Integrin

Integrins, a family of heterodimeric adhesion receptors for diverse extracellular matrices, have consistently been implicated as crucial drivers of ovarian cancer development and progression. A number of the RGD-based members of the integrin family, including α5β1, and αvβ3 or αvβ5 integrins, are markedly elevated in aggressive ovarian tumors. These adhesion receptors appear to promote cell adhesion, survival, motility and invasion during ovarian tumor growth or metastatic progression. Importantly, the functions of these integrins are strongly dependent on the activation of focal adhesion kinase (FAK) and its downstream signaling, including the PI3K/Akt- and Ras/MAPK-dependent pathways.

Integrins are transmembrane proteins and are major receptors for cell-extracellular matrix (ECM) and cell-cell adhesion. Modulation of these molecules, particularly αv integrin family, has exhibited profound effects on fibrosis in multiple organ and disease state. Based on the several studies, the integrins αvβ3, αvβ5, αvβ6, and αvβ8 have been known to modulate the fibrotic process via activation of latent transforming growth factor (TGF)-β in pre-clinical models of fibrosis.

Each integrin is typically formed by the non-covalent pairing of one α subunit, of which, 18 types are known to exist, and one β subunit, of which 8 types are known to exist. Together, 24 distinct heterodimers have been identified to date. The αv subunit can form heterodimers with the β1, β3, β5, β6 or β8 subunits and β1 can associate with many different α subunits from α1 to α11, and αv, indicating that not all theoretically possible α and subunit pairs form. Interestingly, the activation of TGF-β appears to be a common function of multiple αv integrins.
Integrin Inhibitors, Antagonists & Modulators

<table>
<thead>
<tr>
<th>Compound</th>
<th>Cat. No.</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Arg-Gly-Asp-Ser</strong>&lt;br&gt;(RGDS peptide; Fibronectin tetrapeptide)</td>
<td>HY-12290</td>
<td>Arg-Gly-Asp-Ser is an integrin binding sequence that inhibits integrin receptor function, decreases systemic inflammation via inhibition of collagen-triggered activation of leukocytes and attenuates expression of inflammatory cytokines, iNOS and MMP-9. Purity: &gt;98.0% Clinical Data: No Development Reported Size: 10 mM × 1 mL, 5 mg, 10 mg, 50 mg</td>
</tr>
<tr>
<td><strong>ATN-161</strong></td>
<td>HY-13535</td>
<td>ATN-161 is a novel integrin α5β1 antagonist, which inhibits angiogenesis and growth of liver metastases in a murine model. Purity: &gt;98% Clinical Data: Phase 2 Size: 5 mg, 10 mg, 50 mg, 100 mg</td>
</tr>
<tr>
<td><strong>ATN-161 trifluoroacetate salt</strong>&lt;br&gt;(ATN-161 TFA salt)</td>
<td>HY-13535A</td>
<td>ATN-161 trifluoroacetate salt is a novel integrin α5β1 antagonist, which inhibits angiogenesis and growth of liver metastases in a murine model. Purity: &gt;95.0% Clinical Data: Phase 2 Size: 5 mg, 10 mg, 50 mg, 100 mg</td>
</tr>
<tr>
<td><strong>BI-1950</strong></td>
<td>HY-124040</td>
<td>BI-1950 is a highly potent lymphocyte function associated antigen-1 (LFA-1) inhibitor. LFA-1 is an essential component in normal immune system function and a target for drug discovery. Purity: &gt;98% Clinical Data: No Development Reported Size: 1 mg, 5 mg</td>
</tr>
<tr>
<td><strong>BMS-688521</strong></td>
<td>HY-10596</td>
<td>BMS-688521 is a highly potent, orally active inhibitor of the LFA-1/ICAM interaction, with an IC50 of 2.5 nM in the adhesion assay and an IC50 of 60 nM in the MLR assay. BMS-688521 is efficacious in a mouse allergic eosinophilic lung inflammation model. Purity: &gt;98% Clinical Data: No Development Reported Size: 10 mM × 1 mL, 5 mg, 10 mg</td>
</tr>
<tr>
<td><strong>c(phg-isoDGR-(NMe)k)</strong></td>
<td>HY-111413</td>
<td>c(phg-isoDGR-(NMe)k) is a selective and potent α5β1-integrin ligand with an IC50 of 2.9 nM. Purity: &gt;98% Clinical Data: No Development Reported Size: 1 mg, 5 mg, 10 mg</td>
</tr>
<tr>
<td><strong>Cilengitide</strong>&lt;br&gt;(EMD 121974)</td>
<td>HY-16141</td>
<td>Cilengitide is a potent and selective integrin inhibitor for α5β1 and αβ4 receptor, with IC50s of 4 and 79 nM, respectively. Purity: 99.06% Clinical Data: Phase 3 Size: 10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg</td>
</tr>
<tr>
<td>Compound</td>
<td>Cat. No.</td>
<td>Purity</td>
</tr>
<tr>
<td>--------------------------------</td>
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</tr>
<tr>
<td>Cucurbitacin B</td>
<td>HY-N0416</td>
<td>99.92%</td>
</tr>
<tr>
<td>CWHM-12</td>
<td>HY-18644</td>
<td>99.65%</td>
</tr>
<tr>
<td>Cyclo(-RGDFk)</td>
<td>HY-P0023</td>
<td>&gt;98.0%</td>
</tr>
<tr>
<td>Cyclo(RADfK)</td>
<td>HY-P0031</td>
<td>98.03%</td>
</tr>
<tr>
<td>Cyclo(RGDyK)</td>
<td>HY-100563A</td>
<td>&gt;98%</td>
</tr>
<tr>
<td>Cyclo(RGDyK) trifluoroacetate</td>
<td>HY-100563</td>
<td>99.13%</td>
</tr>
<tr>
<td>E7820 (ER68203-00)</td>
<td>HY-14571</td>
<td>99.36%</td>
</tr>
<tr>
<td>Eptifibatide</td>
<td>HY-80686</td>
<td>96.49%</td>
</tr>
<tr>
<td>Firategrast</td>
<td>HY-14951</td>
<td>99.66%</td>
</tr>
</tbody>
</table>

