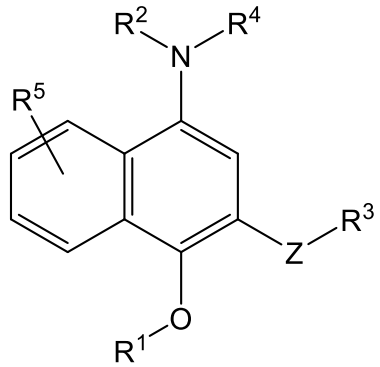
In the prior art, Chinese patent application No. 201910386493.X documents the compound UMI-77 as a mitophagy inducer. However, the researchers discovered in their study that UMI-77 as an mitophagy activator does not selectively induce autophagy in damaged mitochondria, and thus, it also triggers autophagy in healthy mitochondria during treatment, leading to adverse reactions. Furthermore, UMI-77 possess poor metabolic stability and is rapidly eliminated in in vitro metabolic stability experiments and PK experiments in mice, impacting significantly on drugability. Thus, developing a mitophagy activator that can effectively activate autophagy in damaged mitochondria, especially selectively induce autophagy in damaged mitochondria, and possesses desirable metabolic stability is pivotal for suppressing or mitigating many acute chronic diseases triggered by mitophagy dysfunction.

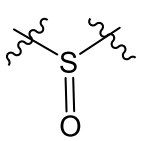
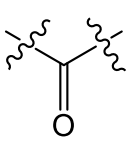
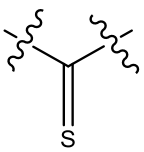
Summary

In an aspect of the present disclosure, there is provided a compound having a structure represented by Formula (I) or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof,



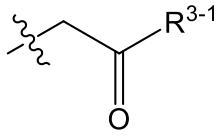
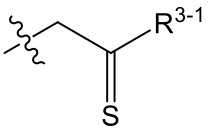
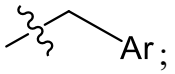
(I)

wherein:

Z is  ,  or  ;

R^1 is hydrogen or $C_{1\sim6}$ alkyl;

R^2 is hydrogen, $C_{1\sim6}$ alkyl, three to six-membered cycloalkyl, three to six-membered epoxyalkyl, phenyl or $C_{1\sim6}$ alkyl substituted phenyl;

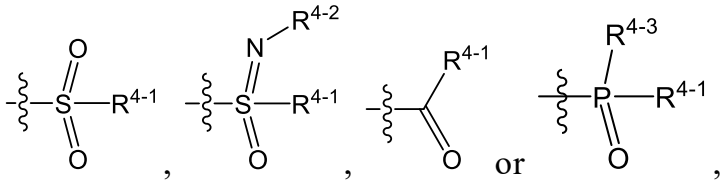
R^3 is  ,  or ;

wherein R^{3-1} is hydrogen, hydroxyl, $C_{1\sim6}$ alkyl, $C_{1\sim6}$ alkoxy, three to six-membered cycloalkyl, three to six-membered epoxyalkyl, amino, $C_{1\sim6}$ amido, $-CH_2C(O)R^{3-2}$, $-CH_2C(O)OR^{3-2}$ or $-CH_2C(O)N(R^{3-2}R^{3-2a})$,

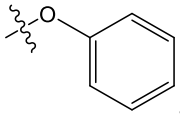
R^{3-2} and R^{3-2a} are each independently hydrogen, $C_{1\sim6}$ alkyl or three to six-membered cycloalkyl,

Ar is phenyl, naphthyl, 5- or 6-membered monocyclic heteroaryl, 8 to 10-membered fused bicyclic heteroaryl, phenyl with at least one hydrogen atom substituted by R^{3-3}, naphthyl with at least one hydrogen atom substituted by R^{3-3}, 5- or 6-membered monocyclic heteroaryl with at least one hydrogen atom substituted by R^{3-3} or 8 to 10-membered fused bicyclic heteroaryl with at least one hydrogen atom substituted by R^{3-3}, the R^{3-3} is hydrogen, halogen, $C_{1\sim6}$ alkyl, three to six-membered cycloalkyl, hydroxyl, $C_{1\sim6}$ alkoxy, three to six-membered epoxyalkyl, $C_{1\sim6}$ haloalkyl, $C_{2\sim6}$ alkenyl, $C_{2\sim6}$ alkynyl, $-N(R^{3-3a}R^{3-3b})$ or phenyl,

R^{3-3a} and R^{3-3b} are each independently hydrogen, $C_{1\sim6}$ alkyl or three to six-membered cycloalkyl;

R^4 is ,

wherein R^{4-1} is phenyl, naphthyl, phenyl with at least one hydrogen atom substituted by R^{4-11}, 5- or 6-membered monocyclic heteroaryl, 5- or 6-membered monocyclic heteroaryl with at least one hydrogen atom substituted by R^{4-11} or 8 to 10- membered fused bicyclic heteroaryl, or 8- to 10- membered fused bicyclic heteroaryl with at least one hydrogen atom substituted by R^{4-11}, and the R^{4-11} is hydrogen, halogen, nitro, nitrile group,

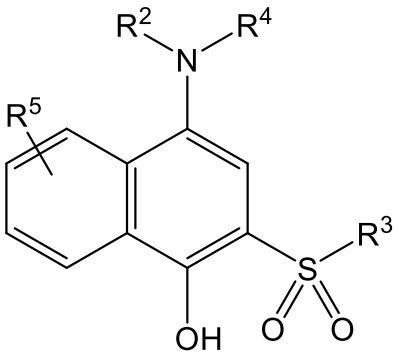
hydroxyl, $C_{1\sim6}$ alkyl, three to six-membered cycloalkyl, $C_{1\sim6}$ alkoxy, $-N(R^{4-1a}R^{4-1b})$, phenyl, $C_{1\sim6}$ haloalkyl, $C_{1\sim6}$ haloalkoxy, $-C(O)OR^{4-12}$, $-C(O)R^{4-12}$, $-C(O)N(R^{4-1a}R^{4-1b})$, $-S(O)_2R^{4-12}$, $-S(O)R^{4-12}$, $-OC(O)R^{4-12}$, $-OC(O)OR^{4-12}$ or , R^{4-12}, R^{4-1a} and R^{4-1b} are each independently hydrogen, $C_{1\sim6}$ alkyl, three to six-membered cycloalkyl, $C_{2\sim6}$ alkenyl, $C_{2\sim6}$ alkynyl, $C_{1\sim6}$ alkyl with at least one hydrogen substituted by halogen, $C_{2\sim6}$ alkenyl with at least one hydrogen substituted by halogen, three to six-membered cycloalkyl with at least one hydrogen substituted by halogen, or $C_{2\sim6}$ alkynyl with at least one hydrogen substituted by halogen, and R^{4-1a} and R^{4-1b} can be bonded to each other to form a ring,

R^{4-2} is hydrogen, $C_{1\sim6}$ alkyl or three to six-membered cycloalkyl, or when R^2 is $C_{1\sim6}$ alkyl, R^{4-2} and R^2 are bonded to form a 4~8 membered ring,

R^{4-3} is hydrogen, $C_{1\sim6}$ alkyl or $C_{1\sim6}$ alkoxy; and

the number of R^5 is 0~5, and when the number of R^5 is not 0, each R^5 is independently selected from halogen, nitro, nitrile group, $-N^+(R^{5-1})_3$, C_{1-6} haloalkyl, $-C(O)OR^{5-1}$, $-C(O)R^{5-1}$, $-C(O)N(R^{5-1}R^{5-1a})$, $-S(O)_2R^{5-1}$, $-S(O)R^{5-1}$, $-S(O)_2N(R^{5-1}R^{5-1a})$, $-S(O)N(R^{5-1}R^{5-1a})$, $-N=C(R^{5-1}R^{5-1a})$, hydroxyl, $C_{1\sim6}$ alkyl, phenyl, phenyl with at least one hydrogen substituted by R^{5-1}, $C_{1\sim6}$ alkoxy, $-N(R^{5-1}R^{5-1a})$, $-N(R^{5-1})C(O)R^{5-1a}$, $-N(R^{5-1})C(O)OR^{5-1a}$, $-N(R^{5-1})C(O)N(R^{5-1a}R^{5-1b})$, $-OC(O)R^{5-1}$, $-OC(O)OR^{5-1}$, $-OC(O)N(R^{5-1}R^{5-1a})$ and $-SR^{5-1}$, wherein R^{5-1}, R^{5-1a} and R^{5-1b} are each independently hydrogen, $C_{1\sim6}$ alkyl, $C_{2\sim6}$ alkenyl, $C_{2\sim6}$ alkynyl, $C_{1\sim6}$ alkyl with at least one hydrogen substituted by halogen, $C_{2\sim6}$ alkenyl with at least one hydrogen substituted by halogen, or $C_{2\sim6}$ alkynyl with at least one hydrogen substituted by halogen.

