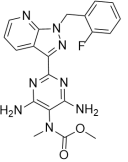
Pralinciguat (IW-1973) is a potent and orally active **soluble guanylate cyclase stimulator**, enhances NO signaling, acts as a vasodilator. Pralinciguat (IW-1973) stimulates sGC in HEK-293 cells with an  $EC_{50}$  of 197 nM.



**Purity:** >98%  
**Clinical Data:** No Development Reported  
**Size:** 5 mg, 10 mg, 50 mg, 100 mg

**Riociguat**  
(BAY 632521) Cat. No.: HY-14779

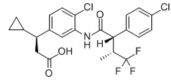
Riociguat is an oral stimulator of soluble guanylate cyclase (sGC) used in the treatment of pulmonary hypertension.



**Purity:** 99.58%  
**Clinical Data:** Launched  
**Size:** 10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg, 200 mg

**Runcaciguat** Cat. No.: HY-109136

Runcaciguat is an orally active stimulator of **soluble guanylate cyclase**, and is used in the research of cardiovascular and renal diseases combined with selective partial adenosine A1 receptor agonists.

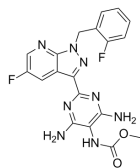


**Purity:** >98%  
**Clinical Data:** No Development Reported  
**Size:** 1 mg, 5 mg

**Vericiguat**  
(BAY1021189)

Cat. No.: HY-16774

Vericiguat (BAY1021189) is a potent, orally available and soluble **guanylate cyclase** stimulator.



**Purity:** 99.09%

**Clinical Data:** Phase 3

**Size:** 10 mM × 1 mL, 2 mg, 5 mg, 10 mg, 50 mg, 100 mg