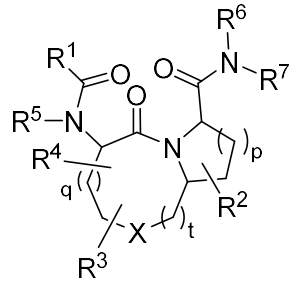


(**I**);

and pharmaceutically acceptable salts and compositions thereof, wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, X, q, t and p are as described herein.

[0006a] In one aspect, the present disclosure provides a compound having the structural formula **I**:



(**I**);

or a pharmaceutically acceptable salt thereof, wherein:

q is 0 or 1 and t is 0, 1, or 2, provided that at least one of q or t is 1;

p is 1 or 2;

X is selected from S, SO_2, -S(=O)=NH, and NR^8;

R^1 is selected from an 8- to 10-membered fused bicyclic heteroaryl substituted with –$CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$, –$CR^{1a}R^{2a}P(O)[OR^{1b}][NH(AA)C(O)OR^T]$, –$P(O)OR^{1b}OR^{2b}$, -$[P(O)[NHR^{Ty}][NH(AA)C(O)OR^T]$, or –$P(O)[OR^{1b}][NH(AA)C(O)OR^T]$; an 8- to 10-membered fused bicyclic heterocyclyl substituted with –$CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$, –$CR^{1a}R^{2a}P(O)[OR^{1b}][NH(AA)C(O)OR^T]$, –$P(O)OR^{1b}OR^{2b}$, -$[P(O)[NHR^{Ty}][NH(AA)C(O)OR^T]$, or –$P(O)[OR^{1b}][NH(AA)C(O)OR^T]$; an aryl substituted with –$CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$, –$CR^{1a}R^{2a}P(O)[OR^{1b}][NH(AA)C(O)OR^T]$, –$P(O)OR^{1b}OR^{2b}$, -$[P(O)[NHR^{Ty}][NH(AA)C(O)OR^T]$, or –$P(O)[OR^{1b}][NH(AA)C(O)OR^T]$, wherein said aryl may be further optionally substituted with 1 or 2 groups independently selected from cyano, (C_1-C_4)alkoxy, and halo; a -(C_1-C_4)alkyl(aryl) wherein said aryl portion of -(C_1-C_4)alkyl(aryl) is substituted with –$CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$, –$CR^{1a}R^{2a}P(O)[OR^{1b}][NH(AA)C(O)OR^T]$, –$P(O)OR^{1b}OR^{2b}$, -$[P(O)[NHR^{Ty}][NH(AA)C(O)OR^T]$, -[P(O)[NH(AA)C(O)ORT][NH(AA)C(O)ORT], or –$P(O)[OR^{1b}][NH(AA)C(O)OR^T]$; and a -

(C_2-C_4)alkenyl(aryl) wherein said aryl portion of -(C_2-C_4)alkenyl(aryl) is substituted with –$CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$, –$CR^{1a}R^{2a}P(O)[OR^{1b}][NH(AA)C(O)OR^{T}]$, –$P(O)OR^{1b}OR^{2b}$, -$[P(O)[NHR^{Ty}][NH(AA)C(O)OR^{T}]$, or –$P(O)[OR^{1b}][NH(AA)C(O)OR^{T}]$;

R^{1a} and R^{2a} are each independently selected from hydrogen, cyano, (C_1-C_4)alkyl, hydroxy(C_1-C_4)alkyl and fluoro; or R^{1a} and R^{2a} taken together with the carbon they are attached form oxo;

R^{1b} and R^{2b} are each independently selected from hydrogen, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, -[(C_1-C_4)alkyl]-OC(O)-[(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-C(O)O-[(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-O-[(C_1-C_{20})alkyl], -[(C_1-C_4)alkyl]-OC(O)-[halo(C_1-C_4)alkyl], [(C_1-C_4)alkyl]-OC(O)O-[5- to 7-membered heterocyclyl], [(C_1-C_4)alkyl]-OC(O)-[5- to 7-membered heterocyclyl], -[(C_1-C_4)alkyl]-OC(O)-[(C_1-C_4)alkyl]-OH, -[(C_1-C_4)alkyl]-OC(O)-[(C_1-C_4)alkyl]-O-[(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-OC(O)O-[(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-OC(O)O-[halo(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-OC(O)O-[(C_1-C_4)alkyl]-OH, -[(C_1-C_4)alkyl]-OC(O)O-[(C_1-C_4)alkyl]-O-[(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-SC(O)-[(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-SC(O)-[halo(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-SC(O)-[(C_1-C_4)alkyl]-OH, -[(C_1-C_4)alkyl]-SC(O)-[(C_1-C_4)alkyl]-O-[(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-OC(O)NH(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-OC(O)N[(C_1-C_4)alkyl]$_2$, and aryl, wherein said 5- to 6- membered heteroaryl and aryl are each optionally and independently substituted with, as valency permits, 1 to 2 groups selected from halo, cyano, and (C_1-C_4)alkyl and wherein said 5- to 7-membered heterocyclyl of [(C_1-C_4)alkyl]-OC(O)O-[5- to 7-membered heterocyclyl] and [(C_1-C_4)alkyl]-OC(O)-[5- to 7-membered heterocyclyl] are each optionally and independently substituted with, as valency permits 1 to 2 groups selected from $C(O)OR^{h}$;

R^2 is selected from hydrogen, halo, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, hydroxy(C_1-C_4)alkyl, cyano, and hydroxyl;

R^3 and R^4 are each independently selected from hydrogen, halo, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, hydroxy(C_1-C_4)alkyl, -(C_1-C_4)alkylphenyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, -(C_1-C_4)alkyl(C_1-C_4)alkoxy, hydroxyl, cyano, $-NR^{a}R^{b}$, phenyl, (C_3-C_6)cycloalkyl, 5- to 6-membered heteroaryl, and 4- to 6-membered heterocyclyl, wherein said phenyl, (C_3-C_6)cycloalkyl, 5- to 6-membered heteroaryl, and 4- to 6-membered heterocyclyl are each optionally substituted with, as valency permits, 1 to 3 groups selected from R^{S};

R^5 and R^6 are each independently selected from hydrogen, phenyl, and (C_1-C_4)alkyl;

R^7 is selected from (C_1-C_4)alkyl, phenyl, 4- to 9-membered monocyclic or bicyclic heterocyclyl, and 5- to 10-membered monocyclic or bicyclic heteroaryl, wherein said (C_1-

C_4)alkyl is optionally substituted with, as valency permits, 1 to 3 groups selected from R^Y and said phenyl, 4- to 9-membered monocyclic or bicyclic heterocyclyl, and 5- to 10-membered monocyclic or bicyclic heteroaryl are each optionally substituted with, as valency permits, 1 to 3 groups selected from R^Z; or