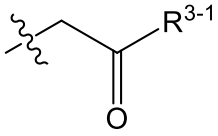
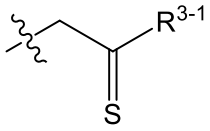
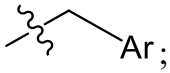
In another aspect of the present disclosure, there is provided a compound having a structure represented by Formula (III), or the pharmaceutically acceptable salt, stereoisomer, or solvate thereof of:



(III)

wherein:

R^2 is hydrogen, $C_{1\sim4}$ alkyl, three to six-membered cycloalkyl or four to six-membered epoxyalkyl;

R^3 is  ,  or  ;

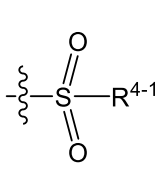
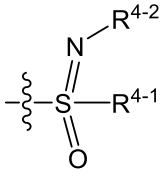
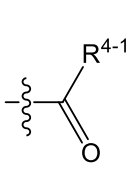
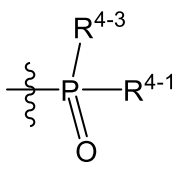
wherein R^{3-1} is hydrogen, hydroxyl, $C_{1\sim4}$ alkyl, $C_{1\sim4}$ alkoxy, three to six-membered cycloalkyl, three to six-membered epoxyalkyl,

$-N(R^{3-2}R^{3-2a})$, $-CH_2C(O)R^{3-2}$, $-CH_2C(O)OR^{3-2}$ or $-CH_2C(O)NR^{3-2}R^{3-2a}$,

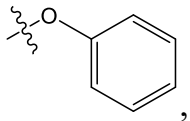
R^{3-2} and R^{3-2a} are each independently hydrogen, $C_{1\sim4}$ alkyl or three to six-membered cycloalkyl,

Ar is phenyl, 5- or 6-membered monocyclic heteroaryl, or 5- or 6-membered monocyclic heteroaryl with at least one hydrogen atom substituted by R^{3-3}, and the R^{3-3} is hydrogen, halogen, $C_{1\sim4}$ alkyl, three to six-membered cycloalkyl, hydroxyl, $C_{1\sim4}$ alkoxy, three to six-membered epoxyalkyl, $C_{1\sim4}$ haloalkyl, $C_{2\sim4}$ alkenyl, $C_{2\sim4}$ alkyne, $-N(R^{3-3a}R^{3-3b})$ or phenyl,

R^{3-3a} and R^{3-3b} are each independently hydrogen, $C_{1\sim4}$ alkyl or three to six-membered cycloalkyl;

R^4 is  ,  ,  or  ,

wherein R^{4-1} is phenyl, phenyl with at least one hydrogen atom

substituted by R^{4-11}, 8 to 10- membered fused bicyclic heteroaryl, or 8 to 10- membered fused bicyclic heteroaryl with at least one hydrogen atom substituted by R^{4-11}, and the R^{4-11} is hydrogen, halogen, nitro, $C_{1\sim4}$ alkyl, three to six-membered cycloalkyl, $C_{1\sim4}$ alkoxy, -N($R^{4-1a}R^{4-1b}$), phenyl, $C_{1\sim4}$ haloalkyl, $C_{1\sim4}$ haloalkoxy or , R^{4-1a} and R^{4-1b} are each independently hydrogen, $C_{1\sim4}$ alkyl or three to six-membered cycloalkyl, and R^{4-1a} and R^{4-1b} can be bonded to each other to form a ring,

R^{4-2} is $C_{1\sim4}$ alkyl or three- to six-membered cycloalkyl, or when R^2 is $C_{1\sim4}$ alkyl, R^{4-2} and R^2 are bonded to form a 4 to 8-membered ring,

R^{4-3} is $C_{1\sim4}$ alkyl or $C_{1\sim4}$ alkoxy; and

when the number of R^5 is not 0, each R^5 is independently selected from halogen, nitro, nitrile group, $-N^+(R^{5-1})_3$, $C_{1\sim4}$ haloalkyl, $-C(O)OR^{5-1}$, $-C(O)R^{5-1}$, $-C(O)N(R^{5-1}R^{5-1a})$, $-S(O)_2R^{5-1}$, $-S(O)R^{5-1}$, $-N=C(R^{5-1}R^{5-1a})$, hydroxyl, $C_{1\sim4}$ alkyl, phenyl, phenyl with at least one hydrogen substituted by R^{5-1}, $C_{1\sim4}$ alkoxy, $-N(R^{5-1}R^{5-1a})$, $-N(R^{5-1})C(O)R^{5-1a}$, $-OC(O)R^{5-1}$, $-OC(O)N(R^{5-1}R^{5-1a})$ or $-SR^{5-1}$, wherein R^{5-1}, R^{5-1a} and R^{5-1b} are each independently hydrogen, $C_{1\sim4}$ alkyl, $C_{2\sim4}$ alkenyl, $C_{2\sim4}$ alkynyl, $C_{1\sim4}$ alkyl with at least one hydrogen substituted by halogen, $C_{2\sim4}$ alkenyl with at least one hydrogen substituted by halogen, and $C_{2\sim4}$ alkynyl with at least one hydrogen substituted by halogen.

In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising the compound, or the pharmaceutically acceptable salt, stereoisomer, or solvate thereof disclosed herein.

In another aspect of the present disclosure, there is provided a compound, or the pharmaceutically acceptable salt, stereoisomer, solvate or prodrug thereof disclosed herein, or the pharmaceutical composition disclosed herein, for use in therapy.

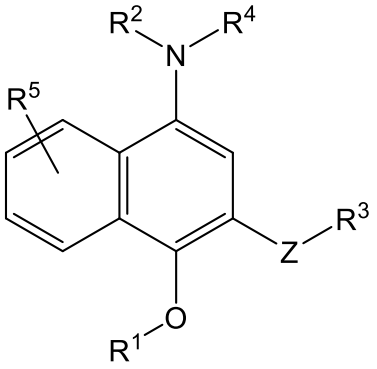
Brief Description of the Invention

In order to solve the above problems, a goal of our current invention is to provide a class of small molecule compounds featuring the structure of naphthylamine and their applications, functioning as mitophagy inducers and capable of selectively activating autophagy in damaged mitochondria without influencing the healthy mitochondria, along with improved metabolic stability and higher bioavailability.

In a first aspect of the present invention, it provides a compound having a structure represented by Formula (I) and a pharmaceutically acceptable salt, stereoisomer, solvate or prodrug thereof,

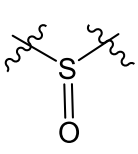
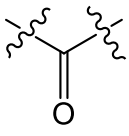
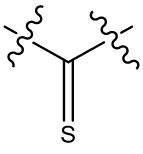
Claims

1. A compound having a structure represented by Formula (I) or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof,



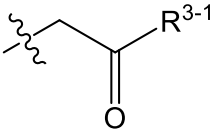
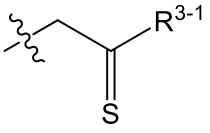
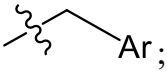
(I)

wherein:

Z is  ,  or  ;

R^1 is hydrogen or $C_{1\sim6}$ alkyl;

R^2 is hydrogen, $C_{1\sim6}$ alkyl, three to six-membered cycloalkyl, three to six-membered epoxyalkyl, phenyl or $C_{1\sim6}$ alkyl substituted phenyl;

R^3 is  ,  or  ;

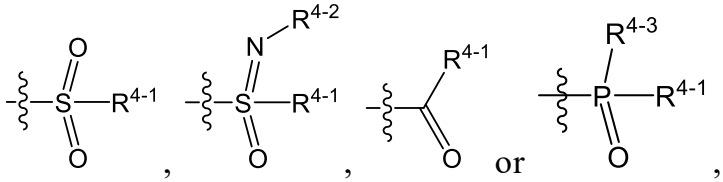
wherein R^{3-1} is hydrogen, hydroxyl, $C_{1\sim6}$ alkyl, $C_{1\sim6}$ alkoxy, three to six-membered cycloalkyl, three to six-membered epoxyalkyl, amino, $C_{1\sim6}$ amido, $-CH_2C(O)R^{3-2}$, $-CH_2C(O)OR^{3-2}$ or $-CH_2C(O)N(R^{3-2}R^{3-2a})$,

