Epigenetic regulators of gene expression and chromatin state include so-called writers, erasers, and readers of chromatin modifications. Well-characterized examples of reader domains include bromodomains typically binding acetyllysine and chromatin organization modifier (chromo), malignant brain tumor (MBT), plant homeodomain (PHD), and Tudor domains generally associating with methyllysine. Research on epigenetic readers has been tremendously influenced by the discovery of selective inhibitors targeting the bromodomain and extraterminal motif (BET) family of acetyl-lysine readers. The human genome encodes 46 proteins containing 61 bromodomains clustered into eight families. Distinct experimental approaches are used to identify the first BET inhibitors, GSK 525762A and (+)-JQ-1\(^1\).

The Polycomb group (PcG) protein, enhancer of zeste homologue 2 (EZH2), has an essential role in promoting histone H3 lysine 27 trimethylation (H3K27me3) and epigenetic gene silencing. This function of EZH2 is important for cell proliferation and inhibition of cell differentiation, and is implicated in cancer progression. Cyclin-dependent kinases regulate epigenetic gene silencing through phosphorylation of EZH2\(^2\). In many types of cancers including lymphomas and leukemia, EZH2 is postulated to exert its oncogenic effects via aberrant histone and DNA methylation, causing silencing of tumor suppressor genes\(^3\).

p300/CBP is not only a transcriptional adaptor but also a histone acetyltransferase\(^4\).

References:
## Epigenetic Reader Domain Inhibitors & Modulators

<table>
<thead>
<tr>
<th>Inhibitor</th>
<th>Cat. No.</th>
<th>Bioactivity</th>
<th>Purity</th>
<th>Clinical Data</th>
<th>Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+)-JQ-1</td>
<td>HY-13030</td>
<td>(+)-JQ-1 is a BET bromodomain inhibitor, with IC\textsubscript{50} of 77 nM/33 nM for the first and second bromodomain (BRD4(1/2)).</td>
<td>99.86%</td>
<td>10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg, 200 mg, 500 mg, 1 g.</td>
<td>5 g</td>
</tr>
<tr>
<td>(R)-(-)-JQ1 Enantiomer</td>
<td>HY-13030A</td>
<td>(-)-JQ-1 is the stereoisomer of (+)-JQ1. (+)-JQ1 potently decreases expression of both BRD4 target genes, whereas (-)-JQ1 has no effect.</td>
<td>99.61%</td>
<td>10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg, 200 mg, 500 mg, 1 g.</td>
<td>5 g</td>
</tr>
<tr>
<td>3-Deazaneplanocin A</td>
<td>HY-10442</td>
<td>3-Deazaneplanocin A is a potent histone methyltransferase EZH2 inhibitor.</td>
<td>&gt;98%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-Deazaneplanocin A (hydrochloride)</td>
<td>HY-12186</td>
<td>3-Deazaneplanocin A hydrochloride is a potent histone methyltransferase EZH2 inhibitor.</td>
<td>96.03%</td>
<td>10mM x 1mL in DMSO, 1 mg, 5 mg, 10 mg, 25 mg</td>
<td></td>
</tr>
<tr>
<td>ARV-825</td>
<td>HY-16954</td>
<td>ARV-825 is a BRD4 inhibitor with DC50 (50% of maximum degradation) 1nM for Burkitt’s lymphoma (BL) cell lines. Affinity to BD1 and BD2 of BRD4 by ARV-825 is 90 and 28 nM, respectively.</td>
<td>99.35%</td>
<td>10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg</td>
<td></td>
</tr>
<tr>
<td>BET-BAY 002</td>
<td>HY-12421</td>
<td>BET-BAY 002 is a potent BET inhibitor; shows efficacy in a multiple myeloma model.</td>
<td>99.73%</td>
<td>10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg</td>
<td></td>
</tr>
<tr>
<td>BET-BAY 002 (S enantiomer)</td>
<td>HY-12421B</td>
<td>BET-BAY 002 S enantiomer is the S-enantiomer of BET-BAY 002. BET-BAY 002 is a BET inhibitor.</td>
<td>&gt;98%</td>
<td>10mM x 1mL in DMSO, 2 mg.</td>
<td>5 mg</td>
</tr>
<tr>
<td>BI 2536</td>
<td>HY-50698</td>
<td>BI 2536 is a potent and selective inhibitor of PI3K with IC\textsubscript{50} of 0.83 nM, and is also a potent inhibitor of BRD4 with IC\textsubscript{50} of 25 nM.</td>
<td>99.19%</td>
<td>10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg</td>
<td></td>
</tr>
<tr>
<td>BI-7273</td>
<td>HY-100351</td>
<td>BI-7273 is a selective, and cell-permeable BRD9 BD inhibitor.</td>
<td>99.65%</td>
<td>10mM x 1mL in DMSO, 5 mg, 10 mg, 25 mg, 50 mg</td>
<td></td>
</tr>
</tbody>
</table>

