# IMMUNOMODULATORS AND IMMUNOMODULATOR CONJUGATES

## CROSS REFERENCE TO RELATED APPLICATIONS

**[0001]** This application claims priority from U.S. Provisional Application No. 63/152,003, filed on February 22, 2021, and US. Provisional Application No. 63/273,081, filed on October 28, 2021, which are hereby incorporated by reference in their entireties.

## INCORPORATION BY REFERENCE

**[0002]** All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

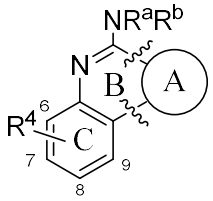
## BACKGROUND OF THE DISCLOSURE

**[0003]** Toll-like receptor (TLR) modulators can be used in various therapeutic settings, e.g., as vaccine adjuvants. However, many factors have limited the efficacy of TLR modulating compounds such as imiquimod. As an example, although such compounds can induce proinflamatory cytokines, they may also concurrently induce significant levels of anti-inflammatory cytokines such as IL-10. Thus, there exists an unmet need to develop TLR modulating compounds that can trigger a more desirable ratio of pro- to anti-inflammatory cytokines.

## SUMMARY OF THE DISCLOSURE

**[0004]** TLR modulating compounds that can trigger a more desirable ratio of pro- to anti-inflammatory cytokines are disclosed. In some instances, such TLR modulating compounds can be a compound of Formula I:

(I)




wherein:

the fused ring A is selected from the group consisting of:

wherein rings B and C in Formula I can optionally be further substituted on one or more carbons with one or more groups independently selected from the group consisting of halo, hydroxy, nitro, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkenyl, $(C_1\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_1\text{-}C_6)$alkoxycarbonyl, trifluoromethyl, trifluoromethoxy, cyano, and $NR^pR^q$;

each $R^p$ and $R^q$ is independently H or $(C_1\text{-}C_6)$alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more $(C_1\text{-}C_6)$alkyl; and

$R^r$ is H, aryl, or $(C_1\text{-}C_{10})$alkyl that is optionally substituted with halo or aryl;

$R^s$ is H, aryl, or $(C_1\text{-}C_{10})$alkyl that is optionally substituted with halo or aryl;

each $R^u$ and $R^v$ is independently H or $(C_1\text{-}C_6)$alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more $(C_1\text{-}C_6)$alkyl;

$R^w$ is H, aryl, or $(C_1\text{-}C_{10})$alkyl that is optionally substituted with halo or aryl;

each $R^x$ and $R^y$ is independently H or $(C_1\text{-}C_6)$alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more $(C_1\text{-}C_6)$alkyl;

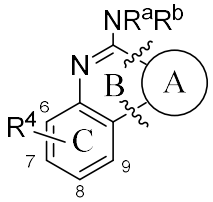
$R^z$ is H, aryl, or $(C_1\text{-}C_{10})$alkyl that is optionally substituted with halo or aryl; and

$R^{aa}$ is aryl that is optionally substituted with one or more groups independently selected from the group consisting of hydroxy, halo, nitro, cyano, $(C_1\text{-}C_6)$alkoxy, and $(C_1\text{-}C_6)$alkyl that is optionally substituted with one or more halo;

or a pharmaceutically acceptable salt thereof.

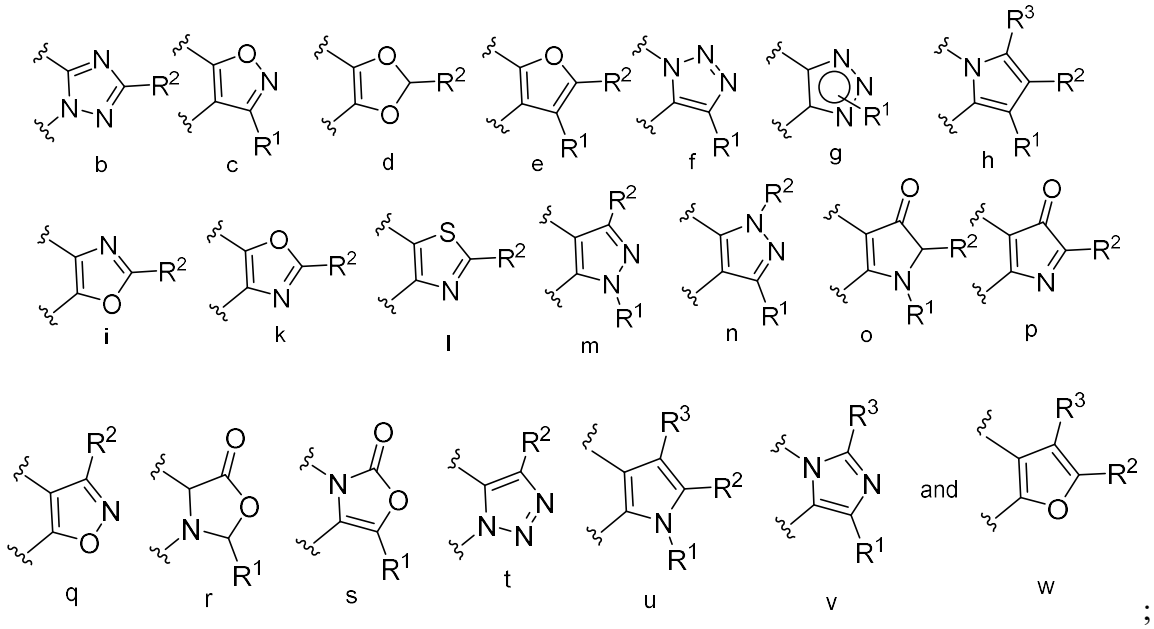
**[0004a]** In one aspect, the present disclosure provides a compound of Formula I:

(I)




wherein:

the fused ring A is selected from the group consisting of:



;

$R^1$ is H, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, aryl, heteroaryl, heterocycle, $NR^gR^h$, or $R^mR^nNC(=O)$-, wherein any $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, aryl, heteroaryl, and heterocycle, is optionally substituted with one or more groups independently selected from the group consisting of halo, cyano, oxo, oxiranyl, $(C_3\text{-}C_8)$cycloalkyl, aryl, that is optionally substituted with alkyl that is substituted with $NR^uR^v$, aryl that is substituted with carboxy, heteroaryl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkylthio, $OR^z$, $-N(H)S(O)_2R^r$, $R^sC(=O)O$-, -S-$R^w$, $-NR^xR^y$, $(C_1\text{-}C_6)$alkoxycarbonyl, and carboxy;

$R^2$ is H, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, aryl, heteroaryl, heterocycle, $NR^gR^h$, or $R^mR^nNC(=O)$-, wherein any $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, aryl, heteroaryl, and heterocycle, is optionally substituted with one or more groups independently selected from the group consisting of hydroxy, halo, -SH, cyano, oxo, oxiranyl, $(C_3\text{-}C_8)$cycloalkyl, aryl, heteroaryl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkylthio, and $NR^gR^h$;