Cucurbitacin B belongs to a class of highly oxidized tetracyclic triterpenoids; could repress cancer cell progression.

CWHM-12 is a potent inhibitor of αV integrins with IC₅₀ of 0.2, 0.8, 1.5, and 1.8 nM for αvβ8, αvβ3, αvβ6, and αvβ1.

Cyclo(-RGDFk) is a potent and selective inhibitor of the αβ₃ integrin, with an IC₅₀ of 0.94 nM.

Cyclo(RADfK) is a selective α(v)β(3) integrin ligand that has been extensively used for research, therapy, and diagnosis of neoangiogenesis.

Cyclo(RGDyK) is a potent and selective α(β3) integrin inhibitor with an IC₅₀ of 20 nM.

Cyclo(RGDyK) trifluoroacetate is a potent and selective αvβ₃ integrin inhibitor with an IC₅₀ of 20 nM.

E7820 is an angiogenesis inhibitor by suppressing integrin α2, a cell adhesion molecule expressed on endothelial cells.

Eptifibatide is a cyclic heptapeptide, acts as a competitive antagonist for the activated platelet glycoprotein IIb/IIIa receptor, with anti-platelet activity.

Firategrast is an orally bioavailable α4β1/α4β7 integrin antagonist.
| **Fradafiban**  
(BIBU-52) | **Cat. No.: HY-101720** |
|---|---|
| Fradafiban is a nonpeptide platelet glycoprotein  
IIb/IIIa antagonist, which binds to the human  
platelet GP IIb/IIIa complex with a $K_d$ value of  
148 nM. | |
| Purity: $>98\%$  
Clinical Data: Phase 1  
Size: 1 mg, 5 mg, 10 mg, 20 mg | |

| **GLPG0187**  
| **Cat. No.: HY-100506** |
|---|---|
| GLPG0187 is a broad spectrum integrin receptor  
antagonist with antitumor activity; inhibits  
$\alpha_\beta_3$-integrin with an $IC_{50}$ of 1.3 nM.  
Purity: 98.97%  
Clinical Data: Phase 1  
Size: 10 mM × 1 mL, 1 mg, 5 mg, 10 mg, 50 mg, 100 mg | |