R^6 and R^7 together with the nitrogen atom to which they are attached form a 4- to 14-membered monocyclic or bicyclic heterocyclyl or a 5- to 12-membered monocyclic or bicyclic heteroaryl, each of which being optionally substituted with, as valency permits, 1 to 3 groups selected from R^Q;

R^8 is selected from hydrogen, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_3-C_6)cycloalkyl, 5- to 7-membered heterocyclyl, -(C_1-C_4)[5- to 7-membered heterocyclyl], 5- to 10-membered heteroaryl, -(C_1-C_4)[5- to 10-membered heteroaryl], phenyl, -(C_1-C_4)alkylphenyl, –C(O)R^{Ha}, –C(O)OR^{Ha}, -C(O)N$R^{Ha}R^{Hb}$, -C(O)OR^{Ha}, -SO$R^{Ha}R^{Hb}$ and -SO_2R^{Ha}, wherein said (C_3-C_6)cycloalkyl, 5- to 7-membered heterocyclyl, 5- to 10-membered heteroaryl, phenyl, the phenyl on (C_1-C_4)alkylphenyl, the 5- to 7-membered heterocyclyl on -(C_1-C_4)[5- to 7-membered heterocyclyl], and the 5- to 6-membered heteroaryl on -(C_1-C_4)[5- to 6-membered heteroaryl] are each optionally substituted with, as valency permits, 1 to 3 groups selected from R^U;

R^{Ha} is selected from (C_1-C_{10})alkyl, (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, phenyl, 5- to 10-membered monocyclic or bicyclic heteroaryl, and 4- to 10-membered monocyclic or bicyclic heterocyclyl, wherein said (C_1-C_{10})alkyl, (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl are each optionally substituted with, as valency permits, 1 to 2 groups selected from R^O and wherein said 5-to 10-membered monocyclic or bicyclic heteroaryl and said 4-to 10-membered monocyclic or bicyclic heterocyclyl are each optionally substituted with, as valency permits, 1 to 3 groups selected from halo, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, oxo, cyano, and 4- to 6-membered heterocyclyl optionally substituted with C_1-C_4alkyl;

R^O is selected from halo, (C_1-C_4)alkoxy, OH, phenyl, NH_2, -NH(C_1-C_{10})alkyl, -N[(C_1-C_{10})alkyl], ($C_{3\text{-}6}$cycloalkyl), 4- to 10-membered monocyclic or fused bicyclic heterocyclyl and 5-to 10-membered monocyclic or bicyclic heteroaryl, wherein said 5- to 10-membered monocyclic or bicyclic heteroaryl and said 4-to 10-membered monocyclic or bicyclic heterocyclyl are each optionally substituted with, as valency permits, 1 to 3 groups selected from halo, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, oxo, and cyano;

R^{Hb} is hydrogen or (C_1-C_4)alkyl;

AA is the residue of an alpha or beta natural or non-natural amino acid;

R^T and R^{Ty} are each independently selected from (C_1-C_4)alkyl, benzyl, and phenyl, wherein said phenyl is optionally substituted with 1 or 2 groups selected from halo, (C_1-C_4)alkyl, and halo(C_1-C_4)alkyl;

R^Q and R^U are each independently selected from halo, (C_2-C_4)alkenyl, (C_1-C_4)alkyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, cyano, phenyl, hydroxyl, 4- to 9-membered monocyclic or bicyclic heterocyclyl, 5- to 10-membered monocyclic or bicyclic heteroaryl, (C_3-C_6)cycloalkyl, oxo, imino, -OR^e, -$C(O)R^g$, -$C(O)OR^e$, -$NR^cC(O)R^e$, -$C(O)NR^cR^d$, -NR^aR^b, -$S(O)R^eR^f$, -$S(O)_2R^f$, -$S(O)$=NH(C_1-C_4)alkyl, -$S(O)NR^eR^f$, and -$S(O)_2NR^eR^f$, wherein said (C_2-C_4)alkenyl and (C_1-C_4)alkyl are each optionally and independently substituted with, as valency permits, 1 to 3 groups selected from R^M, and wherein said phenyl, 5- to 10-membered monocyclic or bicyclic heteroaryl, (C_3-C_6)cycloalkyl, and 4- to 9-membered monocyclic or bicyclic heterocyclyl are each optionally and independently substituted with, as valency permits, 1 to 3 groups selected from R^F;

R^Y is selected from halo, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, cyano, -$C(O)R^g$, -$C(O)OR^e$, -$NHC(O)R^e$, -NR^aR^b, -$S(O)R^eR^f$, -$S(O)_2R^f$, -$S(O)NR^eR^f$, -$S(O)$=NH(C_1-C_4)alkyl, -$S(O)_2NR^eR^f$, hydroxyl, phenyl, 4- to 6-membered heterocyclyl, and 5- to 10-membered monocyclic or bicyclic heteroaryl, wherein said phenyl, 4- to 6-membered heterocyclyl, and 5- to 10-membered monocyclic or bicyclic heteroaryl are each optionally substituted with, as valency permits, 1 to 3 groups selected from R^X;

R^M and R^J are each independently selected from halo, (C_1-C_4)alkyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, cyano, -$C(O)R^g$, -$C(O)OR^e$, -$NHC(O)R^e$, -$C(O)NR^cR^d$, -NR^aR^b, -$S(O)R^eR^f$, -$S(O)_2R^f$, -$S(O)NR^eR^f$, -$S(O)$=NH(C_1-C_4)alkyl, -$S(O)_2NR^eR^f$, hydroxyl, phenyl, 4- to 6-membered heterocyclyl, and 5- to 10-membered monocyclic or bicyclic heteroaryl, wherein said phenyl, 4- to 6-membered heterocyclyl, and 5- to 10-membered monocyclic or bicyclic heteroaryl are each optionally substituted with, as valency permits, 1 to 3 groups selected from R^X;

R^F, R^S, R^X, and R^Z are each independently selected from halo, cyano, (C_1-C_4)alkyl, (C_3-C_6cycloalkyl), halo(C_1-C_4)alkyl, -(C_1-C_4)alkyl(C_1-C_4)alkoxy, hydroxy(C_1-C_4)alkyl, -(C_1-C_4)alkylphenyl, -(C_1-C_4)alkylheteroaryl, (C_2-C_4)alkenyl, halo(C_2-C_4)alkenyl, (C_2-C_4)alkynyl, halo(C_2-C_4)alkynyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, -OR^e, oxo, imino, phenyl, 4- to 6-membered heterocyclyl, -$S(O)R^eR^f$, -$S(O)_2R^f$, -$S(O)$=NH(C_1-C_4)alkyl, -$S(O)NR^eR^f$, and -$S(O)_2NR^eR^f$, -$C(O)OR^e$, -$NR^cC(O)R^e$, -(C_1-C_4alkyl)$C(O)R^g$, -$C(O)R^g$, -(C_1-