$R^3$ is H, halo, hydroxy, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, aryl, heteroaryl, heterocycle, $NR^gR^h$, or $R^mR^nNC(=O)$-, wherein any $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, aryl, heteroaryl, and heterocycle, is optionally substituted with one or more groups independently selected from

the group consisting of hydroxy, halo, -SH, cyano, oxo, oxiranyl, ($C_3$-$C_8$)cycloalkyl, aryl, heteroaryl, ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)alkylthio, and $NR^gR^h$;

$R^4$ is $R^k$-C(=O)-, $R^k$-O-C(=O)-, $R^k$-S(O)$_2$-O-, $R^cR^dNC(=O)$-, $R^cR^dNS(O)_2$-, $R^eC(=O)N(R^e)$-, $R^eS(O)_2NR^f$-, or 1-ethylene that is substituted at the 2-position with $R^k$-C(=O)-, $R^k$-O-C(=O)-, $R^k$-S(O)$_2$-O-, $R^cR^dNC(=O)$-, $R^cR^dNS(O)_2$-, $R^eC(=O)N(R^e)$-, or $R^eS(O)_2NR^f$-;

$R^a$ is H, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_2$-$C_6$)alkynyl, ($C_1$-$C_6$)alkanoyl, ($C_1$-$C_6$)alkoxycarbonyl, ($C_3$-$C_6$)cycloalkyl, aryl, or heteroaryl, wherein any ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_2$-$C_6$)alkynyl, ($C_1$-$C_6$)alkanoyl, ($C_1$-$C_6$)alkoxycarbonyl, ($C_3$-$C_6$)cycloalkyl, aryl, and heteroaryl is optionally substituted with one or more groups independently selected from the group consisting of hydroxy, halo, -SH, cyano, oxiranyl, ($C_3$-$C_8$)cycloalkyl, aryl, heteroaryl, ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)alkylthio, and $NR^gR^h$;

$R^b$ is H or X-Y;

each $R^c$ and $R^d$ is independently H, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_3$-$C_8$)cycloalkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, aryl, aryl($C_1$-$C_6$)alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more ($C_1$-$C_6$)alkyl;

$R^e$ is H, ($C_1$-$C_6$)alkyl, or $R^{aa}$;

$R^f$ is H or ($C_1$-$C_6$)alkyl;

each $R^g$ and $R^h$ is independently H, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_3$-$C_8$)cycloalkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, aryl, aryl($C_1$-$C_6$)alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more ($C_1$-$C_6$)alkyl;

$R^k$ is H, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_2$-$C_6$)alkynyl, ($C_3$-$C_8$)cycloalkyl, trifluoromethyl, aryl, or aryl($C_1$-$C_6$)alkyl, wherein each ($C_1$-$C_6$)alkyl can optionally be substituted with one or more halo, ($C_1$-$C_6$)alkanoyloxy, ($C_1$-$C_6$)alkoxy, ($C_3$-$C_8$)cycloalkyl;

each $R^m$ and $R^n$ is independently H, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_3$-$C_8$)cycloalkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, aryl, aryl($C_1$-$C_6$)alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more ($C_1$-$C_6$)alkyl;

X is a linking group; and

Y is a peptide, a protein, or maleimide;

wherein rings B and C in formula I can optionally be further substituted on one or more carbons with one or more groups independently selected from the group consisting of halo, hydroxy, nitro, ($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkenyl, ($C_1$-$C_6$)alkynyl, ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)alkanoyl,

($C_1$-$C_6$)alkanoyloxy, ($C_1$-$C_6$)alkoxycarbonyl, trifluoromethyl, trifluoromethoxy, cyano, and $NR^pR^q$;

each $R^p$ and $R^q$ is independently H or ($C_1$-$C_6$)alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more ($C_1$-$C_6$)alkyl; and

$R^r$ is H, aryl, or ($C_1$-$C_{10}$)alkyl that is optionally substituted with halo or aryl;

$R^s$ is H, aryl, or ($C_1$-$C_{10}$)alkyl that is optionally substituted with halo or aryl;

each $R^u$ and $R^v$ is independently H or ($C_1$-$C_6$)alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more ($C_1$-$C_6$)alkyl;

$R^w$ is H, aryl, or ($C_1$-$C_{10}$)alkyl that is optionally substituted with halo or aryl;

each $R^x$ and $R^y$ is independently H or ($C_1$-$C_6$)alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more ($C_1$-$C_6$)alkyl;

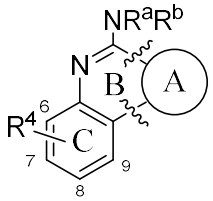
$R^z$ is H, aryl, or ($C_1$-$C_{10}$)alkyl that is optionally substituted with halo or aryl; and

$R^{aa}$ is aryl that is optionally substituted with one or more groups independently selected from the group consisting of hydroxy, halo, nitro, cyano, ($C_1$-$C_6$)alkoxy, and ($C_1$-$C_6$)alkyl that is optionally substituted with one or more halo;

or a pharmaceutically acceptable salt thereof.

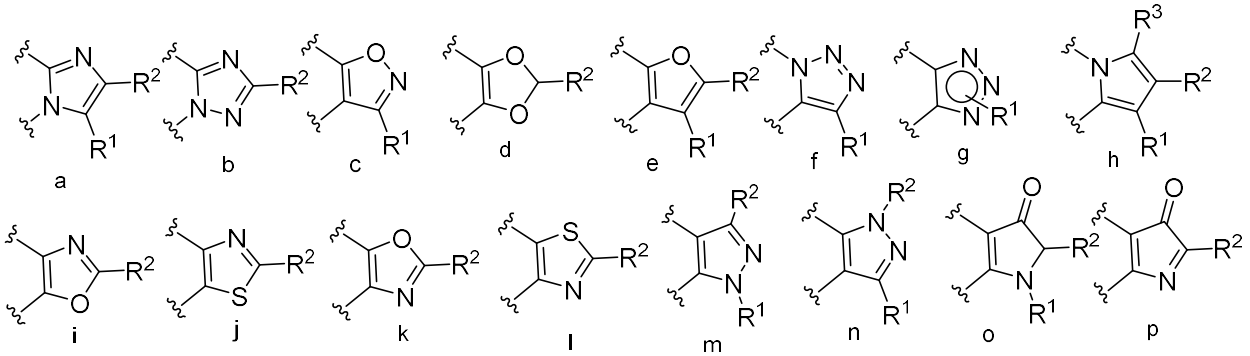
**[0004b]** In another aspect, the present disclosure provides a compound of Formula I:

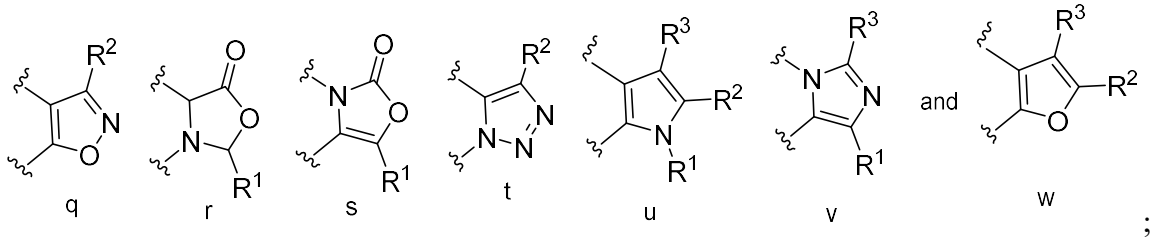
(I)




wherein:

the fused ring A is selected from the group consisting of:





;

$R^1$ is H, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, heterocycle, $NR^gR^h$, or $R^mR^nNC(=O)$-, wherein any $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, and heterocycle, is optionally substituted with one or more groups independently selected from the group consisting of halo, cyano, oxo, oxiranyl, $(C_3\text{-}C_8)$cycloalkyl, aryl, that is optionally substituted with alkyl that is substituted with $NR^uR^v$, aryl that is substituted with carboxy, heteroaryl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkylthio, $OR^z$, $-N(H)S(O)_2R^r$, $R^sC(=O)O$-, $-S\text{-}R^w$, $-NR^xR^y$, $(C_1\text{-}C_6)$alkoxycarbonyl, and carboxy;

$R^2$ is H, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, aryl, heteroaryl, heterocycle, $NR^gR^h$, or $R^mR^nNC(=O)$-, wherein any $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, aryl, heteroaryl, and heterocycle, is optionally substituted with one or more groups independently selected from the group consisting of hydroxy, halo, -SH, cyano, oxo, oxiranyl, $(C_3\text{-}C_8)$cycloalkyl, aryl, heteroaryl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkylthio, and $NR^gR^h$;

$R^3$ is H, halo, hydroxy, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, aryl, heteroaryl, heterocycle, $NR^gR^h$, or $R^mR^nNC(=O)$-, wherein any $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, aryl, heteroaryl, and heterocycle, is optionally substituted with one or more groups independently selected from the group consisting of hydroxy, halo, -SH, cyano, oxo, oxiranyl, $(C_3\text{-}C_8)$cycloalkyl, aryl, heteroaryl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkylthio, and $NR^gR^h$;

$R^4$ is $R^k\text{-}C(=O)$-, $R^k\text{-}O\text{-}C(=O)$-, $R^k\text{-}S(O)_2\text{-}O$-, $R^cR^dNC(=O)$-, $R^cR^dNS(O)_2$-, $R^eS(O)_2NR^f$-, or 1-ethylene that is substituted at the 2-position with $R^k\text{-}C(=O)$-, $R^k\text{-}O\text{-}C(=O)$-, $R^k\text{-}S(O)_2\text{-}O$-, $R^cR^dNC(=O)$-, $R^cR^dNS(O)_2$-, $R^eC(=O)N(R^e)$-, or $R^eS(O)_2NR^f$-;

$R^a$ is H, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, or $(C_1\text{-}C_6)$alkoxycarbonyl, wherein any $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, and $(C_1\text{-}C_6)$alkoxycarbonyl, is optionally substituted with one or more groups independently

selected from the group consisting of hydroxy, halo, -SH, cyano, oxiranyl, ($C_3$-$C_8$)cycloalkyl, aryl, heteroaryl, ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)alkylthio, and $NR^gR^h$;

$R^b$ is H or X-Y;

each $R^c$ and $R^d$ is independently H, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_3$-$C_8$)cycloalkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, aryl, aryl($C_1$-$C_6$)alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more ($C_1$-$C_6$)alkyl;

$R^e$ is H, ($C_1$-$C_6$)alkyl, or $R^{aa}$;

$R^f$ is H or ($C_1$-$C_6$)alkyl;

each $R^g$ and $R^h$ is independently H, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_3$-$C_8$)cycloalkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, aryl, aryl($C_1$-$C_6$)alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more ($C_1$-$C_6$)alkyl;

$R^k$ is H, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_2$-$C_6$)alkynyl, ($C_3$-$C_8$)cycloalkyl, trifluoromethyl, aryl, or aryl($C_1$-$C_6$)alkyl, wherein each ($C_1$-$C_6$)alkyl can optionally be substituted with one or more halo, ($C_1$-$C_6$)alkanoyloxy, ($C_1$-$C_6$)alkoxy, ($C_3$-$C_8$)cycloalkyl;

each $R^m$ and $R^n$ is independently H, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_3$-$C_8$)cycloalkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, aryl, aryl($C_1$-$C_6$)alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more ($C_1$-$C_6$)alkyl;

X is a linking group; and

Y is a peptide, a protein, or maleimide;

wherein rings B and C in formula I can optionally be further substituted on one or more carbons with one or more groups independently selected from the group consisting of halo, hydroxy, nitro, ($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkenyl, ($C_1$-$C_6$)alkynyl, ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)alkanoyl, ($C_1$-$C_6$)alkanoyloxy, ($C_1$-$C_6$)alkoxycarbonyl, trifluoromethyl, trifluoromethoxy, cyano, and $NR^pR^q$;

each $R^p$ and $R^q$ is independently H or ($C_1$-$C_6$)alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more ($C_1$-$C_6$)alkyl; and

$R^r$ is H, aryl, or ($C_1$-$C_{10}$)alkyl that is optionally substituted with halo or aryl;

$R^s$ is H, aryl, or ($C_1$-$C_{10}$)alkyl that is optionally substituted with halo or aryl;

each $R^u$ and $R^v$ is independently H or $(C_1$-$C_6)$alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more $(C_1$-$C_6)$alkyl;

$R^w$ is H, aryl, or $(C_1$-$C_{10})$alkyl that is optionally substituted with halo or aryl;

each $R^x$ and $R^y$ is independently H or $(C_1$-$C_6)$alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more $(C_1$-$C_6)$alkyl;

$R^z$ is H, aryl, or $(C_1$-$C_{10})$alkyl that is optionally substituted with halo or aryl; and

$R^{aa}$ is aryl that is optionally substituted with one or more groups independently selected from the group consisting of hydroxy, halo, nitro, cyano, $(C_1$-$C_6)$alkoxy, and $(C_1$-$C_6)$alkyl that is optionally substituted with one or more halo;

or a pharmaceutically acceptable salt thereof.

**[0005]** In some examples, Y is an antigen.

**[0006]** In another aspect, the present disclosure provides a pharmaceutical composition comprising a compound as disclosed herein. The present disclosure also provides a pharmaceutical composition comprising a compound of Formula I, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent and/or carrier.

**[0007]** Further provided herein is a method for treating a pathological condition (e.g. a viral infection, a bacterial infection, or a cancer) in an animal (e.g., a mammal such as a human) comprising administering to the animal a compound of Formula I, or a pharmaceutically acceptable salt thereof, and/or a pharmaceutical composition comprising such compound.