*Bioactivity, Size and purity values are provided for reference. Clinical data specifics may vary depending on the source.*
### BI-9564
(BI 9564; BI9564)

**Cat. No.: HY-100352**

**Bioactivity:** BI-9564 is a selective, and cell-permeable BRD9 BD inhibitor, with $K_d$ of 5.9 nM for BRD9, and IC$_{50}$ of > 100 μM for BET family.

| Purity: 99.55% |
| Clinical Data: Size: 10mM x 1mL in DMSO, 2 mg, 5 mg, 10 mg, 50 mg, 100 mg, 200 mg |

![BI-9564](image)

### Bromosporine

**Cat. No.: HY-15815**

**Bioactivity:** Bromosporine is a broad spectrum inhibitor for bromodomains with IC50 of 0.41 μM, 0.29 μM, 0.122 μM and 0.017 μM for BRD2, BRD4, BRD9 and CECR2, respectively.

| Purity: 99.4% |
| Clinical Data: Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg |

![Bromosporine](image)

### CPI-169
(CPI169 R-enantiomer; CPI 169 R-enantiomer)

**Cat. No.: HY-15956A**

**Bioactivity:** CPI-169 is the R enantiomer of CPI-169, which is a novel and potent EZH2 inhibitor, with IC$_{50}$ of 0.24 nM, 0.51 nM, and 6.1 nM for EZH2 WT, EZH2 Y641N, and EZH1, respectively.

| Purity: >98% |
| Clinical Data: Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg |

![CPI-169](image)

### CPI-169 racemate

**Cat. No.: HY-15956**

**Bioactivity:** CPI-169 racemate is the racemate form of CPI-169, which is a novel and potent EZH2 inhibitor with IC50 of 0.5 nM and 2.5 nM nM for wt EZH2 and Y641N EZH2, respectively.

| Bioactivity: 98.33% |
| Clinical Data: Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg |

![CPI-169 racemate](image)

### CPI-203
(CPI203; CPI 203)

**Cat. No.: HY-15846**

**Bioactivity:** CPI-203 is a novel potent, selective and cell permeable inhibitor of BET bromodomain, with an IC$_{50}$ value of appr 37 nM (BRD4 α-screen assay).

| Purity: 99.38% |
| Clinical Data: Size: 10mM x 1mL in DMSO, 2 mg, 5 mg, 10 mg, 25 mg |

![CPI-203](image)

### CPI-360
(CPI360; CPI 360)

**Cat. No.: HY-15955**

**Bioactivity:** CPI-360 is a potent, selective EZH2 inhibitor with IC50 of 0.5 nM and 2.5 nM nM for wt EZH2 and Y641N EZH2, respectively.

| Bioactivity: 97.21% |
| Clinical Data: Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg |

![CPI-360](image)

### CPI-637
(CPI637; CPI 637)

**Cat. No.: HY-100482**

**Bioactivity:** CPI-637 is a potent and selective CBP/EP300 bromodomains inhibitor with IC50 of 0.03±0.01μM and 11.0±0.6 μM for CBP/EP300 and BRD4, respectively.