C_4alkyl)C(O)NR^cR^d, -C(O)NR^cR^d, -NO_2, and -NR^aR^b, wherein the (C_1-C_4)alkyl is optionally substituted with cyano, wherein said phenyl, said 4- to 6-membered heterocyclyl, and said phenyl for -(C_1-C_4)alkylphenyl are each optionally and independently substituted with, as valency permits 1 to 3 groups selected from halo, cyano, oxo, (C_1-C_{10})alkyl, (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, halo(C_1-C_{10})alkyl, (C_1-C_{10})alkoxy, and halo(C_1-C_{10})alkoxy, wherein said (C_1-C_{10})alkyl, (C_2-C_{10})alkenyl and (C_2-C_{10})alkynyl are each optionally substituted with, as valency permits a 5-to 10-membered monocyclic or bicyclic heteroaryl or a 4-to 10-membered monocyclic or bicyclic heterocyclyl each of said 5-to 10-membered monocyclic and bicyclic heteroaryl or a 4-to 10-membered monocyclic or bicyclic heterocyclyl being optionally substituted with oxo or a 5- to 7-membered heterocyclyl that is optionally substituted with 1 to 2 oxo; and

R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are each independently selected from, as valency permits, hydrogen, (C_1-C_4)alkyl, (C_2-C_4)alkynyl, -(C_1-C_4)alkylphenyl, phenyl, (C_3-C_6)cycloalkyl, 4- to 6-membered heterocyclyl and 5- to 6-membered heteroaryl, wherein said (C_1-C_4)alkyl is optionally substituted with, as valency permits, 1 to 3 groups selected from R^J, and said phenyl, (C_3-C_6)cycloalkyl, 4- to 6-membered heterocyclyl, and 5- to 6-membered heteroaryl are each independently optionally substituted with, as valency permits, 1 to 3 groups selected from halo, cyano, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, hydroxyl, phenyl, and benzyl.

[0007] The disclosed compounds of Formula **I** and pharmaceutically acceptable salts thereof inhibit STAT3 and/or STAT6, and are useful in a variety of therapeutic applications such as, for example, in treating cancer and inflammatory conditions.

[0007a] In another aspect, the present disclosure provides use of a compound as disclosed herein or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of conditions associated with modulation of STAT3 or STAT6, wherein said condition is a cancer or an inflammatory condition.

[0007b] In another aspect, the present disclosure provides a compound as disclosed herein or a pharmaceutically acceptable salt thereof, for use in therapy.

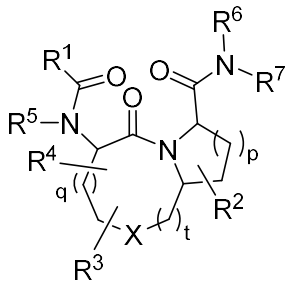
[0008] Pharmaceutical compositions comprising the compounds and pharmaceutically acceptable salts of the disclosed compounds of Formula **I**, as well as methods for their preparation are also included.

[0009] Methods of treating conditions responsive to the modulation of STAT3 and/or STAT6 using the disclosed compounds, pharmaceutically acceptable salts, and compositions thereof are also included.

DETAILED DESCRIPTION

1. *General Description of Compounds*

[0010] In a second embodiment, provided herein is a compound of structural Formula **I**:



(**I**);

q is 0 or 1 and t is 0, 1, or 2, provided that at least one of q or t is 1;

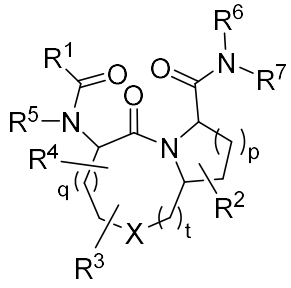
p is 1 or 2;

X is selected from S, SO_2, -S(=O)=NH, and NR^8;

R^1 is selected from an 8- to 10-membered fused bicyclic heteroaryl substituted with –$CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$, –$CR^{1a}R^{2a}P(O)[OR^{1b}][NH(AA)C(O)OR^T]$, –$P(O)OR^{1b}OR^{2b}$, -$[P(O)[NHR^{Ty}][NH(AA)C(O)OR^T]$, or –$P(O)[OR^{1b}][NH(AA)C(O)OR^T]$; an 8- to 10-membered fused bicyclic heterocyclyl substituted with –$CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$, –

Listing of Claims:

1. A compound having the structural formula **I**:



(**I**);

or a pharmaceutically acceptable salt thereof, wherein:

q is 0 or 1 and t is 0, 1, or 2, provided that at least one of q or t is 1;

p is 1 or 2;

X is selected from S, SO_2, -S(=O)=NH, and NR^8;

R^1 is selected from an 8- to 10-membered fused bicyclic heteroaryl substituted with –$CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$, –$CR^{1a}R^{2a}P(O)[OR^{1b}][NH(AA)C(O)OR^T]$, –$P(O)OR^{1b}OR^{2b}$, -$[P(O)[NHR^{Ty}][NH(AA)C(O)OR^T]$, or –$P(O)[OR^{1b}][NH(AA)C(O)OR^T]$; an 8- to 10-membered fused bicyclic heterocyclyl substituted with –$CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$, –$CR^{1a}R^{2a}P(O)[OR^{1b}][NH(AA)C(O)OR^T]$, –$P(O)OR^{1b}OR^{2b}$, -$[P(O)[NHR^{Ty}][NH(AA)C(O)OR^T]$, or –$P(O)[OR^{1b}][NH(AA)C(O)OR^T]$; an aryl substituted with –$CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$, –$CR^{1a}R^{2a}P(O)[OR^{1b}][NH(AA)C(O)OR^T]$, –$P(O)OR^{1b}OR^{2b}$, -$[P(O)[NHR^{Ty}][NH(AA)C(O)OR^T]$, or –$P(O)[OR^{1b}][NH(AA)C(O)OR^T]$, wherein said aryl may be further optionally substituted with 1 or 2 groups independently selected from cyano, (C_1-C_4)alkoxy, and halo; a -(C_1-C_4)alkyl(aryl) wherein said aryl portion of -(C_1-C_4)alkyl(aryl) is substituted with –$CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$, –$CR^{1a}R^{2a}P(O)[OR^{1b}][NH(AA)C(O)OR^T]$, –$P(O)OR^{1b}OR^{2b}$, -$[P(O)[NHR^{Ty}][NH(AA)C(O)OR^T]$, -[P(O)[NH(AA)C(O)ORT][NH(AA)C(O)ORT], or –$P(O)[OR^{1b}][NH(AA)C(O)OR^T]$; and a -($C_2$-$C_4$)alkenyl(aryl) wherein said aryl portion of -(C_2-C_4)alkenyl(aryl) is substituted with –$CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$, –$CR^{1a}R^{2a}P(O)[OR^{1b}][NH(AA)C(O)OR^T]$, –$P(O)OR^{1b}OR^{2b}$, -$[P(O)[NHR^{Ty}][NH(AA)C(O)OR^T]$, or –$P(O)[OR^{1b}][NH(AA)C(O)OR^T]$;