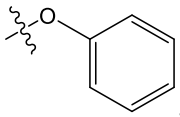
R^{3-2} and R^{3-2a} are each independently hydrogen, $C_{1\sim6}$ alkyl or three to six-membered cycloalkyl,

Ar is phenyl, naphthyl, 5- or 6-membered monocyclic heteroaryl, 8 to 10-membered fused bicyclic heteroaryl, phenyl with at least one hydrogen atom substituted by R^{3-3}, naphthyl with at least one hydrogen atom substituted by R^{3-3}, 5- or 6-membered monocyclic heteroaryl with at least

one hydrogen atom substituted by R^{3-3} or 8 to 10-membered fused bicyclic heteroaryl with at least one hydrogen atom substituted by R^{3-3}, the R^{3-3} is hydrogen, halogen, $C_{1\sim6}$ alkyl, three to six-membered cycloalkyl, hydroxyl, $C_{1\sim6}$ alkoxy, three to six-membered epoxyalkyl, $C_{1\sim6}$ haloalkyl, $C_{2\sim6}$ alkenyl, $C_{2\sim6}$ alkynyl, -N($R^{3-3a}R^{3-3b}$) or phenyl,

R^{3-3a} and R^{3-3b} are each independently hydrogen, $C_{1\sim6}$ alkyl or three to six-membered cycloalkyl;

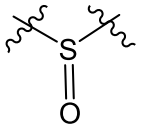
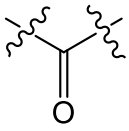
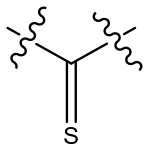
R^4 is ,

wherein R^{4-1} is phenyl, naphthyl, phenyl with at least one hydrogen atom substituted by R^{4-11}, 5- or 6-membered monocyclic heteroaryl, 5- or 6-membered monocyclic heteroaryl with at least one hydrogen atom substituted by R^{4-11} or 8 to 10- membered fused bicyclic heteroaryl, or 8- to 10- membered fused bicyclic heteroaryl with at least one hydrogen atom substituted by R^{4-11}, and the R^{4-11} is hydrogen, halogen, nitro, nitrile group, hydroxyl, $C_{1\sim6}$ alkyl, three to six-membered cycloalkyl, $C_{1\sim6}$ alkoxy, -N($R^{4-1a}R^{4-1b}$), phenyl, $C_{1\sim6}$ haloalkyl, $C_{1\sim6}$ haloalkoxy, -C(O)OR^{4-12}, -C(O)R^{4-12}, -C(O)N($R^{4-1a}R^{4-1b}$), -S(O)$_2R^{4-12}$, -S(O)R^{4-12}, -OC(O)R^{4-12}, -OC(O)OR^{4-12} or , R^{4-12}, R^{4-1a} and R^{4-1b} are each independently hydrogen, $C_{1\sim6}$ alkyl, three to six-membered cycloalkyl, $C_{2\sim6}$ alkenyl, $C_{2\sim6}$ alkynyl, $C_{1\sim6}$ alkyl with at least one hydrogen substituted by halogen, $C_{2\sim6}$ alkenyl with at least one hydrogen substituted by halogen, three to six-membered cycloalkyl with at least one hydrogen substituted by halogen, or $C_{2\sim6}$ alkynyl with at least one hydrogen substituted by halogen, and R^{4-1a} and R^{4-1b} can be bonded to each other to form a ring,

R^{4-2} is hydrogen, $C_{1\sim6}$ alkyl or three to six-membered cycloalkyl, or when R^2 is $C_{1\sim6}$ alkyl, R^{4-2} and R^2 are bonded to form a 4~8 membered ring,

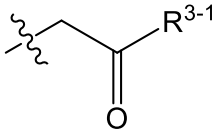
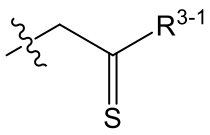
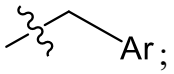
R^{4-3} is hydrogen, $C_{1\sim6}$ alkyl or $C_{1\sim6}$ alkoxy; and

the number of R^5 is 0~5, and when the number of R^5 is not 0, each R^5 is independently selected from halogen, nitro, nitrile group, $-N^+(R^{5-1})_3$, C_{1-6} haloalkyl, $-C(O)OR^{5-1}$, $-C(O)R^{5-1}$, $-C(O)N(R^{5-1}R^{5-1a})$, $-S(O)_2R^{5-1}$, $-S(O)R^{5-1}$, $-S(O)_2N(R^{5-1}R^{5-1a})$, $-S(O)N(R^{5-1}R^{5-1a})$, $-N=C(R^{5-1}R^{5-1a})$, hydroxyl, $C_{1\sim6}$ alkyl, phenyl, phenyl with at least one hydrogen substituted by R^{5-1}, $C_{1\sim6}$ alkoxy, $-N(R^{5-1}R^{5-1a})$, $-N(R^{5-1})C(O)R^{5-1a}$, $-N(R^{5-1})C(O)OR^{5-1a}$, $-N(R^{5-1})C(O)N(R^{5-1a}R^{5-1b})$, $-OC(O)R^{5-1}$, $-OC(O)OR^{5-1}$, $-OC(O)N(R^{5-1}R^{5-1a})$ and $-SR^{5-1}$, wherein R^{5-1}, R^{5-1a} and R^{5-1b} are each independently hydrogen, $C_{1\sim6}$ alkyl, $C_{2\sim6}$ alkenyl, $C_{2\sim6}$ alkynyl, $C_{1\sim6}$ alkyl with at least one hydrogen substituted by halogen, $C_{2\sim6}$ alkenyl with at least one hydrogen substituted by halogen, or $C_{2\sim6}$ alkynyl with at least one hydrogen substituted by halogen.

2. The compound or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof of claim 1, wherein Z is  ,  or  ;

R^1 is hydrogen or $C_{1\sim4}$ alkyl;

R^2 is hydrogen, $C_{1\sim4}$ alkyl, three to six-membered cycloalkyl or four to six-membered epoxyalkyl;

R^3 is  ,  or  ;

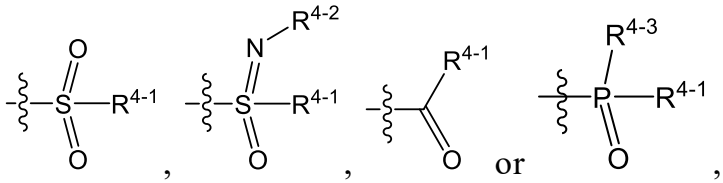
wherein, R^{3-1} is hydrogen, hydroxyl, $C_{1\sim4}$ alkyl, $C_{1\sim4}$ alkoxy or $-N(R^{3-2}R^{3-2a})$,

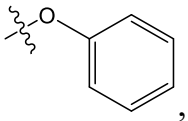
R^{3-2} and R^{3-2a} are each independently hydrogen or $C_{1\sim4}$ alkyl,

Ar is phenyl, 5- or 6-membered monocyclic heteroaryl, or a 5- or 6-membered monocyclic heteroaryl with at least one hydrogen atom

substituted by R^{3-3}, and the R^{3-3} is hydrogen, halogen, $C_{1\sim4}$ alkyl, hydroxyl, $C_{1\sim4}$ alkoxy, $C_{1\sim4}$ haloalkyl or $-N(R^{3-3a}R^{3-3b})$,

R^{3-3a} and R^{3-3b} are each independently hydrogen or $C_{1\sim4}$ alkyl;

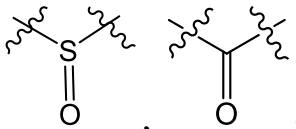
R^4 is  ,

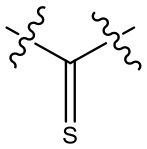
wherein, R^{4-1} is phenyl, phenyl with at least one hydrogen atom substituted by R^{4-11}, 5- or 6-membered monocyclic heteroaryl, or 5- or 6-membered monocyclic heteroaryl with at least one hydrogen atom substituted by R^{4-11}, and the R^{4-11} is hydrogen, halogen, nitro, $C_{1\sim4}$ alkyl, three to six-membered cycloalkyl, $C_{1\sim4}$ alkoxy, $-N(R^{4-1a}R^{4-1b})$, phenyl, $C_{1\sim4}$ haloalkyl, $C_{1\sim4}$ haloalkoxy or , R^{4-1a} and R^{4-1b} are each independently hydrogen, $C_{1\sim4}$ alkyl or three to six membered cycloalkyl, and R^{4-1a} and R^{4-1b} can be bonded to each other to form a ring,

R^{4-2} is $C_{1\sim4}$ alkyl, three- to six-membered cycloalkyl, or when R^2 is $C_{1\sim4}$ alkyl, R^{4-2} and R^2 are bonded to form a 4~8membered ring,