| Bioactivity: 96.34% |
| Clinical Data: Size: 5 mg, 10 mg, 50 mg, 100 mg |

![CPI-637](image)

### EI1
(Ezh2 inhibitor; EI-1; EI 1)

**Cat. No.: HY-15573**

**Bioactivity:** EI1 is a potent and selective EZH2 inhibitor with IC$_{50}$ of 15 nM and 13 nM for EZH2 (WT) and EZH2 (Y641F), respectively.

| Bioactivity: 96.34% |
| Clinical Data: Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg |

![EI1](image)

### EPZ-6438
(Tazemetostat; EPZ6438; EPZ 6438; E-7438)

**Cat. No.: HY-13803**

**Bioactivity:** EPZ-6438 inhibits the activity of human PRC2-containing wild-type EZH2 with $K_i$ of 2.5±0.5 nM.

| Bioactivity: 98.97% |
| Clinical Data: Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg |

![EPZ-6438](image)

### EPZ005687
(EPZ-005687; EPZ 005687)

**Cat. No.: HY-15555**

**Bioactivity:** EPZ005687 is a potent and selective inhibitor of Epigenetic Reader Domain with $K_i$ of 24 nM, and has 50-fold selectivity against EZH1 and 500-fold selectivity against 15 other protein methyltransferases.

| Bioactivity: 98.97% |
| Clinical Data: Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg |

![EPZ005687](image)
EPZ011989 (EPZ-011989)
Cat. No.: HY-16986

Bioactivity: EPZ011989 is a potent, selective orally bioavailable EZH2 inhibitor with \( K_i < 3 \text{ nM} \) for EZH2 wt and EZH2 Y646; 15-fold selectivity over EZH1 and >3000-fold selectivity over other HMTase.

Purity: 98.93%
Clinical Data: Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg

EPZ011989 (trifluoroacetate) (EPZ-011989 trifluoroacetate)
Cat. No.: HY-16986A

Bioactivity: EPZ011989 trifluoroacetate is a potent, selective orally bioavailable EZH2 inhibitor with \( K_i < 3 \text{ nM} \) for EZH2 wt and EZH2 Y646; 15-fold selectivity over EZH1 and >3000-fold selectivity over other HMTase.

Purity: 99.31%
Clinical Data: Size: 5 mg, 10 mg, 50 mg, 100 mg

GSK 525762A (GSK525762A; GSK-525762A; I-BET762; I-BET 762)
Cat. No.: HY-13032

Bioactivity: GSK 525762A is a BET bromodomain inhibitor with \( IC_{50} \) of 32.5-42.5nM.

Purity: 99.69%
Clinical Data: Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg, 200 mg

GSK 525768A (GSK525768A; GSK-525768A)
Cat. No.: HY-13032A

Bioactivity: GSK 525768A is a bromodomain inhibitor, competitively inhibit the binding of acetylated lysine-containing peptides to bromodomains.

Purity: 99.62%
Clinical Data: Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg

GSK 5959
Cat. No.: HY-18665

Bioactivity: GSK-5959 is a potent, selective and cell permeable BRPF1 bromodomain inhibitor with \( IC_{50} \) = 80 nM. Exhibits >100-fold selectivity for BRPF1 over a panel of 35 other bromodomains, including BRPF2/3 and BET family bromodomains.

Purity: 98.07%
Clinical Data: Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg

GSK126 (EZH2 inhibitor; GSK-126; GSK 126; GSK2816126A; GSK-2816126A)
Cat. No.: HY-13470

Bioactivity: GSK126 is a potent, highly selective inhibitor of EZH2 methyltransferase activity with \( IC_{50} \) of 9.9 nM.

Purity: 99.41%
Clinical Data: Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg, 200 mg

GSK1324726A (I-BET726; GSK 1324726A; GSK-1324726A; I-BET 726)
Cat. No.: HY-13960

Bioactivity: GSK1324726A is a novel, potent, and selective inhibitor of BET proteins with high affinity to BRD2 \( IC_{50} = 41 \text{ nM} \), BRD3 \( IC_{50} = 31 \text{ nM} \), and BRD4 \( IC_{50} = 22 \text{ nM} \).