| **Gly-Arg-Gly-Asp-Ser**  
| **Cat. No.: HY-P0295** |
|---|---|
| Gly-Arg-Gly-Asp-Ser is a pentapeptide that forms  
the cell-binding domain of a glycoprotein,  
osteopontin. Gly-Arg-Gly-Asp-Ser binds to integrin  
receptors $\alpha\beta_3$ and $\alpha\beta_5$ with estimated $IC_{50}$ of  
5 and 6.5 μM.  
Purity: 98.12%  
Clinical Data: No Development Reported  
Size: 2 mg, 5 mg, 10 mg, 25 mg | |

| **Gly-Arg-Gly-Asp-Ser (TFA)**  
| **Cat. No.: HY-P0295A** |
|---|---|
| Gly-Arg-Gly-Asp-Ser (TFA) is a pentapeptide that  
forms the cell-binding domain of a glycoprotein,  
osteopontin. Gly-Arg-Gly-Asp-Ser binds to integrin  
receptors $\alpha\beta_3$ and $\alpha\beta_5$ with estimated $IC_{50}$ of  
5 and 6.5 μM.  
Purity: $>98\%$  
Clinical Data:  
Size: 1 mg, 5 mg | |

| **GRGDSP**  
| **Cat. No.: HY-P0290** |
|---|---|
| GRGDSP, a synthetic linear RGD peptide, is an integrin inhibitor. | |
| Purity: $>98\%$  
Clinical Data: No Development Reported  
Size: 1 mg, 5 mg, 10 mg | |

| **GRGDSP TFA**  
| **Cat. No.: HY-P0290A** |
|---|---|
| GRGDSP (TFA) is an integrin inhibitor.  
Purity: 98.53%  
Clinical Data: No Development Reported  
Size: 10 mM × 1 mL, 1 mg, 5 mg, 10 mg | |

| **ILK-IN-2**  
(OSU-T315 analog)  
| **Cat. No.: HY-18676B** |
|---|---|
| ILK-IN-2 (OSU-T315 analog) is an ILK inhibitor. | |
| Purity: $>98.0\%$  
Clinical Data: No Development Reported  
Size: 2 mg, 5 mg, 10 mg | |

| **Integrin Antagonists 27**  
| **Cat. No.: HY-18668** |
|---|---|
| Integrin Antagonists 27 is a small molecule integrin $\alpha\beta_3$ antagonist with binding affinity of 18 nM, as a novel anticancer agent.  
Purity: $>98.0\%$  
Clinical Data: No Development Reported  
Size: 10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg | |

| **Integrin-IN-2**  
| **Cat. No.: HY-130119** |
|---|---|
| Integrin-IN-2 (compound 39) is an orally bioavailable pan $\alpha\beta$ integrin inhibitor. Integrin-IN-2 can increases the $\alpha\beta_6$, $\alpha\beta_3$,  
$\alpha\beta_5$ and $\alpha\beta_8$ binding affinities with $pIC_{50}$ values of 7.8, 8.4, 8.4 and 7.4, respectively.  
Purity: $>98\%$  
Clinical Data: No Development Reported  
Size: 100 mg, 250 mg, 500 mg | |