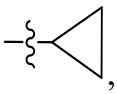
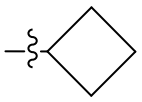
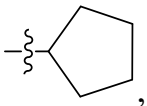
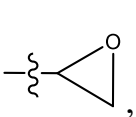
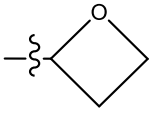
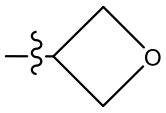
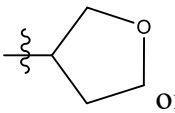
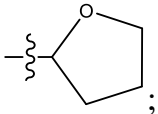
R^{4-3} is $C_{1\sim4}$ alkyl or $C_{1\sim4}$ alkoxy; and

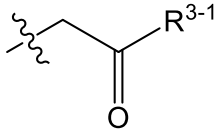
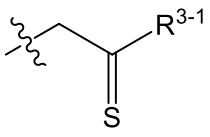
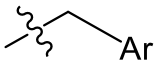
when the number of R^5 is not 0, each R^5 is independently selected from halogen, nitro, nitrile group, $-N^+(R^{5-1})_3$, $C_{1\sim4}$ haloalkyl, $-C(O)OR^{5-1}$, $-C(O)R^{5-1}$, $-C(O)N(R^{5-1}R^{5-1a})$, $-S(O)_2R^{5-1}$, $-S(O)R^{5-1}$, $-N=C(R^{5-1}R^{5-1a})$, hydroxyl, $C_{1\sim4}$ alkyl, phenyl, phenyl with at least one hydrogen substituted by R^{5-1}, $C_{1\sim4}$ alkoxy, $-N(R^{5-1}R^{5-1a})$, $-N(R^{5-1})C(O)R^{5-1a}$ and $-OC(O)R^{5-1}$, wherein R^{5-1}, R^{5-1a} and R^{5-1b} are each independently hydrogen, $C_{1\sim4}$ alkyl, and $C_{1\sim4}$ alkyl with at least one hydrogen substituted by halogen.

3. The compound or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof of claim 1, wherein Z is  or


;

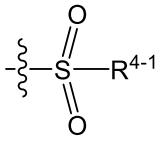
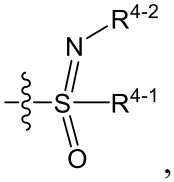
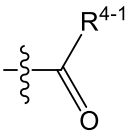
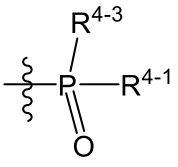
and/or, R^1 is hydrogen;

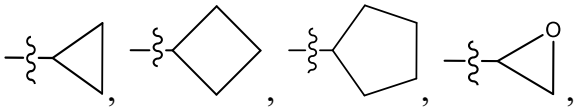
and/or, R^2 is hydrogen, methyl, ethyl, n-propyl, isopropyl, , , , , , ,  or ;

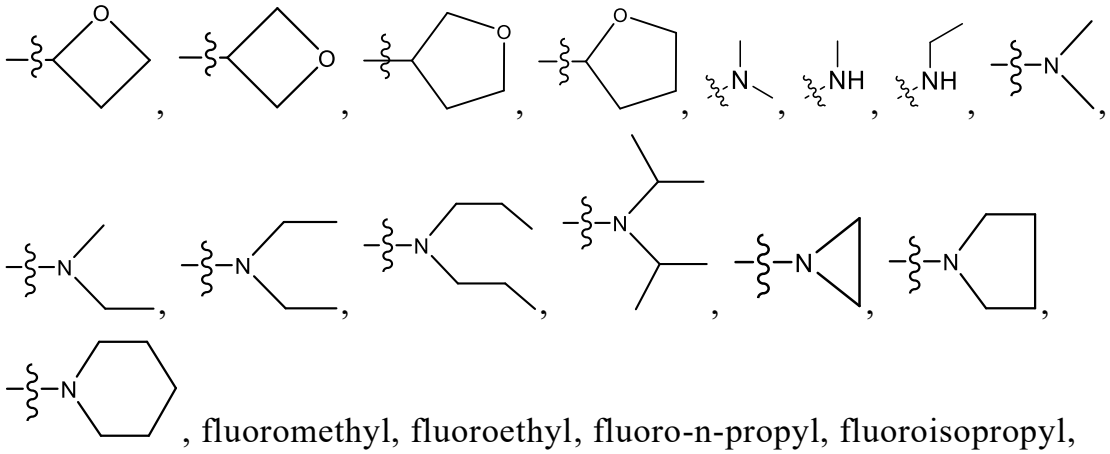
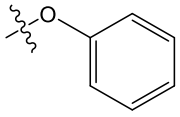
and/or, R^3 is ,  or ;

wherein R^{3-1} is hydrogen, hydroxyl, methyl, ethyl, n-propyl, isopropyl, methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, tert-butoxy, sec-butoxy or isobutoxy,

Ar is phenyl, 5- or 6-membered nitrogen-containing monocyclic heteroaryl;

and/or, R^4 is , ,  or ,

wherein R^{4-1} is phenyl, phenyl with at least one hydrogen atom substituted by R^{4-11}, 5- or 6-membered monocyclic heteroaryl, and 5- or 6-membered monocyclic heteroaryl with at least one hydrogen atom substituted by R^{4-11}, 8 to 10- membered fused bicyclic heteroaryl, or 8 to 10- membered fused bicyclic heteroaryl with at least one hydrogen atom substituted by R^{4-11}, and the R^{4-11} is hydrogen, halogen, nitrogen methyl, ethyl, n-propyl, isopropyl, ,


, fluoromethyl, fluoroethyl, fluoro-n-propyl, fluoroisopropyl, chloromethyl, chloroethyl, chloro-n-propyl, chloroisopropyl, bromomethyl, bromoethyl, bromo-n-propyl, bromoisopropyl, iodomethyl, iodoethyl, iodo-n-propyl, iodoisopropyl, fluoromethoxy, fluoroethoxy, fluoro-n-propoxy, fluoroisopropoxy, chloromethoxy, chloroethoxy, chloro-n-propoxy, chloroisopropoxy, bromomethoxy, bromoethoxy, bromo-n-propoxy, bromoisopropoxy, iodooxymethyl, iodoethoxy, iodo-n-propoxy, iodoisopropoxy or ,

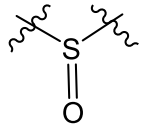
R^{4-2} is methyl, ethyl, n-propyl or isopropyl, or when R^2 is methyl, ethyl or n-propyl, R^{4-2} and R^2 are bonded to form a 4-8 membered ring,

R^{4-3} is methyl, ethyl, n-propyl, isopropyl, methoxy, ethoxy, n-propoxy or isopropoxy;

and/or, when the number of R^5 is not 0, each R^5 is independently selected from halogen, nitro, nitrile, $-N^+(R^{5-1})_3$, fluoromethyl, fluoroethyl, fluoro-n-propyl, fluoroisopropyl, chloromethyl, chloroethyl, chloro-n-propyl, chloroisopropyl, bromomethyl, bromoethyl, bromo-n-propyl, bromoisopropyl, $-C(O)OR^{5-1}$, $-C(O)R^{5-1}$, $-C(O)N(R^{5-1}R^{5-1a})$,$-S(O)_2R^{5-1}$, $-S(O)R^{5-1}$, $-N=C(R^{5-1}R^{5-1a})$, hydroxyl, methyl, ethyl, n-propyl, isopropyl, phenyl, phenyl with at least one hydrogen substituted by R^{5-1}, methoxy, ethoxy, n-propoxy, isopropoxy, $-N(R^{5-1}R^{5-1a})$, $-N(R^{5-1})C(O)R^{5-1a}$ and $-OC(O)R^{5-1}$, wherein R^{5-1}, R^{5-1a} and R^{5-1b} are each independently hydrogen, methyl, ethyl, n-propyl, isopropyl, fluoromethyl, fluoroethyl, fluoro-n-

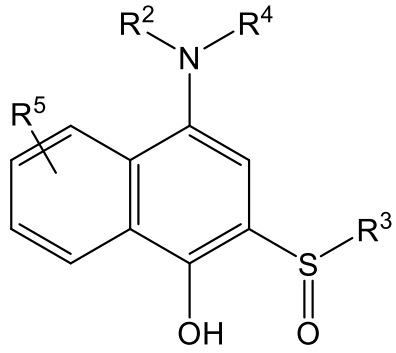
propyl, fluoroisopropyl, chloromethyl, chloroethyl, chloro-n-propyl, chloroisopropyl, bromomethyl, bromoethyl, bromo-n-propyl or bromoisopropyl.