**[0008]** Further provided herein is a method for stimulating an immune response in an animal (e.g., a mammal such as a human), the method comprising administering to the animal a

compound of Formula I, or a pharmaceutically acceptable salt thereof, and/or a pharmaceutical composition comprising such compound.

**[0008a]** In another aspect, the present disclosure provides use of a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as disclosed herein in the manufacture of a medicament for stimulating an immune response in an animal.

**[0009]** In another aspect, there is provided a compound as disclosed herein or a pharmaceutical composition as disclosed herein for use in therapy. Further provided herein is a compound of Formula I, or a pharmaceutically acceptable salt thereof, for use in the prophylactic and/or therapeutic treatment of a pathological condition (e.g. a viral infection, a bacterial infection, or a cancer) in an animal (e.g., a mammal such as a human). Further provided herein is a compound of Formula I, or a pharmaceutically acceptable salt thereof, for use in medical therapy. In another aspect, there is provided use of a compound as disclosed herein or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as disclosed herein in the manufacture of a medicament for the treatment of a pathological condition in an animal.The present disclosure also provides the use of a compound of Formula I, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament useful for the treatment of a pathological condition (e.g. a viral infection, a bacterial infection, or a cancer) in an animal (e.g., a mammal such as a human). In another aspect, the present disclosure provides use of a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as disclosed herein in the manufacture of a medicament for the treatment of a cancer in an animal.

**[0010]** The disclosure further provides processes and intermediates disclosed herein that are useful for preparing compounds of Formula I-IV, or pharmaceutically acceptable salts thereof.

**[0011]** In another aspect, the present disclosure provides a method of synthesizing a compound as disclosed herein, the method comprising performing a reaction according to any one of reaction **SCHEMES 1-5**. Further provided herein are methods for synthesizing compounds of Formulae I-IV and intermediates thereof, the methods comprising performing a reaction according to any one of reaction **SCHEMES 1-5**.

## DETAILED DESCRIPTION

### I. Introduction

**[0012]** The present disclosure provides compounds (e.g., those of Formulae I-IV) capable of interacting with one or more Toll-like receptors (TLRs), e.g., TLR-7, TLR-8, or a combination thereof. In some embodiments, the compounds of the present disclosure are agonistic to one or

more TLRs. Thus, in some embodiments, the compounds provided herein can initiate an immune response in a subject, which can be used to treat a disease or pathological condition in the subject. Further provided herein are conjugates that can comprise a compound of the present disclosure (e.g., one of Formulae I-IV) coupled to another molecule. Such other molecule can be a small molecule, a peptide, a protein, or a nucleic acid. In some cases, a conjugate herein comprises a compound of any one of Formulae I-IV coupled to a peptide or protein. The compound can be coupled (e.g., covalently coupled) to the peptide or protein via a linker, as further described herein.

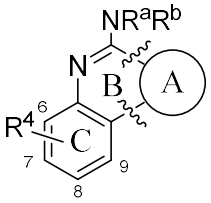
**[0013]** Number ranges are to be understood as inclusive, i.e., including the indicated lower and upper limits. Furthermore, the term "about", as used herein, and unless clearly indicated otherwise, generally refers to and encompasses plus or minus 10% of the indicated numerical

## CLAIMS

WHAT IS CLAIMED IS:

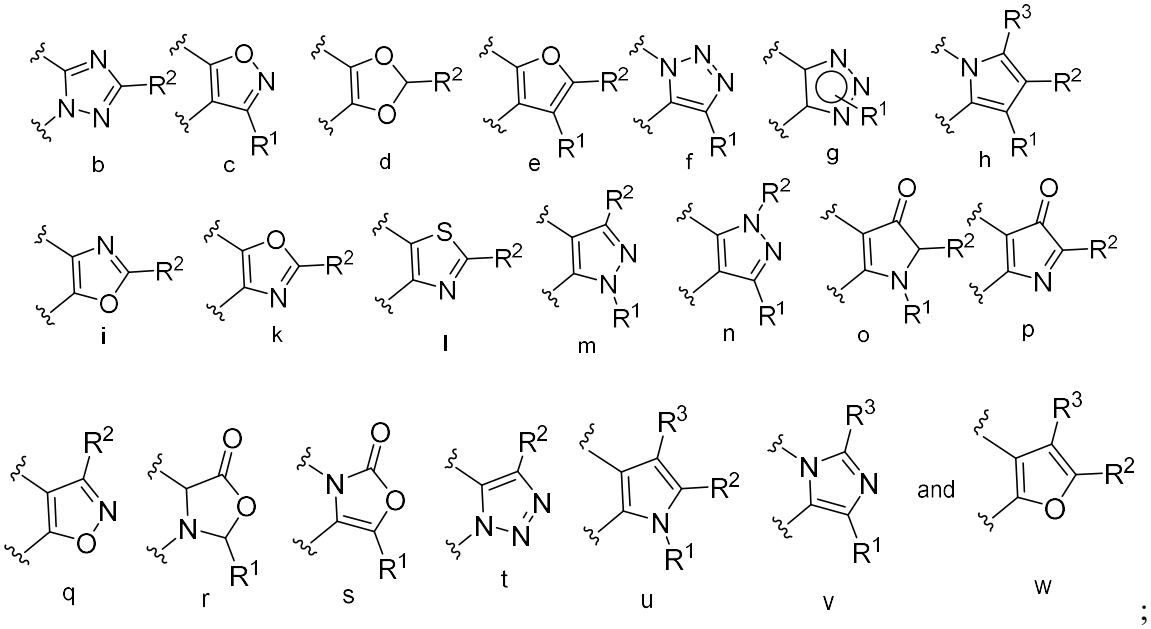
1. A compound of Formula I:

(I)



wherein:

the fused ring A is selected from the group consisting of:



;

$R^1$ is H, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, aryl, heteroaryl, heterocycle, $NR^gR^h$, or $R^mR^nNC(=O)$-, wherein any $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, aryl, heteroaryl, and heterocycle, is optionally substituted with one or more groups independently selected from the group consisting of halo, cyano, oxo, oxiranyl, $(C_3\text{-}C_8)$cycloalkyl, aryl, that is optionally substituted with alkyl that is substituted with $NR^uR^v$, aryl that is substituted with carboxy, heteroaryl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkylthio, $OR^z$, $-N(H)S(O)_2R^r$, $R^sC(=O)O$-, -S-$R^w$, $-NR^xR^y$, $(C_1\text{-}C_6)$alkoxycarbonyl, and carboxy;