R^{1a} and R^{2a} are each independently selected from hydrogen, cyano, (C_1-C_4)alkyl, hydroxy(C_1-C_4)alkyl and fluoro; or R^{1a} and R^{2a} taken together with the carbon they are attached form oxo;

R^{1b} and R^{2b} are each independently selected from hydrogen, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, -[(C_1-C_4)alkyl]-OC(O)-[(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-C(O)O-[(C_1-C_4)alkyl], -[(C_1-

C_4)alkyl]-O-[(C_1-C_{20})alkyl], -[(C_1-C_4)alkyl]-OC(O)-[halo(C_1-C_4)alkyl], [(C_1-C_4)alkyl]-OC(O)O-[5- to 7-membered heterocyclyl], [(C_1-C_4)alkyl]-OC(O)-[5- to 7-membered heterocyclyl], -[(C_1-C_4)alkyl]-OC(O)-[(C_1-C_4)alkyl]-OH, -[(C_1-C_4)alkyl]-OC(O)-[(C_1-C_4)alkyl]-O-[(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-OC(O)O-[(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-OC(O)O-[halo(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-OC(O)O-[(C_1-C_4)alkyl]-OH, -[(C_1-C_4)alkyl]-OC(O)O-[(C_1-C_4)alkyl]-O-[(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-SC(O)-[(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-SC(O)-[halo(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-SC(O)-[(C_1-C_4)alkyl]-OH, -[(C_1-C_4)alkyl]-SC(O)-[(C_1-C_4)alkyl]-O-[(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-OC(O)NH(C_1-C_4)alkyl], -[(C_1-C_4)alkyl]-OC(O)N[(C_1-C_4)alkyl]$_2$, and aryl, wherein said 5- to 6- membered heteroaryl and aryl are each optionally and independently substituted with, as valency permits, 1 to 2 groups selected from halo, cyano, and (C_1-C_4)alkyl and wherein said 5- to 7-membered heterocyclyl of [(C_1-C_4)alkyl]-OC(O)O-[5- to 7-membered heterocyclyl] and [(C_1-C_4)alkyl]-OC(O)-[5- to 7-membered heterocyclyl] are each optionally and independently substituted with, as valency permits 1 to 2 groups selected from C(O)OR^h;

R^2 is selected from hydrogen, halo, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, hydroxy(C_1-C_4)alkyl, cyano, and hydroxyl;

R^3 and R^4 are each independently selected from hydrogen, halo, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, hydroxy(C_1-C_4)alkyl, -(C_1-C_4)alkylphenyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, -(C_1-C_4)alkyl(C_1-C_4)alkoxy, hydroxyl, cyano, -NR^{a}R^b, phenyl, (C_3-C_6)cycloalkyl, 5- to 6-membered heteroaryl, and 4- to 6-membered heterocyclyl, wherein said phenyl, (C_3-C_6)cycloalkyl, 5- to 6-membered heteroaryl, and 4- to 6-membered heterocyclyl are each optionally substituted with, as valency permits, 1 to 3 groups selected from R^S;

R^5 and R^6 are each independently selected from hydrogen, phenyl, and (C_1-C_4)alkyl;

R^7 is selected from (C_1-C_4)alkyl, phenyl, 4- to 9-membered monocyclic or bicyclic heterocyclyl, and 5- to 10-membered monocyclic or bicyclic heteroaryl, wherein said (C_1-C_4)alkyl is optionally substituted with, as valency permits, 1 to 3 groups selected from R^Y and said phenyl, 4- to 9-membered monocyclic or bicyclic heterocyclyl, and 5- to 10-membered monocyclic or bicyclic heteroaryl are each optionally substituted with, as valency permits, 1 to 3 groups selected from R^Z; or

R^6 and R^7 together with the nitrogen atom to which they are attached form a 4- to 14-membered monocyclic or bicyclic heterocyclyl or a 5- to 12-membered monocyclic or bicyclic heteroaryl, each of which being optionally substituted with, as valency permits, 1 to 3 groups selected from R^Q;

R^8 is selected from hydrogen, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_3-C_6)cycloalkyl, 5- to 7-membered heterocyclyl, -(C_1-C_4)[5- to 7-membered heterocyclyl], 5- to 10-membered heteroaryl, -(C_1-C_4)[5- to 10-membered heteroaryl], phenyl, -(C_1-C_4)alkylphenyl, –C(O)R^{Ha}, –C(O)OR^{Ha}, -C(O)N$R^{Ha}R^{Hb}$, -C(O)OR^{Ha}, -SO$R^{Ha}R^{Hb}$ and -SO_2R^{Ha}, wherein said (C_3-C_6)cycloalkyl, 5- to 7-membered heterocyclyl, 5- to 10-membered heteroaryl, phenyl, the phenyl on (C_1-C_4)alkylphenyl, the 5- to 7-membered heterocyclyl on -(C_1-C_4)[5- to 7-membered heterocyclyl], and the 5- to 6-membered heteroaryl on -(C_1-C_4)[5- to 6-membered heteroaryl] are each optionally substituted with, as valency permits, 1 to 3 groups selected from R^U;

R^{Ha} is selected from (C_1-C_{10})alkyl, (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, phenyl, 5- to 10-membered monocyclic or bicyclic heteroaryl, and 4- to 10-membered monocyclic or bicyclic heterocyclyl, wherein said (C_1-C_{10})alkyl, (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl are each optionally substituted with, as valency permits, 1 to 2 groups selected from R^O and wherein said 5-to 10-membered monocyclic or bicyclic heteroaryl and said 4-to 10-membered monocyclic or bicyclic heterocyclyl are each optionally substituted with, as valency permits, 1 to 3 groups selected from halo, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, oxo, cyano, and 4- to 6-membered heterocyclyl optionally substituted with C_1-C_4alkyl;

R^O is selected from halo, (C_1-C_4)alkoxy, OH, phenyl, NH_2, -NH(C_1-C_{10})alkyl, -N[(C_1-C_{10})alkyl], ($C_{3\text{-}6}$cycloalkyl), 4- to 10-membered monocyclic or fused bicyclic heterocyclyl and 5-to 10-membered monocyclic or bicyclic heteroaryl, wherein said 5- to 10-membered monocyclic or bicyclic heteroaryl and said 4-to 10-membered monocyclic or bicyclic heterocyclyl are each optionally substituted with, as valency permits, 1 to 3 groups selected from halo, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, oxo, and cyano;

R^{Hb} is hydrogen or (C_1-C_4)alkyl;

AA is the residue of an alpha or beta natural or non-natural amino acid;

R^T and R^{Ty} are each independently selected from (C_1-C_4)alkyl, benzyl, and phenyl, wherein said phenyl is optionally substituted with 1 or 2 groups selected from halo, (C_1-C_4)alkyl, and halo(C_1-C_4)alkyl;