4. The compound or the pharmaceutically acceptable salt, stereoisomer, or solvate thereof of any one of claims 1-3, wherein Z is



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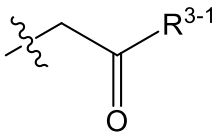
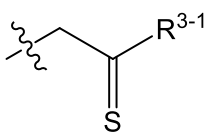
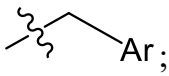
5. The compound or the pharmaceutically acceptable salt, stereoisomer, or solvate thereof of claim 1 or 2, wherein the compound has a structure represented by Formula (II):



(II)

wherein:

R^2 is hydrogen, $C_{1\sim4}$ alkyl, three to six-membered cycloalkyl or four to six-membered epoxyalkyl;

R^3 is ,  or ;

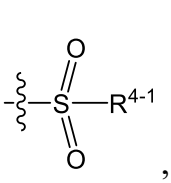
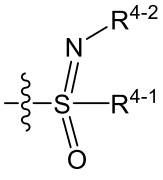
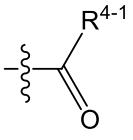
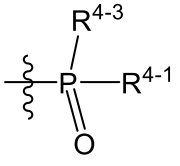
wherein R^{3-1} is hydrogen, hydroxyl, $C_{1\sim4}$ alkyl, $C_{1\sim4}$ alkoxy, three to six-membered cycloalkyl, three to six-membered epoxyalkyl, $-N(R^{3-2}R^{3-2a})$, $-CH_2C(O)R^{3-2}$, $-CH_2C(O)OR^{3-2}$ or $-CH_2C(O)NR^{3-2}R^{3-2a}$,

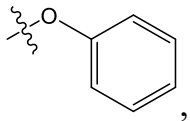
R^{3-2} and R^{3-2a} are each independently hydrogen, $C_{1\sim4}$ alkyl or three to

six-membered cycloalkyl,

Ar is phenyl, 5- or 6-membered monocyclic heteroaryl, or 5- or 6-membered monocyclic heteroaryl with at least one hydrogen atom substituted by R^{3-3}, and the R^{3-3} is hydrogen, halogen, $C_{1\sim4}$ alkyl, three to six-membered cycloalkyl, hydroxyl, $C_{1\sim4}$ alkoxy, three to six-membered epoxyalkyl, $C_{1\sim4}$ haloalkyl, $C_{2\sim4}$ alkenyl, $C_{2\sim4}$ alkynyl, -N(R^{3-3a} R^{3-3b}) or phenyl,

R^{3-3a} and R^{3-3b} are each independently hydrogen, $C_{1\sim4}$ alkyl or three to six-membered cycloalkyl;

R^4 is  ,  ,  or  ,

wherein R^{4-1} is phenyl, phenyl with at least one hydrogen atom substituted by R^{4-11}, 5- or 6-membered monocyclic heteroaryl, and 5- or 6-membered monocyclic heteroaryl with at least one hydrogen atom substituted by R^{4-11}, 8 to 10- membered fused bicyclic heteroaryl, or 8 to 10- membered fused bicyclic heteroaryl with at least one hydrogen atom substituted by R^{4-11}, wherein R^{4-11} is hydrogen, halogen, nitro, $C_{1\sim4}$ alkyl, three to six-membered cycloalkyl, $C_{1\sim4}$ alkoxy, -N($R^{4-1a}R^{4-1b}$), phenyl, $C_{1\sim4}$ haloalkyl, $C_{1\sim4}$ haloalkoxy or  , R^{4-1a} and R^{4-1b} are each independently hydrogen, $C_{1\sim4}$ alkyl or three to six-membered cycloalkyl, and R^{4-1a} and R^{4-1b} can be bonded to each other to form a ring,

R^{4-2} is a $C_{1\sim4}$ alkyl, a three- to six-membered cycloalkyl, or when R^2 is a $C_{1\sim4}$ alkyl, R^{4-2} and R^2 are bonded to form a 4 to 8-membered ring,

R^{4-3} is $C_{1\sim4}$ alkyl or $C_{1\sim4}$ alkoxy; and

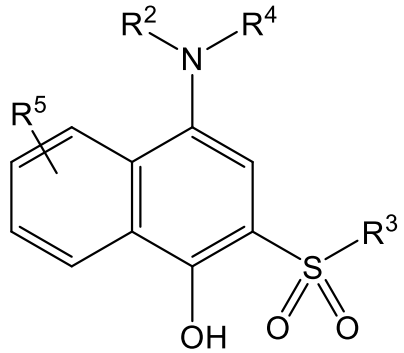
when the number of R^5 is not 0, each R^5 is independently selected from halogen, nitro, nitrile, -$N^+(R^{5-1})_3$, $C_{1\sim4}$ haloalkyl,-C(O)OR^{5-1}, -C(O)R^{5-1}, -C(O)N($R^{5-1}R^{5-1a}$), -$S(O)_2R^{5-1}$, -S(O)R^{5-1}, -N=C($R^{5-1}R^{5-1a}$),

hydroxyl, $C_{1\sim4}$ alkyl, phenyl, phenyl with at least one hydrogen substituted by R^{5-1}, $C_{1\sim4}$ alkoxy, $-N(R^{5-1}R^{5-1a})$, $-N(R^{5-1})C(O)R^{5-1a}$, $-OC(O)R^{5-1}$, $-OC(O)N(R^{5-1}R^{5-1a})$ and $-SR^{5-1}$, wherein R^{5-1}, R^{5-1a} and R^{5-1b} are each independently hydrogen, $C_{1\sim4}$ alkyl, $C_{2\sim4}$ alkenyl, $C_{2\sim4}$ alkynyl , $C_{1\sim4}$ alkyl with at least one hydrogen substituted by halogen, $C_{2\sim4}$ alkenyl with at least one hydrogen substituted by halogen, or $C_{2\sim4}$ alkynyl with at least one hydrogen substituted by halogen.

6. The compound or the pharmaceutically acceptable salt, stereoisomer, or solvate thereof of claim 5, wherein when the number of R^5 is not 0, each R^5 is independently selected from halogen, nitro, nitrile, $-N^+(R^{5-1})_3$, $C_{1\sim4}$ haloalkyl, $-C(O)OR^{5-1}$, $-C(O)R^{5-1}$, $-C(O)N(R^{5-1}R^{5-1a})$, $-S(O)_2R^{5-1}$, $-S(O)R^{5-1}$ and $-N=C(R^{5-1}R^{5-1a})$;

wherein R^{5-1} and R^{5-1a} are each independently hydrogen, $C_{1\sim4}$ alkyl, $C_{2\sim4}$ alkenyl, $C_{2\sim4}$ alkynyl, and $C_{1\sim4}$ alkyl with at least one hydrogen substituted by halogen, $C_{2\sim4}$ alkenyl with at least one hydrogen substituted by halogen or $C_{2\sim4}$ alkynyl group with at least one hydrogen substituted by halogen.

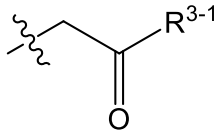
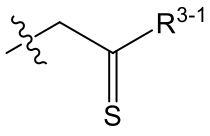
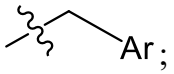
7. A compound having a structure represented by Formula (III), or the pharmaceutically acceptable salt, stereoisomer, or solvate thereof of:



(III)

wherein:

R^2 is hydrogen, $C_{1\sim4}$ alkyl, three to six-membered cycloalkyl or four to six-membered epoxyalkyl;

R^3 is  ,  or ;

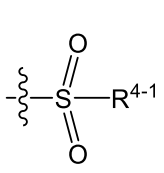
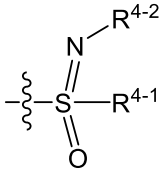
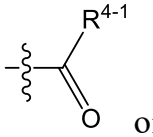
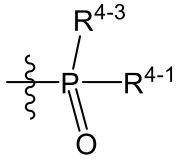
wherein R^{3-1} is hydrogen, hydroxyl, $C_{1\sim4}$ alkyl, $C_{1\sim4}$ alkoxy, three to six-membered cycloalkyl, three to six-membered epoxyalkyl,

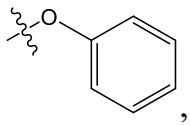
$-N(R^{3-2}R^{3-2a})$, $-CH_2C(O)R^{3-2}$, $-CH_2C(O)OR^{3-2}$ or $-CH_2C(O)NR^{3-2}R^{3-2a}$,

R^{3-2} and R^{3-2a} are each independently hydrogen, $C_{1\sim4}$ alkyl or three to six-membered cycloalkyl,