$R^2$ is H, $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkanoyl, $(C_1$-$C_6)$alkoxycarbonyl, $(C_1$-$C_6)$alkanoyloxy, $(C_3$-$C_6)$cycloalkyl, aryl, heteroaryl, heterocycle, $NR^gR^h$, or $R^mR^nNC(=O)$-, wherein any $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkanoyl, $(C_1$-$C_6)$alkoxycarbonyl, $(C_1$-$C_6)$alkanoyloxy, $(C_3$-$C_6)$cycloalkyl, aryl, heteroaryl, and heterocycle, is optionally substituted with one or more groups independently selected from the group consisting of hydroxy, halo, -SH, cyano, oxo, oxiranyl, $(C_3$-$C_8)$cycloalkyl, aryl, heteroaryl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylthio, and $NR^gR^h$;

$R^3$ is H, halo, hydroxy, $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkanoyl, $(C_1$-$C_6)$alkoxycarbonyl, $(C_1$-$C_6)$alkanoyloxy, $(C_3$-$C_6)$cycloalkyl, aryl, heteroaryl, heterocycle, $NR^gR^h$, or $R^mR^nNC(=O)$-, wherein any $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkanoyl, $(C_1$-$C_6)$alkoxycarbonyl, $(C_1$-$C_6)$alkanoyloxy, $(C_3$-$C_6)$cycloalkyl, aryl, heteroaryl, and heterocycle, is optionally substituted with one or more groups independently selected from the group consisting of hydroxy, halo, -SH, cyano, oxo, oxiranyl, $(C_3$-$C_8)$cycloalkyl, aryl, heteroaryl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylthio, and $NR^gR^h$;

$R^4$ is $R^k$-C(=O)-, $R^k$-O-C(=O)-, $R^k$-$S(O)_2$-O-, $R^cR^dNC(=O)$-, $R^cR^dNS(O)_2$-, $R^eC(=O)N(R^e)$-, $R^eS(O)_2NR^f$-, or 1-ethylene that is substituted at the 2-position with $R^k$-C(=O)-, $R^k$-O-C(=O)-, $R^k$-$S(O)_2$-O-, $R^cR^dNC(=O)$-, $R^cR^dNS(O)_2$-, $R^eC(=O)N(R^e)$-, or $R^eS(O)_2NR^f$-;

$R^a$ is H, $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkanoyl, $(C_1$-$C_6)$alkoxycarbonyl, $(C_3$-$C_6)$cycloalkyl, aryl, or heteroaryl, wherein any $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkanoyl, $(C_1$-$C_6)$alkoxycarbonyl, $(C_3$-$C_6)$cycloalkyl, aryl, and heteroaryl is optionally substituted with one or more groups independently selected from the group consisting of hydroxy, halo, -SH, cyano, oxiranyl, $(C_3$-$C_8)$cycloalkyl, aryl, heteroaryl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylthio, and $NR^gR^h$;

$R^b$ is H or X-Y;

each $R^c$ and $R^d$ is independently H, $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_3$-$C_8)$cycloalkyl, $(C_3$-$C_8)$cycloalkyl$(C_1$-$C_6)$alkyl, aryl, aryl$(C_1$-$C_6)$alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more $(C_1$-$C_6)$alkyl;

$R^e$ is H, $(C_1$-$C_6)$alkyl, or $R^{aa}$;

$R^f$ is H or $(C_1$-$C_6)$alkyl;

each $R^g$ and $R^h$ is independently H, $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_3$-$C_8)$cycloalkyl, $(C_3$-$C_8)$cycloalkyl$(C_1$-$C_6)$alkyl, aryl, aryl$(C_1$-$C_6)$alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more $(C_1$-$C_6)$alkyl;

$R^k$ is H, $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_3$-$C_8)$cycloalkyl, trifluoromethyl, aryl, or aryl$(C_1$-$C_6)$alkyl, wherein each $(C_1$-$C_6)$alkyl can optionally be substituted with one or more halo, $(C_1$-$C_6)$alkanoyloxy, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_8)$cycloalkyl;

each $R^m$ and $R^n$ is independently H, $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_3$-$C_8)$cycloalkyl, $(C_3$-$C_8)$cycloalkyl$(C_1$-$C_6)$alkyl, aryl, aryl$(C_1$-$C_6)$alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more $(C_1$-$C_6)$alkyl;

X is a linking group; and

Y is a peptide, a protein, or maleimide;

wherein rings B and C in formula I can optionally be further substituted on one or more carbons with one or more groups independently selected from the group consisting of halo, hydroxy, nitro, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkenyl, $(C_1$-$C_6)$alkynyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkanoyl, $(C_1$-$C_6)$alkanoyloxy, $(C_1$-$C_6)$alkoxycarbonyl, trifluoromethyl, trifluoromethoxy, cyano, and $NR^pR^q$;

each $R^p$ and $R^q$ is independently H or $(C_1$-$C_6)$alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more $(C_1$-$C_6)$alkyl; and

$R^r$ is H, aryl, or $(C_1$-$C_{10})$alkyl that is optionally substituted with halo or aryl;

$R^s$ is H, aryl, or $(C_1$-$C_{10})$alkyl that is optionally substituted with halo or aryl;

each $R^u$ and $R^v$ is independently H or $(C_1$-$C_6)$alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more $(C_1$-$C_6)$alkyl;

$R^w$ is H, aryl, or $(C_1$-$C_{10})$alkyl that is optionally substituted with halo or aryl;

each $R^x$ and $R^y$ is independently H or $(C_1$-$C_6)$alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more $(C_1$-$C_6)$alkyl;

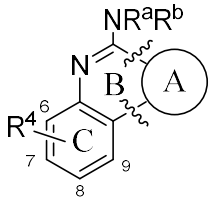
$R^z$ is H, aryl, or $(C_1$-$C_{10})$alkyl that is optionally substituted with halo or aryl; and

$R^{aa}$ is aryl that is optionally substituted with one or more groups independently selected from the group consisting of hydroxy, halo, nitro, cyano, $(C_1$-$C_6)$alkoxy, and $(C_1$-$C_6)$alkyl that is optionally substituted with one or more halo;

or a pharmaceutically acceptable salt thereof.