R^Q and R^U are each independently selected from halo, (C_2-C_4)alkenyl, (C_1-C_4)alkyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, cyano, phenyl, hydroxyl, 4- to 9-membered monocyclic or bicyclic heterocyclyl, 5- to 10-membered monocyclic or bicyclic heteroaryl, (C_3-C_6)cycloalkyl, oxo, imino, -OR^e, -C(O)R^g, -C(O)OR^e, -NR^cC(O)R^e, -C(O)N$R^c R^d$, -N$R^a R^b$, -S(O)$R^e R^f$, -$S(O)_2R^f$, -S(O)=NH(C_1-C_4)alkyl, -S(O)N$R^e R^f$, and -$S(O)_2$N$R^e R^f$, wherein said

(C_2-C_4)alkenyl and (C_1-C_4)alkyl are each optionally and independently substituted with, as valency permits, 1 to 3 groups selected from R^M, and wherein said phenyl, 5- to 10-membered monocyclic or bicyclic heteroaryl, (C_3-C_6)cycloalkyl, and 4- to 9-membered monocyclic or bicyclic heterocyclyl are each optionally and independently substituted with, as valency permits, 1 to 3 groups selected from R^F;

R^Y is selected from halo, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, cyano, -C(O)R^g, -C(O)OR^e, -NHC(O)R^e, -N$R^a$$R^b$, -S(O)$R^e$$R^f$, -S(O)$_2$$R^f$, -S(O)N$R^e$$R^f$, -S(O)=NH($C_1$-$C_4$)alkyl, -S(O)$_2NR^e$$R^f$, hydroxyl, phenyl, 4- to 6-membered heterocyclyl, and 5- to 10-membered monocyclic or bicyclic heteroaryl, wherein said phenyl, 4- to 6-membered heterocyclyl, and 5- to 10-membered monocyclic or bicyclic heteroaryl are each optionally substituted with, as valency permits, 1 to 3 groups selected from R^X;

R^M and R^J are each independently selected from halo, (C_1-C_4)alkyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, cyano, -C(O)R^g, -C(O)OR^e, -NHC(O)R^e, -C(O)N$R^c$$R^d$, -N$R^a$$R^b$, -S(O)$R^e$$R^f$, -S(O)$_2$$R^f$, -S(O)N$R^e$$R^f$, -S(O)=NH($C_1$-$C_4$)alkyl, -S(O)$_2NR^e$$R^f$, hydroxyl, phenyl, 4- to 6-membered heterocyclyl, and 5- to 10-membered monocyclic or bicyclic heteroaryl, wherein said phenyl, 4- to 6-membered heterocyclyl, and 5- to 10-membered monocyclic or bicyclic heteroaryl are each optionally substituted with, as valency permits, 1 to 3 groups selected from R^X;

R^F, R^S, R^X, and R^Z are each independently selected from halo, cyano, (C_1-C_4)alkyl, (C_3-C_6cycloalkyl), halo(C_1-C_4)alkyl, -(C_1-C_4)alkyl(C_1-C_4)alkoxy, hydroxy(C_1-C_4)alkyl, -(C_1-C_4)alkylphenyl, -(C_1-C_4)alkylheteroaryl, (C_2-C_4)alkenyl, halo(C_2-C_4)alkenyl, (C_2-C_4)alkynyl, halo(C_2-C_4)alkynyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, -OR^e, oxo, imino, phenyl, 4- to 6-membered heterocyclyl, -S(O)$R^e$$R^f$, -S(O)$_2$$R^f$, -S(O)=NH($C_1$-$C_4$)alkyl, -S(O)N$R^e$$R^f$, and -S(O)$_2NR^e$$R^f$, -C(O)O$R^e$, -N$R^c$C(O)$R^e$, -($C_1$-$C_4$alkyl)C(O)$R^g$, -C(O)$R^g$, -($C_1$-$C_4$alkyl)C(O)N$R^c$$R^d$, -C(O)N$R^c$$R^d$, -$NO_2$, and -N$R^a$$R^b$, wherein the ($C_1$-$C_4$)alkyl is optionally substituted with cyano, wherein said phenyl, said 4- to 6-membered heterocyclyl, and said phenyl for -(C_1-C_4)alkylphenyl are each optionally and independently substituted with, as valency permits 1 to 3 groups selected from halo, cyano, oxo, (C_1-C_{10})alkyl, (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, halo(C_1-C_{10})alkyl, (C_1-C_{10})alkoxy, and halo(C_1-C_{10})alkoxy, wherein said (C_1-C_{10})alkyl, (C_2-C_{10})alkenyl and (C_2-C_{10})alkynyl are each optionally substituted with, as valency permits a 5-to 10-membered monocyclic or bicyclic heteroaryl or a 4-to 10-membered monocyclic or bicyclic heterocyclyl each of said 5-to 10-membered monocyclic and bicyclic heteroaryl or a 4-to 10-membered monocyclic or bicyclic heterocyclyl being

optionally substituted with oxo or a 5- to 7-membered heterocyclyl that is optionally substituted with 1 to 2 oxo; and

R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are each independently selected from, as valency permits, hydrogen, (C_1-C_4)alkyl, (C_2-C_4)alkynyl, -(C_1-C_4)alkylphenyl, phenyl, (C_3-C_6)cycloalkyl, 4- to 6-membered heterocyclyl and 5- to 6-membered heteroaryl, wherein said (C_1-C_4)alkyl is optionally substituted with, as valency permits, 1 to 3 groups selected from R^J, and said phenyl, (C_3-C_6)cycloalkyl, 4- to 6-membered heterocyclyl, and 5- to 6-membered heteroaryl are each independently optionally substituted with, as valency permits, 1 to 3 groups selected from halo, cyano, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, hydroxyl, phenyl, and benzyl.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein

R^1 is selected from an 8- to 10-membered fused bicyclic heteroaryl substituted with –$CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$, –$CR^{1a}R^{2a}P(O)[OR^{1b}][NH(AA)C(O)OR^T]$, –$P(O)OR^{1b}OR^{2b}$, -$[P(O)[NHR^{Ty}][NH(AA)C(O)OR^T]$, or –$P(O)[OR^{1b}][NH(AA)C(O)OR^T]$; an 8- to 10-membered fused bicyclic heterocyclyl substituted with –$CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$, –$CR^{1a}R^{2a}P(O)[OR^{1b}][NH(AA)C(O)OR^T]$, –$P(O)OR^{1b}OR^{2b}$, -$[P(O)[NHR^{Ty}][NH(AA)C(O)OR^T]$, or –$P(O)[OR^{1b}][NH(AA)C(O)OR^T]$; an aryl substituted with –$CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$, –$CR^{1a}R^{2a}P(O)[OR^{1b}][NH(AA)C(O)OR^T]$, –$P(O)OR^{1b}OR^{2b}$, -$[P(O)[NHR^{Ty}][NH(AA)C(O)OR^T]$, or –$P(O)[OR^{1b}][NH(AA)C(O)OR^T]$; a -($C_1$-$C_4$)alkyl(aryl) wherein said aryl portion of -(C_1-C_4)alkyl(aryl) is substituted with –$CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$, –$CR^{1a}R^{2a}P(O)[OR^{1b}][NH(AA)C(O)OR^T]$, –$P(O)OR^{1b}OR^{2b}$, -$[P(O)[NHR^{Ty}][NH(AA)C(O)OR^T]$, or –$P(O)[OR^{1b}][NH(AA)C(O)OR^T]$; and a -($C_2$-$C_4$)alkenyl(aryl) wherein said aryl portion of -(C_2-C_4)alkenyl(aryl) is substituted with –$CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$, –$CR^{1a}R^{2a}P(O)[OR^{1b}][NH(AA)C(O)OR^T]$, –$P(O)OR^{1b}OR^{2b}$, -$[P(O)[NHR^{Ty}][NH(AA)C(O)OR^T]$, or –$P(O)[OR^{1b}][NH(AA)C(O)OR^T]$;

