

# Mixed Lineage Kinase

**MLKs** 

Mixed lineage kinases (MLKs) are mitogen activated protein kinase kinases (MAPKKKs) with features of both serine-threonine and tyrosine kinases that regulate the c-Jun N-terminal kinase (JNK) mitogen activated protein kinase (MAPK) signaling cascade, and also regulate p38 and extracellular signal-regulated kinase (ERK).

MLK3 (MAP3K11) is the most widely expressed MLK family member, and is expressed in neurons (as well as other cell types). At the cellular level, MLK3 is activated by stress, including reactive oxygen species, ceramide, and TNF $\alpha$ . At the molecular level, it is activated by Cdc42 and Rac, which interact with MLK3, and can cause it to dimerize via a leucine zipper interface, resulting in autophosphorylation and enzyme activation.

## Mixed Lineage Kinase Inhibitors & Activators

## GW806742X

Cat. No.: HY-112292

GW806742X, an ATP mimetic and a potent MLKL (Mixed Lineage Kinase Domain-Like protein) inhibitor, binds the MLKL pseudokinase domain with a  $\rm K_d$  of  $9.3~\mu M$ . GW806742X has activity against VEGFR2 ( $\rm IC_{50}$ =2 nM). GW806742X retards MLKL membrane translocation and inhibits necroptosis.

701101403

**Purity:** 99.91%

Clinical Data: No Development Reported

Size: 5 mg, 10 mg, 25 mg, 50 mg, 100 mg

## GW806742X hydrochloride

Cat. No.: HY-112292A

GW806742X hydrochloride, an ATP mimetic and a potent MLKL (Mixed Lineage Kinase Domain-Like protein) inhibitor, binds the MLKL pseudokinase domain with a  $\rm K_d$  of 9.3  $\mu$ M. GW806742X hydrochloride has activity against VEGFR2 ( $\rm IC_{50}$ =2

nM).

**Purity:** 98.77%

Clinical Data: No Development Reported

Size: 10 mM × 1 mL, 5 mg, 10 mg, 25 mg, 50 mg, 100 mg

## MLK-IN-1

Cat. No.: HY-111351

MLK-IN-1 is a potent, brain penetrant and specific mixed lineage kinase 3 (MLK-3) inhibitor, compound 68, extracted from patent US20140256733A1.

N.N.S

**Purity:** >98%

Clinical Data: No Development Reported

Size: 1 mg, 5 mg

#### MLKL-IN-1

Cat. No.: HY-139878

MLKL-IN-1 is a covalent MLKL inhibitor with a

 $K_p$  of 50  $\mu$ M.

**Purity:** >98%

Clinical Data: No Development Reported

Size: 1 mg, 5 mg

#### MLKL-IN-2

Cat. No.: HY-141889

MLKL-IN-2 is a **MLKL** inhibitor extracted from patent WO2021224505A1, compound (i).

**Purity:** 99.83%

Clinical Data: No Development Reported

Size: 5 mg, 10 mg, 25 mg, 50 mg, 100 mg

## Necrosulfonamide

Cat. No.: HY-100573

Necrosulfonamide is a **necroptosis** inhibitor acting by selectively targeting the mixed lineage kinase domain-like protein (MLKL). Necrosulfonamide prevents MLKL-RIP1-RIP3 necrosome complex from interacting with its downstream effectors.

**Purity:** 98.19%

Clinical Data: No Development Reported

Size: 10 mM × 1 mL, 5 mg, 10 mg, 25 mg, 50 mg, 100 mg

## Necrosulfonamide-d4

Cat. No.: HY-100573S

Necrosulfonamide-d4 is the deuterium labeled Necrosulfonamide. Necrosulfonamide is a **necroptosis** inhibitor acting by selectively targeting the mixed lineage kinase domain-like protein (MLKL).

Purity: >98%

Clinical Data: No Development Reported

Size: 1 mg, 10 mg

## RIP1/RIP3/MLKL activator 1

Cat. No.: HY-144828

RIP1/RIP3/MLKL activator 1 (Compound 6i) is a potent anti-glioma agent. RIP1/RIP3/MLKL activator 1 induces necroptosis through RIP1/RIP3/MLKL pathway. RIP1/RIP3/MLKL activator 1 exerts acceptable BBB permeability.



**Purity:** >98%

Clinical Data: No Development Reported

Size: 1 mg, 5 mg

## TC13172

Cat. No.: HY-101524

TC13172 is a mixed lineage kinase domain-like protein (MLKL) inhibitor with an  $EC_{50}$  value of 2 nM for HT-29 cells.

**Purity:** 98.88%

Clinical Data: No Development Reported

Size:  $10 \text{ mM} \times 1 \text{ mL}$ , 5 mg, 10 mg, 50 mg, 100 mg

## URMC-099

Cat. No.: HY-12599

URMC-099 is an orally bioavailable and potent mixed lineage kinase type 3 (MLK3) (IC $_{50}$ =14 nM) inhibitor with with excellent blood-brain barrier penetration properties.



Purity: 99.90%

Clinical Data: No Development Reported

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