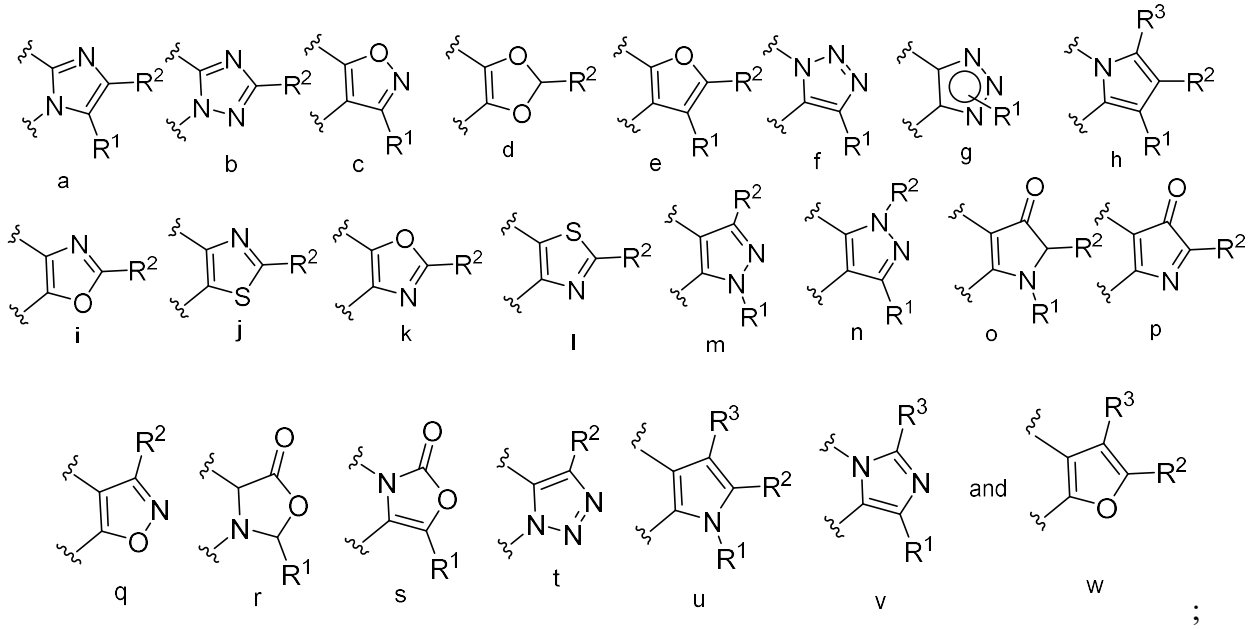
2. A compound of Formula I:

(I)



wherein:

the fused ring A is selected from the group consisting of:



;

$R^1$ is H, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, heterocycle, $NR^gR^h$, or $R^mR^nNC(=O)$-, wherein any $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, and heterocycle, is optionally substituted with one or more groups independently selected from the group consisting of halo, cyano, oxo, oxiranyl, $(C_3\text{-}C_8)$cycloalkyl, aryl, that is optionally substituted with alkyl that is substituted with $NR^uR^v$, aryl that is substituted with carboxy, heteroaryl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkylthio, $OR^z$, $-N(H)S(O)_2R^r$, $R^sC(=O)O$-, $-S\text{-}R^w$, $-NR^xR^y$, $(C_1\text{-}C_6)$alkoxycarbonyl, and carboxy;

$R^2$ is H, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, aryl, heteroaryl, heterocycle, $NR^gR^h$, or $R^mR^nNC(=O)$-, wherein any $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_3\text{-}C_6)$cycloalkyl, aryl, heteroaryl, and heterocycle, is optionally substituted with one or more groups independently selected from the

group consisting of hydroxy, halo, -SH, cyano, oxo, oxiranyl, ($C_3$-$C_8$)cycloalkyl, aryl, heteroaryl, ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)alkylthio, and $NR^gR^h$;

$R^3$ is H, halo, hydroxy, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_2$-$C_6$)alkynyl, ($C_1$-$C_6$)alkanoyl, ($C_1$-$C_6$)alkoxycarbonyl, ($C_1$-$C_6$)alkanoyloxy, ($C_3$-$C_6$)cycloalkyl, aryl, heteroaryl, heterocycle, $NR^gR^h$, or $R^mR^nNC(=O)$-, wherein any ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_2$-$C_6$)alkynyl, ($C_1$-$C_6$)alkanoyl, ($C_1$-$C_6$)alkoxycarbonyl, ($C_1$-$C_6$)alkanoyloxy, ($C_3$-$C_6$)cycloalkyl, aryl, heteroaryl, and heterocycle, is optionally substituted with one or more groups independently selected from the group consisting of hydroxy, halo, -SH, cyano, oxo, oxiranyl, ($C_3$-$C_8$)cycloalkyl, aryl, heteroaryl, ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)alkylthio, and $NR^gR^h$;

$R^4$ is $R^k$-C(=O)-, $R^k$-O-C(=O)-, $R^k$-$S(O)_2$-O-, $R^cR^dNC(=O)$-, $R^cR^dNS(O)_2$-, $R^eS(O)_2NR^f$-, or 1-ethylene that is substituted at the 2-position with $R^k$-C(=O)-, $R^k$-O-C(=O)-, $R^k$-$S(O)_2$-O-, $R^cR^dNC(=O)$-, $R^cR^dNS(O)_2$-, $R^eC(=O)N(R^e)$-, or $R^eS(O)_2NR^f$-;

$R^a$ is H, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_2$-$C_6$)alkynyl, ($C_1$-$C_6$)alkanoyl, or ($C_1$-$C_6$)alkoxycarbonyl, wherein any ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_2$-$C_6$)alkynyl, ($C_1$-$C_6$)alkanoyl, and ($C_1$-$C_6$)alkoxycarbonyl, is optionally substituted with one or more groups independently selected from the group consisting of hydroxy, halo, -SH, cyano, oxiranyl, ($C_3$-$C_8$)cycloalkyl, aryl, heteroaryl, ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)alkylthio, and $NR^gR^h$;

$R^b$ is H or X-Y;

each $R^c$ and $R^d$ is independently H, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_3$-$C_8$)cycloalkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, aryl, aryl($C_1$-$C_6$)alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more ($C_1$-$C_6$)alkyl;

$R^e$ is H, ($C_1$-$C_6$)alkyl, or $R^{aa}$;

$R^f$ is H or ($C_1$-$C_6$)alkyl;

each $R^g$ and $R^h$ is independently H, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_3$-$C_8$)cycloalkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, aryl, aryl($C_1$-$C_6$)alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more ($C_1$-$C_6$)alkyl;

$R^k$ is H, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_2$-$C_6$)alkynyl, ($C_3$-$C_8$)cycloalkyl, trifluoromethyl, aryl, or aryl($C_1$-$C_6$)alkyl, wherein each ($C_1$-$C_6$)alkyl can optionally be substituted with one or more halo, ($C_1$-$C_6$)alkanoyloxy, ($C_1$-$C_6$)alkoxy, ($C_3$-$C_8$)cycloalkyl;

each $R^m$ and $R^n$ is independently H, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_3$-$C_8$)cycloalkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, aryl, aryl($C_1$-$C_6$)alkyl; or taken together with the nitrogen to which

they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more ($C_1$-$C_6$)alkyl;

X is a linking group; and

Y is a peptide, a protein, or maleimide;

wherein rings B and C in formula I can optionally be further substituted on one or more carbons with one or more groups independently selected from the group consisting of halo, hydroxy, nitro, ($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkenyl, ($C_1$-$C_6$)alkynyl, ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)alkanoyl, ($C_1$-$C_6$)alkanoyloxy, ($C_1$-$C_6$)alkoxycarbonyl, trifluoromethyl, trifluoromethoxy, cyano, and $NR^pR^q$;

each $R^p$ and $R^q$ is independently H or ($C_1$-$C_6$)alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more ($C_1$-$C_6$)alkyl; and