Purity: 98.21%
Clinical Data: Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg

GSK2801 (GSK-2801)
Cat. No.: HY-15658

Bioactivity: GSK2801 is a potent, selective and cell active acetyl-lysine competitive inhibitor of BAZ2A \( K_d = 136 \text{ nM} \) and BAZ2B \( K_d = 257 \text{ nM} \) bromodomains.

Purity: 99.62%
Clinical Data: Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg

GSK343 (GSK-343; GSK 343)
Cat. No.: HY-13500

Bioactivity: GSK343 is a highly potent, selective, and cell-active EZH2 inhibitor with \( IC_{50} \) of 4 nM.

Purity: 99.58%
Clinical Data: Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 25 mg, 50 mg, 100 mg

GSK503 (GSK-503)
Cat. No.: HY-12856

Bioactivity: GSK-503 is a potent EZH2 inhibitor with potential anticancer activity.

Purity: 99.29%
Clinical Data: Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg
GSK6853 (GSK-6853; GSK 6853)  
Cat. No.: HY-100220

Bioactivity: GSK6853 is a potent and selective inhibitor of the BRPF1 bromodomain. Shows excellent BRPF1 potency (pKd 9.5) and greater than 1600-fold selectivity over all other bromodomains tested.

Purity: 99.31%
Clinical Data:  
Size: 10mM x 1mL in DMSO, 2 mg, 5 mg, 10 mg, 50 mg, 100 mg

I-BET151 (GSK1210151A; I-BET 151; GSK-1210151A)  
Cat. No.: HY-13235

Bioactivity: I-BET151 is a BET bromodomain inhibitor, inhibits BRD4, BRD2, and BRD3 with pIC50 of 6.1, 6.3, and 6.6, respectively.

Purity: 99.16%
Clinical Data:  
Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg

I-BRD9  
Cat. No.: HY-18975

Bioactivity: I-BRD9 is the first selective cellular chemical probe for BRD9 (pIC50=7.3).

Purity: 98.09%
Clinical Data:  
Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 25 mg, 50 mg, 100 mg

JQ-1 (carboxylic acid) ((+)-JQ1 carboxylic acid; 6H-Thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-6-acetic acid)  
Cat. No.: HY-78695

Bioactivity: (+)-JQ1 carboxylic acid is the carboxylic acid form of (+)-JQ1 for derivative synthesis.

Purity: 99.49%
Clinical Data:  
Size: 10mM x 1mL in DMSO, 10 mg

KU-57788 (KU 57788; NU-7441; KUS7788; NU7441; NU 7441)  
Cat. No.: HY-11006

Bioactivity: KU-57788 is a potent and selective DNA-dependent protein kinase (DNA-PK) inhibitor with IC50 of 14 nM; also is a modest inhibitor of BRD4 and BRDT with IC50s of 1 and 3 nM, respectively.

Purity: 98.74%
Clinical Data:  
Size: 10mM x 1mL in DMSO, 10 mg, 50 mg, 100 mg

MS436 (MS-436; MS 436)  
Cat. No.: HY-13959

Bioactivity: MS436 is a new class of bromodomain inhibitor, exhibits potent affinity of an estimated Kp = 30-50 nM for the BRD4 BrD1 and a 10-fold selectivity over the BrD2.

Purity: 98.02%
Clinical Data:  
Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg

OF-1  
Cat. No.: HY-12518

Bioactivity: OF-1 is a selective BRPF1B and BRPF2 bromodomain inhibitor with Kd values of 100 nM/500 nM for BRPF1B/BRPF2; 39-fold selectivity over BRD4.

Purity: 99.5%
Clinical Data:  
Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg

OTX-015 (OTX 015; OTX015; MK-8628; MK 8628; MK8628)  
Cat. No.: HY-15743

Bioactivity: OTX-015 is a new potent BRD2/3/4 inhibitor for cell adhesion with IC50 values from 92 to 112 nM.