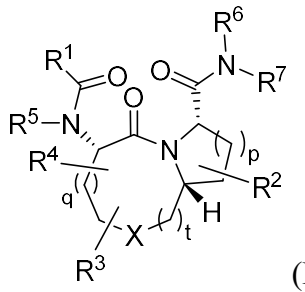
R^8 is selected from hydrogen, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_3-C_6)cycloalkyl, 5- to 7-membered heterocyclyl, -(C_1-C_4)[5- to 7-membered heterocyclyl], 5- to 6-membered heteroaryl, -(C_1-C_4)[5- to 6-membered heteroaryl], phenyl, -(C_1-C_4)alkylphenyl, –$C(O)R^{Ha}$, –$C(O)OR^{Ha}$, -$C(O)NR^{Ha}R^{Hb}$, -$C(O)OR^{Ha}$, -$SOR^{Ha}R^{Hb}$ and -SO_2R^{Ha}, wherein said (C_3-C_6)cycloalkyl, 5- to 7-membered heterocyclyl, 5- to 6-membered heteroaryl, phenyl, the phenyl on (C_1-C_4)alkylphenyl, the 5- to 7-membered heterocyclyl on -(C_1-C_4)[5- to 7-membered heterocyclyl], and the 5- to 6-membered heteroaryl on -(C_1-C_4)[5- to 6-membered

heteroaryl] are each optionally substituted with, as valency permits, 1 to 3 groups selected from R^U;

R^{Ha} is selected from $(C_1\text{-}C_{10})$alkyl, $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, phenyl, 5- to 10-membered monocyclic or bicyclic heteroaryl, and 4- to 10-membered monocyclic or bicyclic heterocyclyl, wherein said $(C_1\text{-}C_{10})$alkyl, $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl are each optionally substituted with, as valency permits, 1 to 2 groups selected from R^O and wherein said 5-to 10-membered monocyclic or bicyclic heteroaryl and said 4-to 10-membered monocyclic or bicyclic heterocyclyl are each optionally substituted with, as valency permits, 1 to 3 groups selected from halo, $(C_1\text{-}C_4)$alkyl, halo$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy, halo$(C_1\text{-}C_4)$alkoxy, oxo, and cyano; and

R^O is selected from halo, $(C_1\text{-}C_4)$alkoxy, OH, phenyl, NH_2, -NH$(C_1\text{-}C_{10})$alkyl, -N[$(C_1\text{-}C_{10})$alkyl], 4- to 10-membered monocyclic or fused bicyclic heterocyclyl and 5-to 10-membered monocyclic or bicyclic heteroaryl, wherein said 5- to 10-membered monocyclic or bicyclic heteroaryl and said 4-to 10-membered monocyclic or bicyclic heterocyclyl are each optionally substituted with, as valency permits, 1 to 3 groups selected from halo, $(C_1\text{-}C_4)$alkyl, halo$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy, halo$(C_1\text{-}C_4)$alkoxy, oxo, and cyano.

3. The compound of Claim 1 or 2, wherein the compound is of the structural formula **II**:



(**II**);

or a pharmaceutically acceptable salt thereof.

4. The compound of any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein p is 1.

5. The compound of any one of Claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein R^2 is hydrogen.

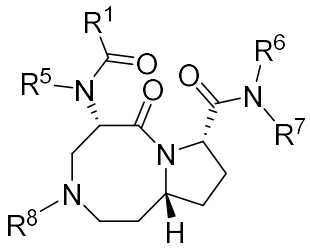
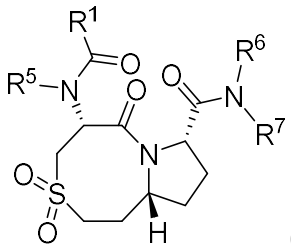
6. The compound of any one of Claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein R^3 is hydrogen.

7. The compound of any one of Claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein R^4 is hydrogen.

8. The compound of any one of Claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein q is 1 and t is 1.

9. The compound of any one of Claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein q is 0 and t is 2.

10. The compound of any one of Claims 1 to 7, wherein the compound is of the structural formula **III**, **IV**, **V**, **VI**, **VII**, or **VIII**:


(**III**),

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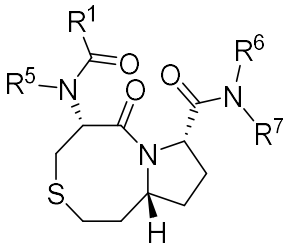
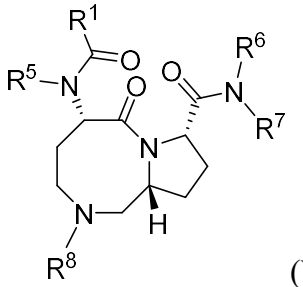
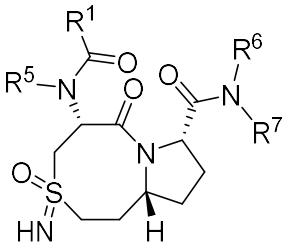
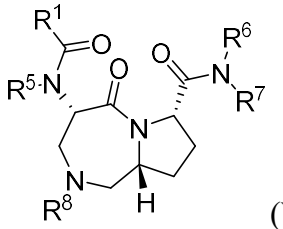
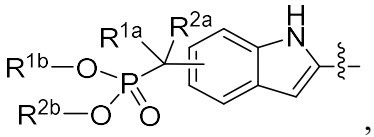

(**V**),

(**VI**),

(**VII**), or

(**VIII**); or a pharmaceutically acceptable salt thereof.

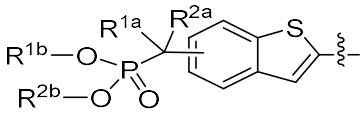
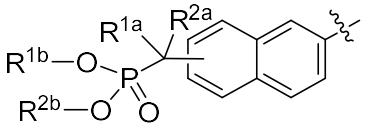
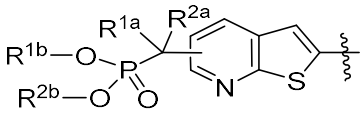
11. The compound of any one of Claims 1 to 10, or a pharmaceutically acceptable salt thereof, wherein R^5 is hydrogen.