$R^r$ is H, aryl, or ($C_1$-$C_{10}$)alkyl that is optionally substituted with halo or aryl;

$R^s$ is H, aryl, or ($C_1$-$C_{10}$)alkyl that is optionally substituted with halo or aryl;

each $R^u$ and $R^v$ is independently H or ($C_1$-$C_6$)alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more ($C_1$-$C_6$)alkyl;

$R^w$ is H, aryl, or ($C_1$-$C_{10}$)alkyl that is optionally substituted with halo or aryl;

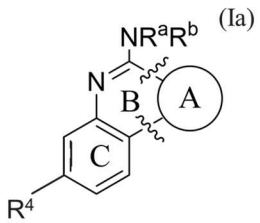
each $R^x$ and $R^y$ is independently H or ($C_1$-$C_6$)alkyl; or taken together with the nitrogen to which they are attached form a aziridino, azetidino, morpholino, piperazino, pyrrolidino or piperidino ring, which ring may optionally be substituted with one or more ($C_1$-$C_6$)alkyl;

$R^z$ is H, aryl, or ($C_1$-$C_{10}$)alkyl that is optionally substituted with halo or aryl; and

$R^{aa}$ is aryl that is optionally substituted with one or more groups independently selected from the group consisting of hydroxy, halo, nitro, cyano, ($C_1$-$C_6$)alkoxy, and ($C_1$-$C_6$)alkyl that is optionally substituted with one or more halo;

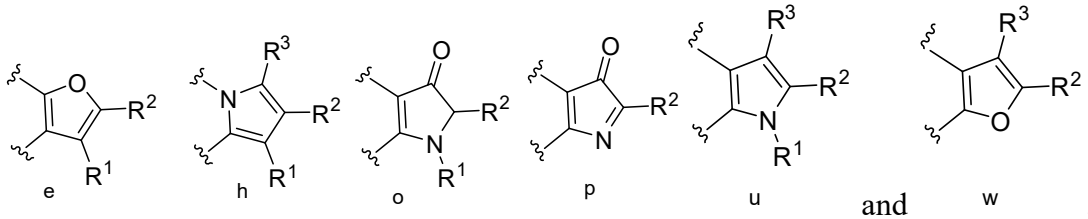
or a pharmaceutically acceptable salt thereof.

3. The compound of claim 1 or 2, wherein the compound of Formula I comprises a structure of Formula (Ia):

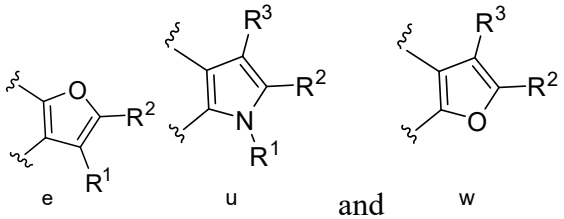


(Ia)

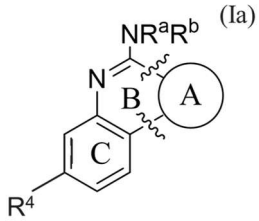
and wherein fused ring A is selected from the group consisting of:




4. The compound of any one of claims 1-3, wherein fused ring A is selected from the group consisting of:

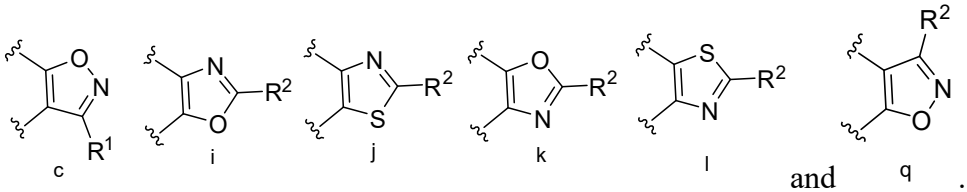



5. The compound of claim 2, wherein the compound of Formula I comprises a structure of Formula (Ia):

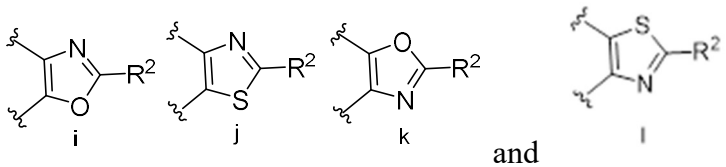



, and

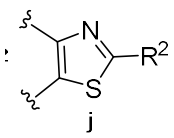
wherein fused ring A is selected from the group consisting of:



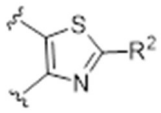

6. The compound of claim 2 or 5, wherein fused ring A is selected from the group consisting of:




7. The compound of any one of claims 2, 5, or 6, wherein fused ring A is selected from the group consisting of:



j

and 

I .

8. The compound of any one of claims 1 to 5 or 8, wherein $R^1$ is H, $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkanoyl, $(C_1$-$C_6)$alkoxycarbonyl, or $-NR^gR^h$, wherein any $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkanoyl, and $(C_1$-$C_6)$alkoxycarbonyl is optionally substituted with one or more groups independently selected from the group consisting of halo, cyano, oxo, oxiranyl, $(C_3$-$C_8)$cycloalkyl, aryl, that is optionally substituted with alkyl that is substituted with $NR^uR^v$, aryl that is substituted with carboxy, heteroaryl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylthio, $OR^z$, $-N(H)S(O)_2R^r$, $R^sC(=O)O-$, $-S-R^w$, $-NR^xR^y$, $(C_1$-$C_6)$alkoxycarbonyl, and carboxy.

9. The compound of any one of claims 1 to 5, 8 or 9, wherein $R^1$ is H, $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, or $-NR^gR^h$, wherein any $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, and $(C_2$-$C_6)$alkynyl is optionally substituted with one or more groups independently selected from the group consisting of halo, cyano, oxo, oxiranyl, $(C_3$-$C_8)$cycloalkyl.

10. The compound of any one of claims 1 to 5, 8 or 9, wherein $R^1$ is H or $(C_1$-$C_6)$alkyl.

11. The compound of any one of claims 1 to 10, wherein $R^2$ is H, $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkanoyl, $(C_1$-$C_6)$alkoxycarbonyl, or $-NR^gR^h$, wherein any $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkanoyl, and $(C_1$-$C_6)$alkoxycarbonyl is optionally substituted with one or more groups independently selected from the group consisting of hydroxy, halo, -SH, cyano, oxo, oxiranyl, $(C_3$-$C_8)$cycloalkyl, aryl, heteroaryl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylthio, and $NR^gR^h$.

12. The compound of any one of claims 1 to 11, wherein $R^2$ is H or $(C_1$-$C_6)$alkyl optionally substituted with one or more groups independently selected from the group consisting of halo, -SH, cyano, and $NR^gR^h$.