| **iRGD peptide**  
(c(CRGDKGPDC))  
| **Cat. No.: HY-P0122** |
|---|---|
| iRGD peptide is a 9-amino acid cyclic peptide,  
triggers tissue penetration of drugs by first  
binding to $\alpha\beta$ integrins, then proteolytically  
cleaved in the tumor to produce CRGDK/R to  
interact with neuropilin-1, and has  
tumor-targeting and tumor-penetrating properties.  
Purity: 98.62%  
Clinical Data: No Development Reported  
Size: 1 mg, 5 mg, 10 mg | |
<table>
<thead>
<tr>
<th>Compound</th>
<th>Cat. No.:</th>
<th>Purity</th>
<th>Clinical Data</th>
<th>Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irigenin</td>
<td>HY-N2587</td>
<td>&gt;98%</td>
<td>No Development Reported</td>
<td>5 mg, 10 mg, 20 mg</td>
</tr>
<tr>
<td>Lifitragast (SAR 1118; SHP-606)</td>
<td>HY-19344</td>
<td>99.58%</td>
<td>Launched</td>
<td>10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg, 200 mg</td>
</tr>
<tr>
<td>LXW7</td>
<td>HY-P0178</td>
<td>&gt;98%</td>
<td>No Development Reported</td>
<td>100 mg, 250 mg, 500 mg</td>
</tr>
<tr>
<td>MK-0429 (L-000845704)</td>
<td>HY-15102</td>
<td>99.73%</td>
<td>No Development Reported</td>
<td>10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg</td>
</tr>
<tr>
<td>Natalizumab</td>
<td>HY-108831</td>
<td>&gt;98%</td>
<td>No Development Reported</td>
<td>100 mg, 250 mg, 500 mg</td>
</tr>
<tr>
<td>OSU-T315</td>
<td>HY-18676</td>
<td>99.88%</td>
<td>No Development Reported</td>
<td>10 mM × 1 mL, 2 mg, 5 mg, 10 mg, 50 mg</td>
</tr>
<tr>
<td>RGD peptide GRGDNP</td>
<td>HY-P1740</td>
<td>&gt;98%</td>
<td>No Development Reported</td>
<td>1 mg, 5 mg</td>
</tr>
</tbody>
</table>

**Irigenin**

Irigenin is a lead compound, and mediates its anti-metastatic effect by specifically and selectively blocking α9β1 and α4β1 integrins binding sites on C-C loop of Extra Domain A (EDA). Irigenin shows anti-cancer properties.

**Lifitragast (SAR 1118; SHP-606)**

Lifitragast (SAR 1118) is an integrin lymphocyte function-associated antigen-1 (LFA-1) antagonist; inhibits Jurkat T cell attachment to ICAM-1 with an IC50 of 2.98 nM.

**LXW7**

LXW7 is an octamer disulfide cyclic peptide, also a αvβ3 integrin ligand, acts as a potent and specific endothelial progenitor cells (EPCs) and endothelial cells (ECs) targeting ligand. LXW7 increases phosphorylation of VEGFR-2 and activation of ERK1/2.

**MK-0429 (L-000845704)**

MK-0429 (L-000845704) is an orally active, potent, selective and nonpeptide αvβ3 integrin antagonist with an IC50 of 80 nM.

**Natalizumab**

Natalizumab is a recombinant, humanized monoclonal antibody, binds to α4β1-integrin and blocks its interaction with vascular cell adhesion molecule-1 (VCAM-1). Natalizumab can be used for the treatment of relapsing remitting multiple sclerosis and Crohn’s disease.

**OSU-T315**

OSU-T315 (ILK-IN-1) is a small Integrin-linked kinase (ILK) inhibitor with an IC50 of 0.6 μM, inhibiting PI3K/AKT signaling by dephosphorylation of AKT-Ser473 and other ILK targets (GSK-3β and myosin light chain).

**RGD peptide GRGDNP (TFA)**

RGD peptide (GRGDNP) (TFA) acts as an inhibitor of integrin-ligand interactions and plays an important role in cell adhesion, migration, growth, and differentiation.

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**RGD Trifluoroacetate**

RGD Trifluoroacetate is a tripeptide that effectively triggers cell adhesion, addresses certain cell lines and elicits specific cell responses; RGD Trifluoroacetate binds to integrins.
### Risuteganib

**Cat. No.: HY-P1930**

Risuteganib is an anti-integrin that downregulates oxidative stress and restores homeostasis, and targets three integrin receptors that are implicated in dry age-related macular degeneration (AMD) in order to restore homeostasis in the retina.

**Purity:** >98%

**Clinical Data:** No Development Reported

**Size:** 100 mg

### RWJ 50271

**Cat. No.: HY-110086**

RWJ 50271 is a selective inhibitor of lymphocyte function-associated antigen-1/intercellular adhesion molecule-1 (LFA-1/ICAM-1) interaction with an IC₅₀ of 5.0 μM (HL60 cells).

**Purity:** >99.0%

**Clinical Data:** No Development Reported

**Size:** 10 mM × 1 mL, 5 mg

### SR121566A

**Cat. No.: HY-U00235**

SR121566A is a novel non-peptide Glycoprotein IIb/IIIa (GP IIb-IIIa) antagonist, which can inhibit ADP-, arachidonic acid- and collagen-induced human platelet aggregation with IC₅₀ of 46±7.5, 56±6 and 42±3 nM, respectively.