Ar is phenyl, 5- or 6-membered monocyclic heteroaryl, or 5- or 6-membered monocyclic heteroaryl with at least one hydrogen atom substituted by R^{3-3}, and the R^{3-3} is hydrogen, halogen, $C_{1\sim4}$ alkyl, three to six-membered cycloalkyl, hydroxyl, $C_{1\sim4}$ alkoxy, three to six-membered epoxyalkyl, $C_{1\sim4}$ haloalkyl, $C_{2\sim4}$ alkenyl, $C_{2\sim4}$ alkyne, $-N(R^{3-3a}R^{3-3b})$ or phenyl,

R^{3-3a} and R^{3-3b} are each independently hydrogen, $C_{1\sim4}$ alkyl or three to six-membered cycloalkyl;

R^4 is  ,  ,  or  ,

wherein R^{4-1} is phenyl, phenyl with at least one hydrogen atom substituted by R^{4-11}, 8 to 10- membered fused bicyclic heteroaryl, or 8 to 10- membered fused bicyclic heteroaryl with at least one hydrogen atom substituted by R^{4-11}, and the R^{4-11} is hydrogen, halogen, nitro, $C_{1\sim4}$ alkyl, three to six-membered cycloalkyl, $C_{1\sim4}$ alkoxy, $-N(R^{4-1a}R^{4-1b})$, phenyl, $C_{1\sim4}$ haloalkyl, $C_{1\sim4}$ haloalkoxy or  , R^{4-1a} and R^{4-1b} are each independently hydrogen, $C_{1\sim4}$ alkyl or three to six-membered cycloalkyl, and R^{4-1a} and R^{4-1b} can be bonded to each other to form a ring,

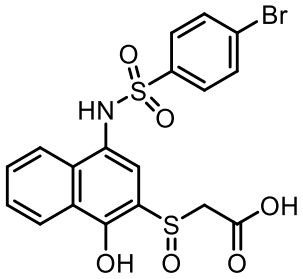
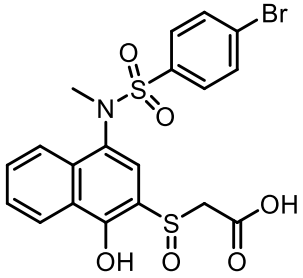
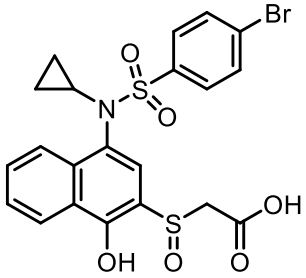
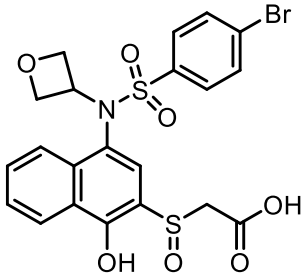
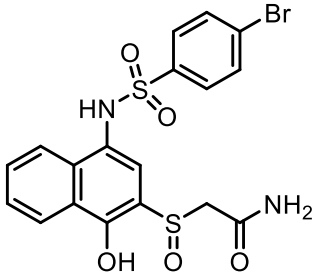
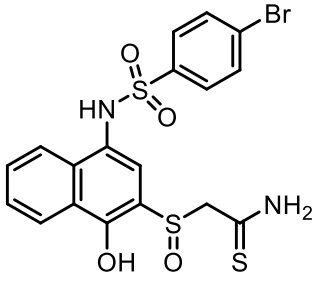
R^{4-2} is $C_{1\sim4}$ alkyl or three- to six-membered cycloalkyl, or when R^2 is $C_{1\sim4}$ alkyl, R^{4-2} and R^2 are bonded to form a 4 to 8-membered ring,

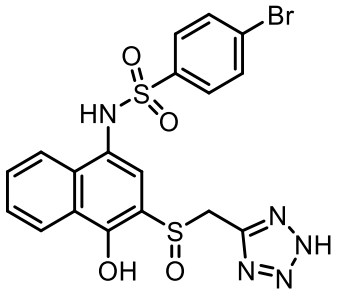
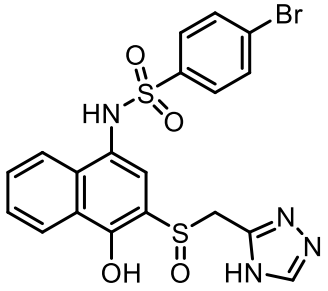
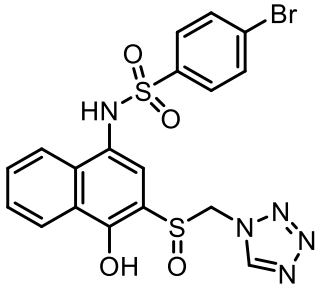
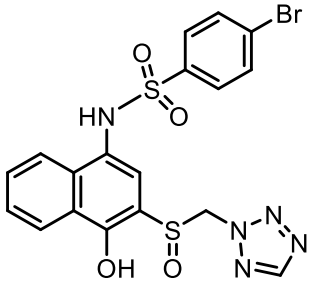
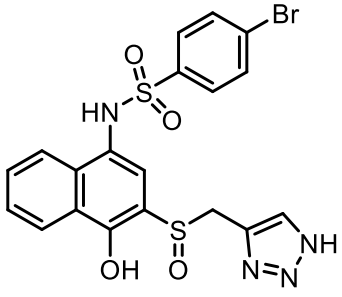
R^{4-3} is $C_{1\sim4}$ alkyl or $C_{1\sim4}$ alkoxy; and

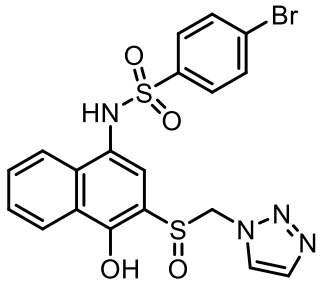
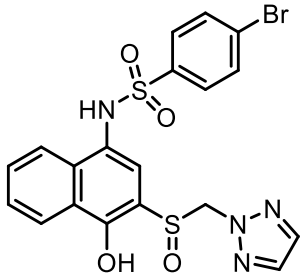
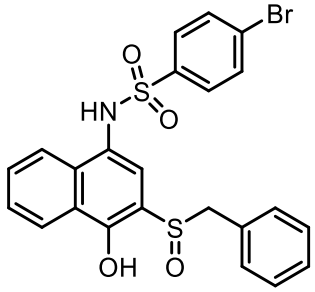
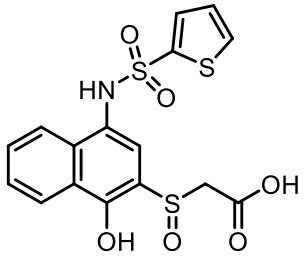
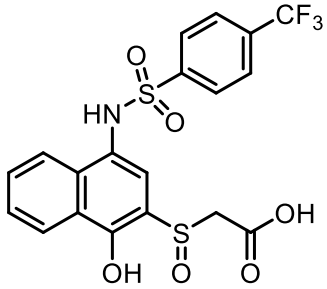
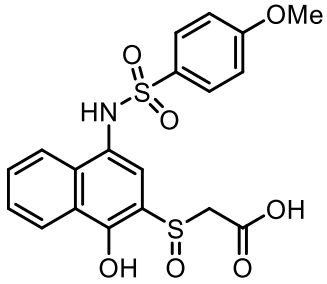
when the number of R^5 is not 0, each R^5 is independently selected from halogen, nitro, nitrile group, $-N^+(R^{5-1})_3$, $C_{1\sim4}$ haloalkyl, $-C(O)OR^{5-1}$, $-C(O)R^{5-1}$, $-C(O)N(R^{5-1}R^{5-1a})$, $-S(O)_2R^{5-1}$, $-S(O)R^{5-1}$, $-N=C(R^{5-1}R^{5-1a})$, hydroxyl, $C_{1\sim4}$ alkyl, phenyl, phenyl with at least one hydrogen substituted by R^{5-1}, $C_{1\sim4}$ alkoxy, $-N(R^{5-1}R^{5-1a})$, $-N(R^{5-1})C(O)R^{5-1a}$, $-OC(O)R^{5-1}$, $-OC(O)N(R^{5-1}R^{5-1a})$ or $-SR^{5-1}$, wherein R^{5-1}, R^{5-1a} and R^{5-1b} are each independently hydrogen, $C_{1\sim4}$ alkyl, $C_{2\sim4}$ alkenyl, $C_{2\sim4}$ alkynyl, $C_{1\sim4}$ alkyl with at least one hydrogen substituted by halogen, $C_{2\sim4}$ alkenyl with at least one hydrogen substituted by halogen, and $C_{2\sim4}$ alkynyl with at least one hydrogen substituted by halogen.