13. The compound of any one of claims 1 to 12, wherein $R^2$ is H or $(C_1$-$C_6)$alkyl.

14. The compound of any one of claims 1 to 4 or 8 to 13, wherein $R^3$ is H, halo, hydroxy, $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkanoyl, $(C_1$-$C_6)$alkoxycarbonyl, or $NR^gR^h$, wherein any $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkanoyl, and $(C_1$-$C_6)$alkoxycarbonyl is optionally substituted with one or more groups independently selected from the group consisting of hydroxy, halo, -SH, cyano, oxo, oxiranyl, $(C_3$-$C_8)$cycloalkyl, aryl, heteroaryl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylthio, and $NR^gR^h$.

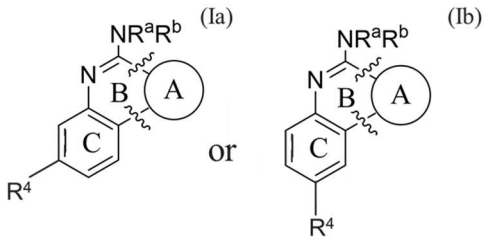
15. The compound of any one of claims 1 to 4 or 8 to 14, wherein $R^3$ is H or $(C_1\text{-}C_6)$alkyl optionally substituted with one or more groups independently selected from the group consisting of halo, -SH, cyano, $(C_3\text{-}C_8)$cycloalkyl, and $NR^gR^h$.

16. The compound of any one of claims 1 to 4 or 8 to 15, wherein $R^3$ is H or $(C_1\text{-}C_6)$alkyl.

17. The compound of any one of claims 1 to 16, wherein $R^4$ is $R^k$-C(=O)-, $R^k$-O-C(=O)-, $R^k$-$S(O)_2$-O-, $R^cR^dNS(O)_2$-, $R^eS(O)_2NR^f$-, or 1-ethylene that is substituted at the 2-position with $R^k$-C(=O)-, $R^k$-O-C(=O)-, $R^k$-$S(O)_2$-O-, $R^cR^dNS(O)_2$-, or $R^eS(O)_2NR^f$-.

18. The compound of any one of claims 1 to 17, wherein $R^4$ is $R^k$-C(=O)- or $R^k$-O-C(=O)-.

19. The compound of any one of claims 1 to 18, wherein the compound of Formula I comprises a structure of Formula (Ia) or Formula (Ib):

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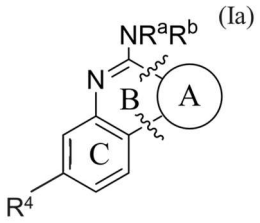
20. The compound of any one of claims 1 to 19, wherein the compound of Formula I comprises a structure of Formula (Ia):

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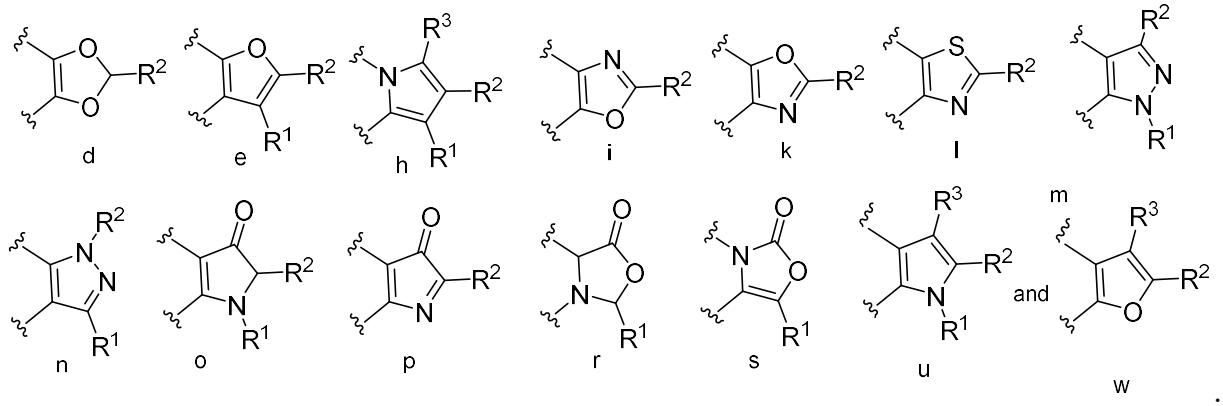
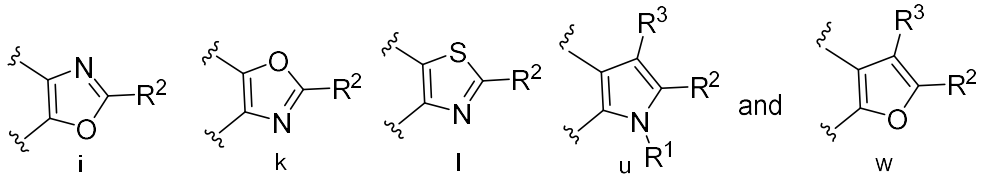
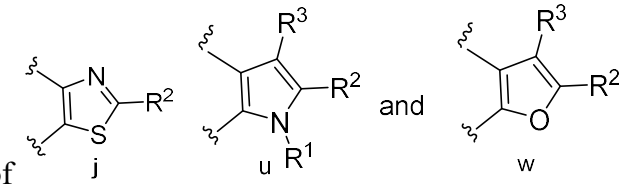
21. The compound of any one of claims 1 to 20, wherein $R^a$ is H or $(C_1\text{-}C_6)$alkyl optionally substituted with one or more groups independently selected from the group consisting of halo, -SH, cyano, and $NR^gR^h$.

22. The compound of any one of claims 1, 2, or 8 to 21, wherein the fused ring A is selected from the group consisting of:




23. The compound of any one of claims 1, 2, or 8 to 22, wherein the fused ring A is selected from the group consisting of:




24. The compound of any one of claims 2 or 8 to 23, wherein fused ring A is selected from the group consisting of 


25. The compound of any one of claims 1-24, wherein $R^b$ is X-Y.

26. The compound of any one of claims 1-25, wherein Y is an antibody.

27. A pharmaceutical composition comprising a compound according to any one of claims 1 to 25.

28. The pharmaceutical composition of claim 27, further comprising a pharmaceutically acceptable diluent or carrier.

29. A compound according to any one of claims 1 to 25 or a pharmaceutical composition according to claim 27 or 28 for use in therapy.

30. Use of a compound according to any one of claims 1 to 25, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 27 or 28 in the manufacture of a medicament for the treatment of a pathological condition in an animal.

31. Use of a compound according to any one of claims 1 to 25, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 27 or 28 in the manufacture of a medicament for stimulating an immune response in an animal.

32. Use of a compound according to any one of claims 1 to 25, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 27 or 28 in the manufacture of a medicament for the treatment of a cancer in an animal.

33. A method of synthesizing a compound of any one of claims 1 to 26, the method comprising performing a reaction according to any one of reaction **SCHEMES 1-5**.