Purity: 99.69%
Clinical Data: Phase 1  
Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg, 200 mg

PF-CBP1 (hydrochloride) (PF CBP1 hydrochloride)  
Cat. No.: HY-19999A

Bioactivity: PF-CBP1 hydrochloride is a highly selective inhibitor of the CREB binding protein bromodomain.

Purity: 99.77%
Clinical Data:  
Size: 10mM x 1mL in DMSO, 5 mg, 10 mg, 25 mg, 50 mg, 100 mg

PFI-1 (PFI 1; PFI1)  
Cat. No.: HY-16586

Bioactivity: PFI-1 is a selective BET (bromodomain-containing protein) inhibitor for BRD4 with IC50 of 0.22 μM in a cell-free assay.

Purity: 99.87%
Clinical Data:  
Size: 10mM x 1mL in DMSO, 10 mg, 50 mg, 100 mg
**PFI-4**

**Cat. No.:** HY-18664

**Bioactivity:** PFI-4 is a potent and selective and cell permeable BRPF1 bromodomain inhibitor (IC50 = 80 nM). Exhibits >100-fold selectivity for BRPF1 over a panel of other bromodomains including BRPF2 (BRD3), BRPF3 and BRD4.

**Purity:** 99.17%

**Clinical Data:**
- Size: 10mM x 1mL in DMSO,
  - 5 mg, 10 mg, 50 mg, 100 mg

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**RVX-208** (Apabetalone; RVX-000222; RVX208; RVX 208; RVX000222; RVX 000222)

**Cat. No.:** HY-16652

**Bioactivity:** RVX-208 is an inhibitor of BET transcriptional regulators with selectivity for the second bromodomain. The IC50's are 87±10 μM and 0.51±0.04 μM for BD1 and BD2, respectively.

**Purity:** 99.33%

**Clinical Data:**
- Discontinued, Phase 2
- Size: 10mM x 1mL in DMSO,
  - 5 mg, 10 mg, 50 mg

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**SGC-CBP30**

**(SGC CBP30; SGCCBP30)**

**Cat. No.:** HY-15826

**Bioactivity:** SGC-CBP30 is a potent CREBBP/EP300 bromodomain inhibitor with IC50 of 21-69 and 38 nM for CREBBP and EP300 bromodomains, respectively.

**Purity:** 99.19%

**Clinical Data:**
- Size: 10mM x 1mL in DMSO,
  - 5 mg, 10 mg, 50 mg, 100 mg

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**TG-101348**

**(Fedratinib; SAR 302503; TG101348; TG 101348)**

**Cat. No.:** HY-10409

**Bioactivity:** TG-101348 is a selective inhibitor of JAK2 with IC50 of 3 nM, 35- and 334-fold more selective for JAK2 versus JAK1 and JAK3, and also inhibits BRD4 with IC50 of 340 nM.

**Purity:** 98.28%

**Clinical Data:**
- Phase 2, Phase 3
- Size: 10mM x 1mL in DMSO,
  - 10 mg, 50 mg, 100 mg

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**TG101209**

**(TG 101209; TG-101209)**

**Cat. No.:** HY-10410

**Bioactivity:** TG101209 is a selective JAK2 inhibitor with IC50 of 6 nM, less potent to FLT3 and RET with IC50 of 25 nM and 17 nM, appr 30-fold selective for JAK2 than JAK3, and selective to JAK2V617F and MPLW515L/K mutations; TG101209 inhibit BRD4 activity with IC50.

**Purity:** 99.20%

**Clinical Data:**
- Phase 2, Phase 3
- Size: 10mM x 1mL in DMSO,
  - 5 mg, 10 mg, 50 mg, 100 mg

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**UNC1999**

**(UNC-1999; UNC 1999)**

**Cat. No.:** HY-15646

**Bioactivity:** UNC1999 is a SAM-competitive, potent and selective inhibitor of EZH2 (IC50<10 nM) and EZH1 (IC50=45±3 nM).

**Purity:** 99.02%

**Clinical Data:**
- Size: 10mM x 1mL in DMSO,
  - 5 mg, 10 mg, 50 mg, 100 mg