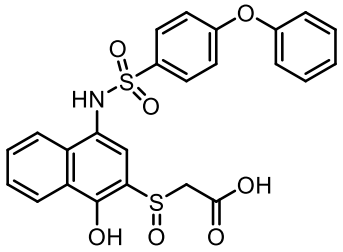
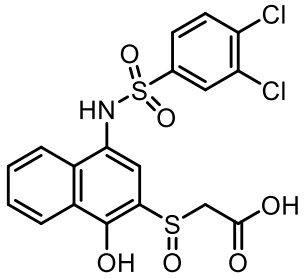
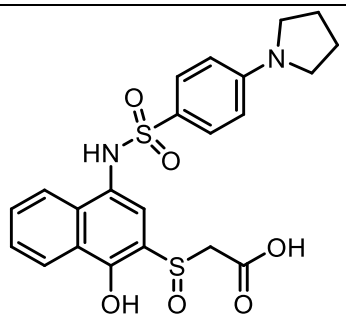
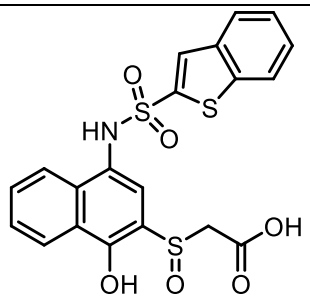
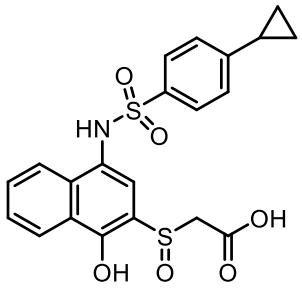
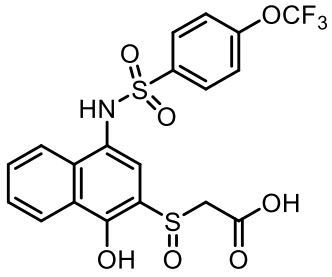
8. The compound or the pharmaceutically acceptable salt, stereoisomer, or solvate thereof of claim 7, wherein when the number of R^5 is not 0, each R^5 is independently selected from hydroxyl, $C_{1\sim4}$ alkyl, phenyl, phenyl with at least one hydrogen substituted by R^{5-1}, $C_{1\sim4}$ alkoxy, $-N(R^{5-1}R^{5-1a})$, $-N(R^{5-1})C(O)R^{5-1a}$, $-OC(O)R^{5-1}$, $-OC(O)N(R^{5-1}R^{5-1a})$ or $-SR^{5-1}$, wherein R^{5-1}, R^{5-1a} and R^{5-1b} are each independently hydrogen, $C_{1\sim4}$ alkyl, $C_{2\sim4}$ alkenyl, $C_{2\sim4}$ alkynyl, $C_{1\sim4}$ alkyl with at least one hydrogen substituted by halogen, $C_{2\sim4}$ alkenyl with at least one hydrogen substituted by halogen and $C_{2\sim4}$ alkynyl with at least one hydrogen substituted by halogen.

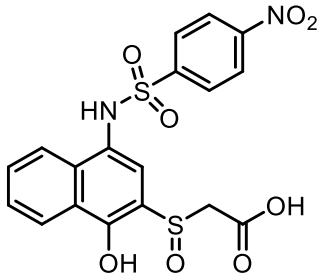
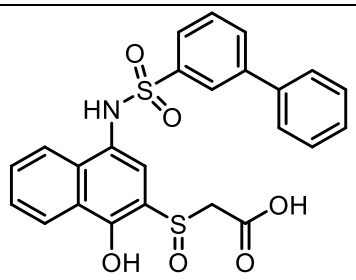
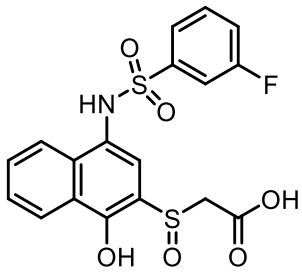
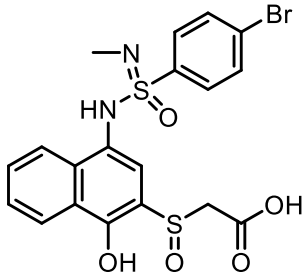
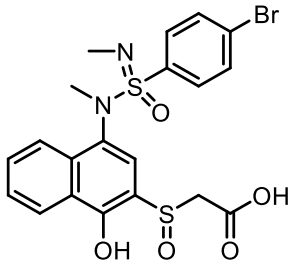
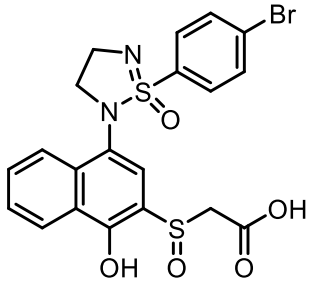
9. The compound or the pharmaceutically acceptable salt, stereoisomer, or solvate thereof of any one of claims 1-3, wherein the compound is selected from any one of the following compounds:

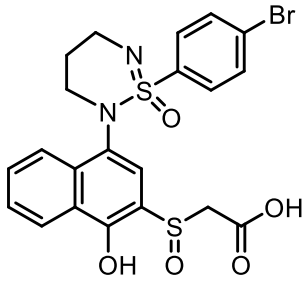
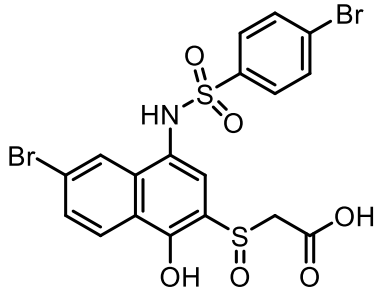
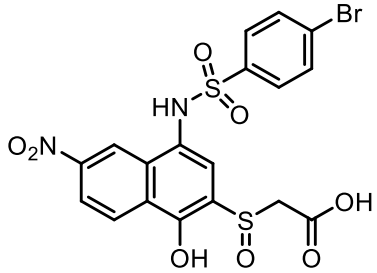
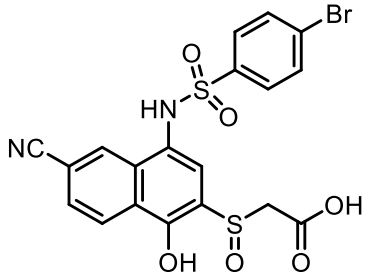
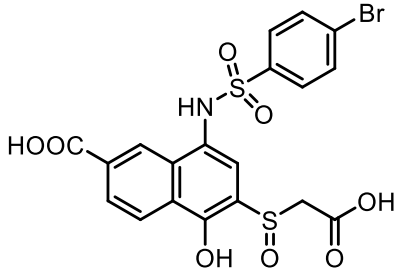
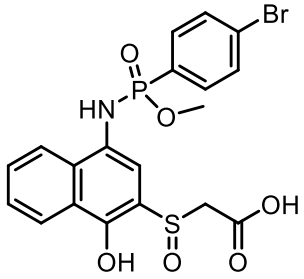
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I- 2	
I- 3	
I- 4	
I- 5	
I- 6	

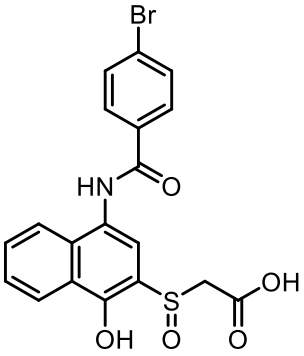
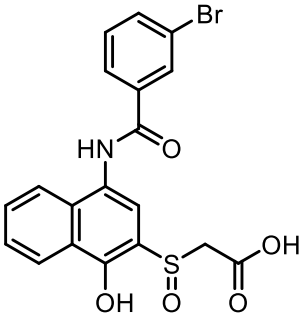
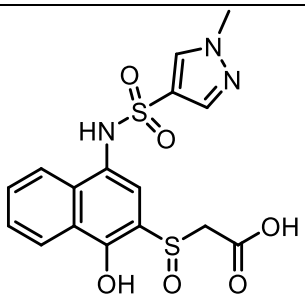
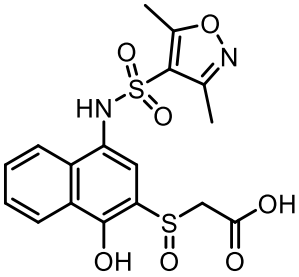
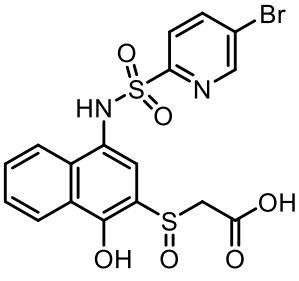
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I- 8	
I - 9-1	
I - 9-2	
I-10	