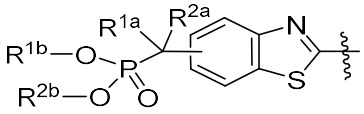
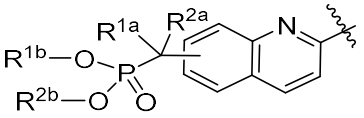
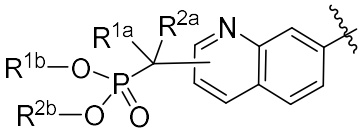
12. The compound of any one of Claims 1 to 11, or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from 8- to 10-membered fused bicyclic heteroaryl and aryl, each of which are substituted with $–CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$.

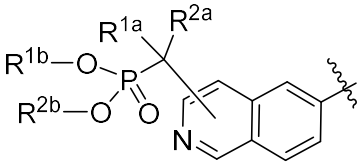
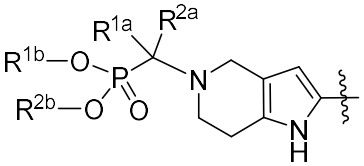
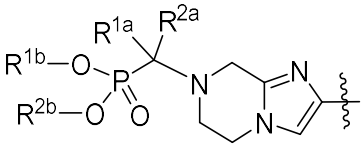
13. The compound of any one of Claims 1 to 12, or a pharmaceutically acceptable salt thereof, wherein, R^1 is selected from benzothiophenyl, indolyl, naphthalenyl, thienopyridinyl,

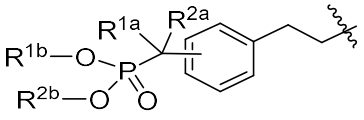
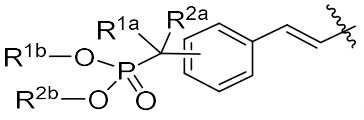
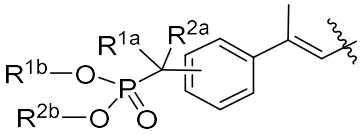
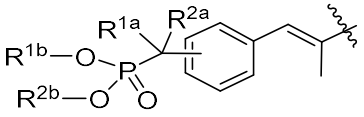
benzothiazoyl, quinolinyl, isoquinolinyl, 4,5,6,7-tetrahydropyrrolopyridinyl, 5,6,7,8-tetrahydroimidazopyrazinyl, each of which are substituted with $–CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$.

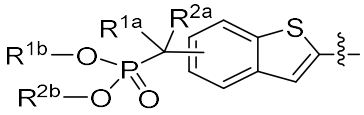
14. The compound of any one of Claims 1 to 13, or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from ,

, , ,

, , ,

, , ,

, , , and .

15. The compound of any one of Claims 1 to 14, or a pharmaceutically acceptable salt thereof, wherein R^1 is .

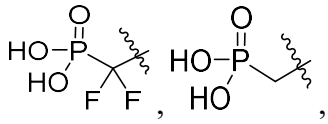
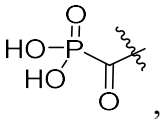
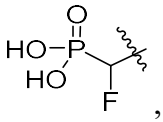
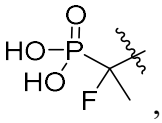
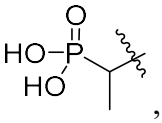
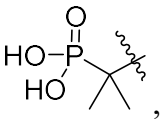
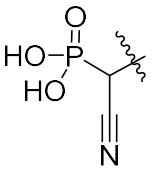
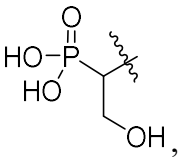
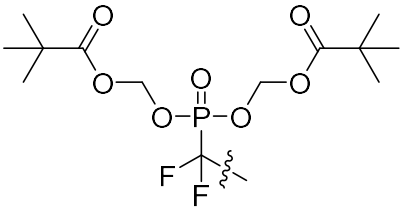
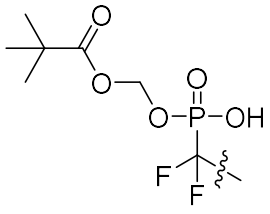
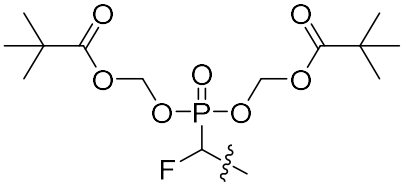
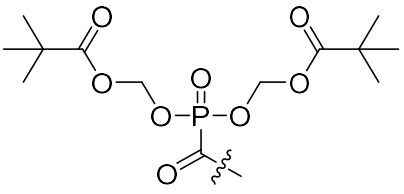
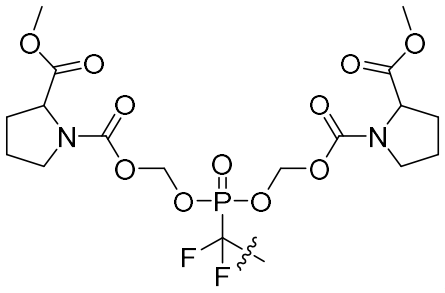
16. The compound of any one of Claims 1 to 15, or a pharmaceutically acceptable salt thereof, wherein R^{1a} is hydrogen and R^{2a} is fluoro or R^{1a} is fluoro and R^{2a} is fluoro.

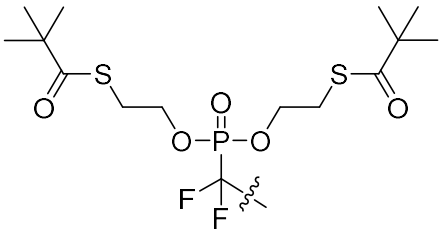
17. The compound of any one of Claims 1 to 16, or a pharmaceutically acceptable salt thereof, wherein R^{1a} and R^{2a} are fluoro.

18. The compound of any one of Claims 1 to 17, or a pharmaceutically acceptable salt thereof, wherein R^{1b} and R^{2b} are each independently selected from hydrogen, $(C_1\text{-}C_4)$alkyl, -[$(C_1\text{-}C_4)$alkyl]-OC(O)-[$(C_1\text{-}C_4)$alkyl], -[$(C_1\text{-}C_4)$alkyl]-OC(O)O-[$(C_1\text{-}C_4)$alkyl], -[$(C_1\text{-}C_4)$alkyl]-SC(O)-[$(C_1\text{-}C_4)$alkyl], -[$(C_1\text{-}C_4)$alkyl]-SC(O)-[halo$(C_1\text{-}C_4)$alkyl], -[$(C_1\text{-}C_4)$alkyl]-OC(O)$NR^{2c}R^{2d}$], [$(C_1\text{-}C_4)$alkyl]-OC(O)O-[5- to 7-membered heterocyclyl], and phenyl, wherein the 5- to 7-membered heterocyclyl of [$(C_1\text{-}C_4)$alkyl]-OC(O)O-[5- to 7-membered heterocyclyl] is optionally substituted with $C(O)OR^{2c}$, wherein any of the $(C_1\text{-}C)_4$alkyl groups are optionally substituted with 1 or 2 $(C_1\text{-}C_4)$alkyl.