**Purity:** >98%

**Clinical Data:** No Development Reported

**Size:** 1 mg, 5 mg, 10 mg, 20 mg

### TCS 2314

**Cat. No.: HY-12308**

TCS 2314 (compound 3) is orally active and selective very late antigen-4 (VLA-4, α4β1, CD49d/CD29) antagonist with an IC₅₀ of 4.4 nM.

**Purity:** >99.0%

**Clinical Data:** No Development Reported

**Size:** 5 mg

### Tirofiban

**Cat. No.: HY-17369B**

Tirofiban (L700462; MK383) is a potent non-peptide, glycoprotein IIb/IIIa (integrins αIIbb3) antagonist that inhibits platelet aggregation and thrombus formation.

**Purity:** >98%

**Clinical Data:** Launched

**Size:** 5 mg, 10 mg

### Tirofiban hydrochloride monohydrate

**Cat. No.: HY-17369**

Tirofiban hydrochloride monohydrate is a potent non-peptide, glycoprotein IIb/IIIa (integrins αIIbb3) antagonist IC₅₀ value: Target: integrin IIb/IIIa Tirofiban hydrochloride monohydrate blocks platelet aggregation and thrombus formation.

**Purity:** 99.99%

**Clinical Data:** Launched

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

### Vedolizumab

**Cat. No.: HY-P9911**

Vedolizumab is a humanized monoclonal antibody that targets the α4β7 integrin for the treatment of ulcerative colitis and Crohn’s disease.

**Purity:** 99.64%

**Clinical Data:** Launched

**Size:** 1 mg, 5 mg

### Zaurategrast

**Cat. No.: HY-70073**

Zaurategrast (CT7758) is a potent and oral-effective α₄-integrin inhibitor.

**Purity:** 98.81%

**Clinical Data:** Phase 2

**Size:** 10 mM × 1 mL, 5 mg, 10 mg, 25 mg

### Zaurategrast ethyl ester

**Cat. No.: HY-75385**

Zaurategrast ethyl ester (CDP323; UCB1184197) is a potent and oral-effective α₄β₁-integrin antagonist used for the treatment of inflammatory and autoimmune disorders.

**Purity:** 99.06%

**Clinical Data:** No Development Reported

**Size:** 10 mM × 1 mL, 5 mg, 10 mg, 25 mg
Zaurategrast ethyl ester sulfate (CDP323 sulfate; UCB1184197 sulfate)  
Cat. No.: HY-75385A

Zaurategrast ethyl ester sulfate (CDP323 sulfate), the ethyl ester prodrug of CT7758, is a \( \alpha 4 \beta 1/\alpha 4 \beta 7 \) integrin antagonist used for the treatment of inflammatory and autoimmune disorders.

Purity: >98%  
Clinical Data: No Development Reported  
Size: 5 mg, 10 mg, 25 mg

\( \alpha 2 \beta 1 \) Integrin Ligand Peptide  
Cat. No.: HY-P1868

\( \alpha 2 \beta 1 \) Integrin Ligand Peptide interacts with the \( \alpha 2 \beta 1 \) integrin receptor on the cell membrane and mediates extracellular signals into cells. It is a potential antagonist of collagen receptors.

Purity: >98%  
Clinical Data: No Development Reported  
Size: 1 mg, 5 mg, 10 mg

\( \alpha 2 \beta 1 \) Integrin Ligand Peptide (TFA)  
Cat. No.: HY-P1868A

\( \alpha 2 \beta 1 \) Integrin Ligand Peptide TFA interacts with the \( \alpha 2 \beta 1 \) integrin receptor on the cell membrane and mediates extracellular signals into cells. It is a potential antagonist of collagen receptors.

Purity: 99.33%  
Clinical Data: No Development Reported  
Size: 1 mg, 5 mg, 10 mg

\( \alpha v \beta 1 \) integrin-IN-1  
Cat. No.: HY-100445

\( \alpha v \beta 1 \) integrin-IN-1 (Compound C8) is a potent and selective \( \alpha v \beta 1 \) integrin inhibitor with an IC\(_{50}\) of 0.63 nM. Antifibrotic effects.

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