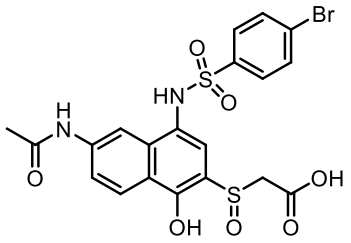
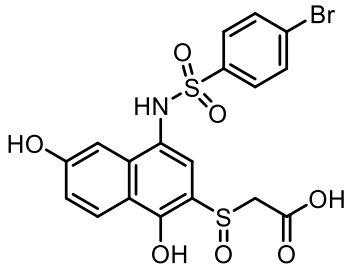
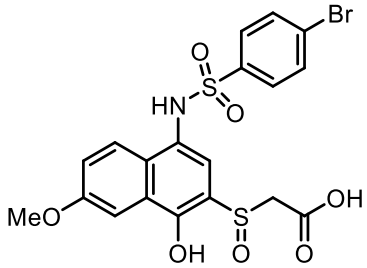
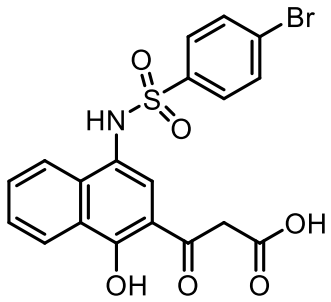
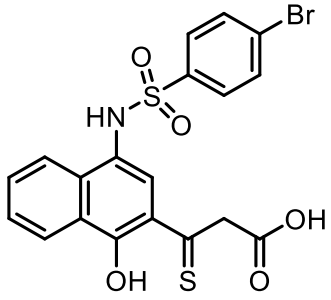
I-11-1	
I-11-2	
I-12	
I-13-1	
I-14-1	
I-15-1	

I-16-1	
I-17-1	
I-18-1	
I-19-1	
I-20-1	
I-21-1	

I-22-1	
I-23-1	
I-24-1	
I-25-1	
I-26	
I-27	

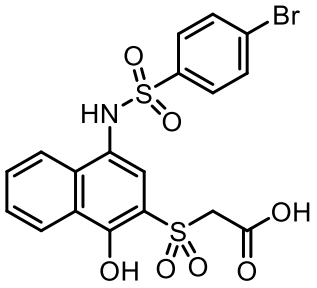
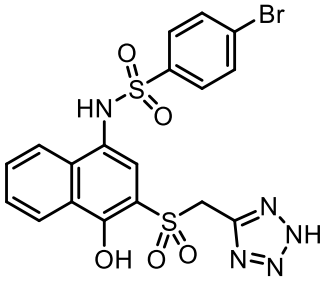
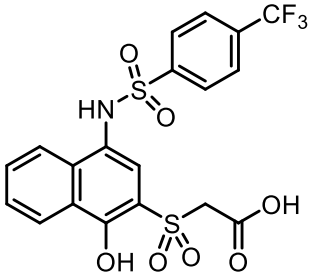
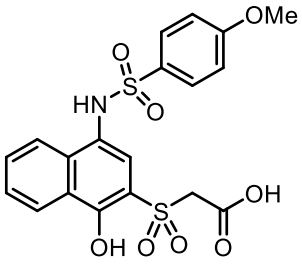
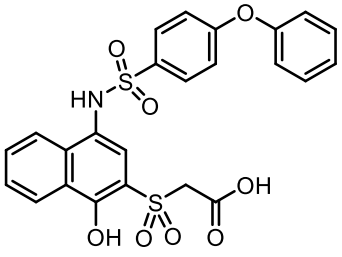
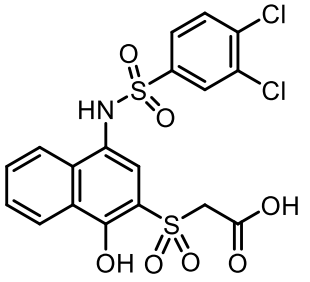
I-28	
I-29	
I-30	
I-31	
I-32	
I-33	

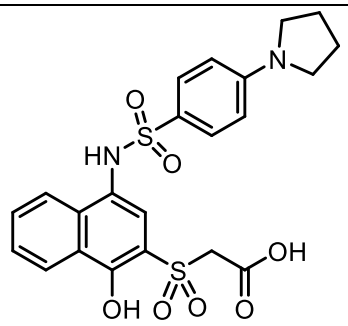
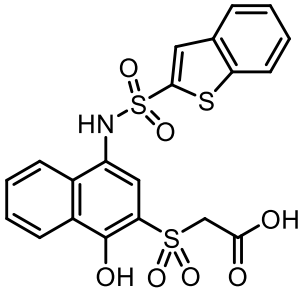
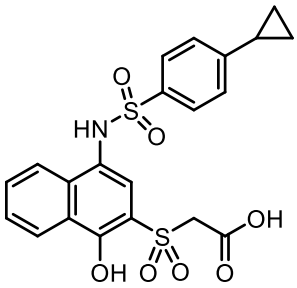
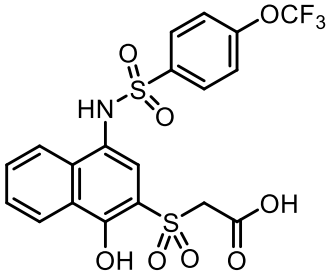
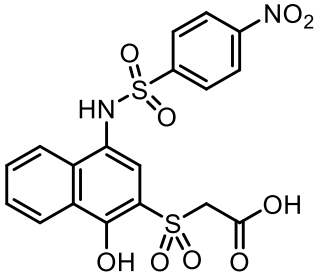
I-34	
I-35-1	
I-36	
I-37	
I-38	

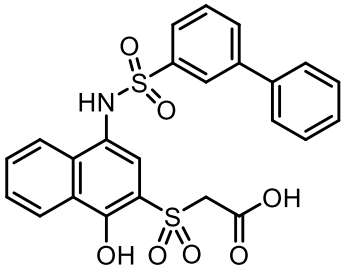
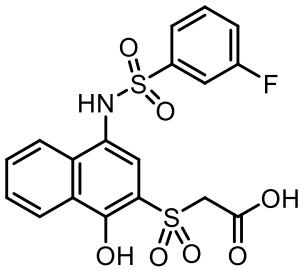
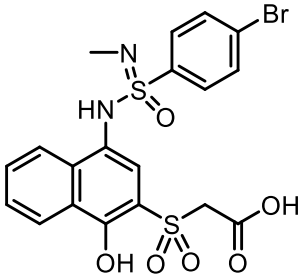
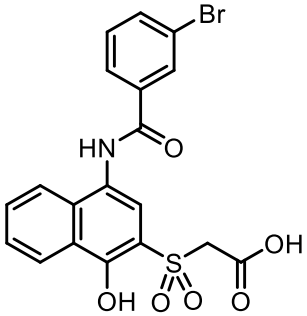
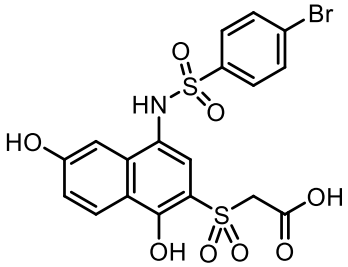
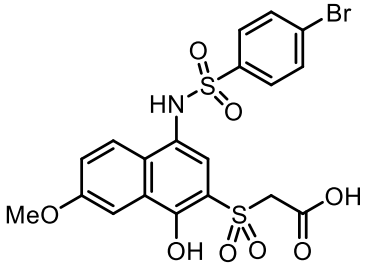
I-39	
I-40-1	
I-41-1	
I-43	
I-44	

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10. The compound or the pharmaceutically acceptable salt, stereoisomer, or solvate thereof of claim 7 or 8, wherein the compound is selected from any one of the following compounds:

I-42	
I-7-2	
I-14-2	
I-15-2	
I-16-2	
I-17-2	

I-18-2	
I-19-2	
I-20-2	
I - 21-2	
I - 22-2	

I - 23-2	
I - 24-2	
I - 25-2	
I - 35-2	
I - 40-2	
I - 41-2	

11. A pharmaceutical composition comprising the compound, or the pharmaceutically acceptable salt, stereoisomer, or solvate thereof of any one of claims 1 to 10.

12. A compound, or the pharmaceutically acceptable salt, stereoisomer, solvate or prodrug thereof of any one of claims 1 to 10, or the pharmaceutical composition of claim 11, for use in therapy.