19. The compound of any one of Claims 1 to 18, or a pharmaceutically acceptable salt thereof, wherein R^{1b} and R^{2b} are each -[$(C_1\text{-}C_4)$alkyl]-OC(O)-[$(C_1\text{-}C_4)$alkyl].

20. The compound of any one of Claims 1 to 18, or a pharmaceutically acceptable salt thereof, wherein R^{1b} and R^{2b} are hydrogen.

21. The compound of any one of Claims 1 to 15 and 18, or a pharmaceutically acceptable salt thereof, wherein $-CR^{1a}R^{2a}P(O)OR^{1b}OR^{2b}$ is selected from , , , , , , , , , , , , , .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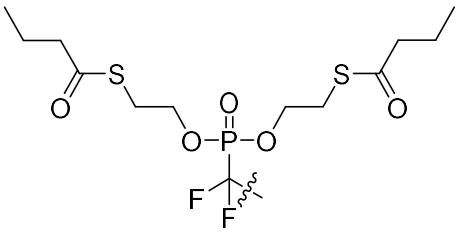
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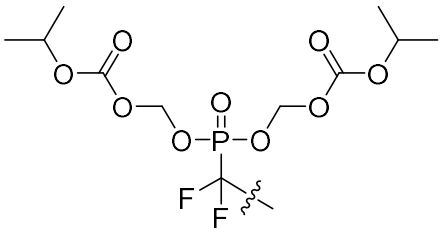
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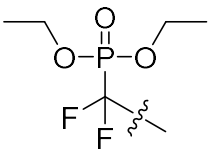
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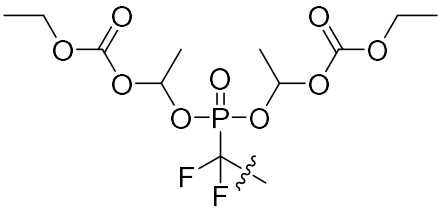
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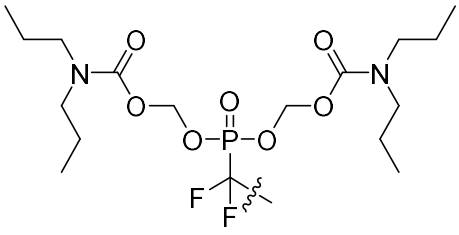
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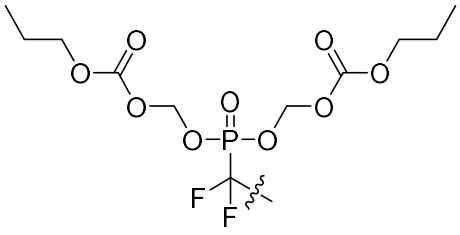
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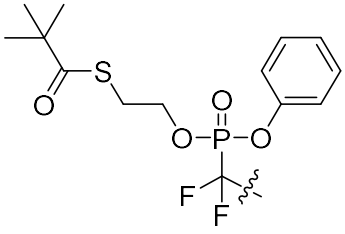
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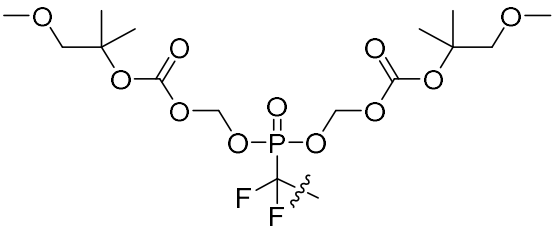
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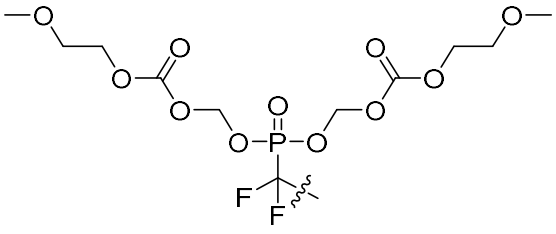
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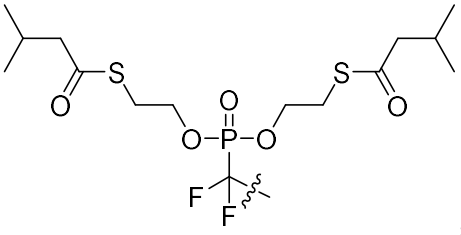
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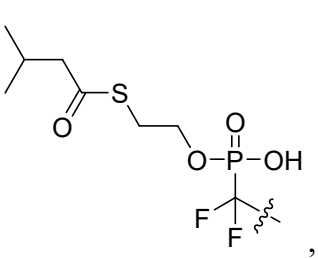
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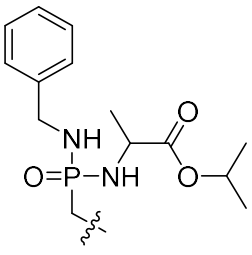
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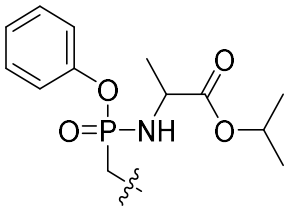
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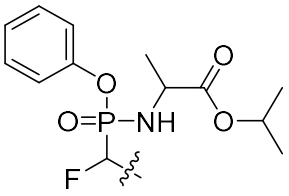
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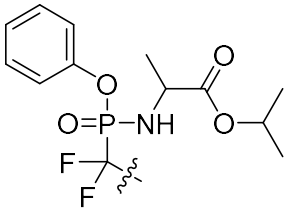
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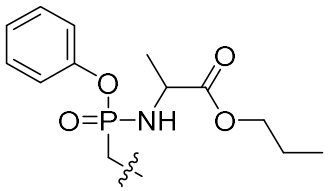
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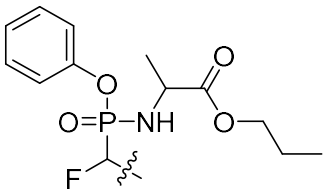
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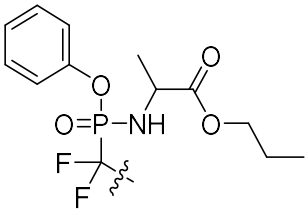
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or a pharmaceutically acceptable salt thereof.

22. The compound of Claim 1, wherein the compound is selected any one of Compounds 1 to 441; or a pharmaceutically acceptable salt thereof.

23. Use of a compound of any one of claims 1 to 22 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of conditions associated with modulation of STAT3 or STAT6, wherein said condition is a cancer or an inflammatory condition.

24. A compound of any one of claims 1 to 22 or a pharmaceutically acceptable salt thereof, for use in therapy.