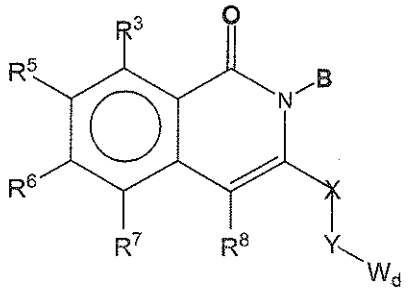
[0007] The delta (δ) isoform of class I PI3K has been implicated, in particular, in a number of diseases and biological processes. PI3K δ is expressed primarily in hematopoietic cells including leukocytes such as T-cells, dendritic cells, neutrophils, mast cells, B-cells, and macrophages. PI3K δ is integrally involved in mammalian immune system functions such as T-cell function, B-cell activation, mast cell activation, dendritic cell function, and neutrophil activity. Due to its integral role in immune system function, PI3K δ is also involved in a number of diseases related to undesirable immune response such as allergic reactions, inflammatory diseases, inflammation mediated angiogenesis, rheumatoid arthritis, auto-immune diseases such as lupus, asthma, emphysema and other respiratory diseases. Other class I PI3K involved in immune system function includes PI3K γ, which plays a role in leukocyte signaling and has been implicated in inflammation, rheumatoid arthritis, and autoimmune diseases such as lupus.

[0008] Downstream mediators of the PI3K signal transduction pathway include Akt and mammalian target of rapamycin (mTOR). Akt possesses a plckstrin homology (PH) domain that binds PIP3, leading to Akt kinase activation. Akt phosphorylates many substrates and is a central downstream effector of PI3K for diverse cellular responses. One important function of Akt is to augment the activity of mTOR, through phosphorylation of TSC2 and other mechanisms. mTOR is a serine-threonine kinase related to the lipid kinases of the PI3K family. mTOR has been implicated in a wide range of biological processes including cell growth, cell proliferation, cell motility and survival. Disregulation of the mTOR pathway has been reported in various types of cancer. mTOR is a multifunctional kinase that integrates growth factor and nutrient signals to regulate protein translation, nutrient uptake, autophagy, and mitochondrial function.

[0009] As such, kinases, particularly PI3Ks are prime targets for drug development. There remains a need for PI3K inhibitors suitable for drug development. The present invention addresses this need and provides related advantages as well by providing new classes of kinase inhibitors.

SUMMARY ~~OF THE INVENTION~~

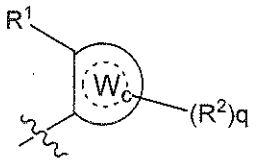
[0010] ~~In one aspect,~~ the present ~~invention~~disclosure provides compounds of Formula I below or pharmaceutically acceptable salts thereof, wherein



Formula I

[0011] W_d is heterocycloalkyl, aryl or heteroaryl;

[0012] B is a moiety of Formula II;



Formula II

[0013] wherein W_c is aryl, heteroaryl, heterocycloalkyl, or cycloalkyl, and q is an integer of 0, 1, 2, 3, or 4;

[0014] X is absent or $-(CH(R^9))_z-$, and z is an integer of 1;

[0015] Y is absent, or $-N(R^9)-$;

[0016] R^1 is hydrogen, alkyl, alkenyl, alkynyl, alkoxy, amido, alkoxycarbonyl, sulfonamido, halo, cyano, or nitro;

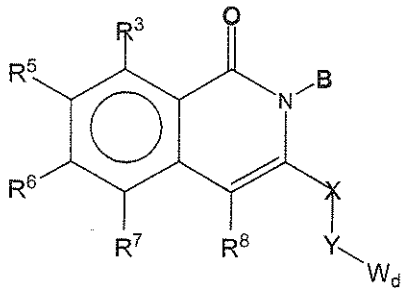
[0017] R^2 is alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, heteroarylalkyl, alkoxy, amino, halo, cyano, hydroxy or nitro;

[0018] R^3 is hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, alkoxy, amido, amino, alkoxycarbonyl sulfonamido, halo, cyano, hydroxy or nitro;

[0019] R^5, R^6, R^7, and R^8 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, hetercycloalkyl, alkoxy, amido, amino, acyl, acyloxy, sulfonamido, halo, cyano, hydroxy or nitro; and

[0020] each instance of R^9 is independently hydrogen, alkyl, cycloalkyl, or heterocycloalkyl.

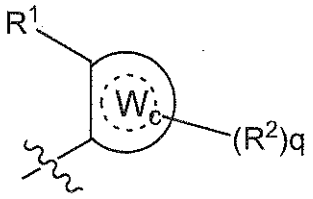
[0021] T~~In another aspect, the~~ present ~~invention~~disclosure also provides compounds which are of Formula I, or their pharmaceutically acceptable salts thereof, wherein



Formula I

[0022] W_d is heterocycloalkyl, aryl or heteroaryl;

[0023] B is alkyl, amino, heteroalkyl, or a moiety of Formula II;



Formula II

[0024] wherein W_c is aryl, heteroaryl, heterocycloalkyl, or cycloalkyl, and q is an integer of 0, 1, 2, 3, or 4;

[0025] X is absent or is $-(CH(R^9))_z-$and z is independently an integer of 1, 2, 3, or 4;

[0026] Y is absent, -O-, -S-, -S(=O)-, $-S(=O)_2-$, $-N(R^9)-$, $-C(=O)-(CHR^9)_z-$, -C(=O)-, $-N(R^9)(C=O)-$, $-N(R^9)(C=O)NH-$, or-$N(R^9)C(R^9)_2-$;

[0027] R^1 is hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, or carbonate;

[0028] R^2 is alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy,nitro, phosphate, urea, or carbonate;

[0029] R^3 is hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, alkoxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, aryl, heteroaryl, or nitro;

[0051] R^2 is alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, heteroarylalkyl, alkoxy, amino, halo, cyano, hydroxy or nitro;

[0052] R^3 is hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, alkoxy, amido, amino, alkoxycarbonyl sulfonamido, halo, cyano, hydroxy or nitro;

[0053] each instance of R^9 is independently hydrogen, C_1-C_{10}alkyl, cycloalkyl, or hetercyclooalkyl; and R^{12} is H, alkyl, alkynyl, alkenyl, halo, aryl, heteroaryl, heterocycloalkyl, or cycloalkyl.

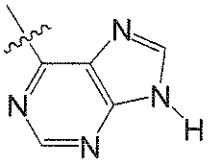
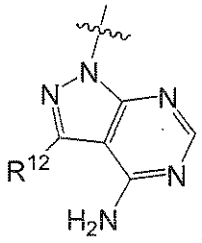
[0054] The disclosure also provides~~In another aspect of the invention~~ a compound and its pharmaceutically acceptable salts having the structure of Formula I ~~is provided~~, wherein:

[0055] B is alkyl, amino, heteroalkyl, or a moiety of Formula II;

[0056] wherein W_c is aryl, heteroaryl, heterocycloalkyl, or cycloalkyl, and q is an integer of 0, 1, 2, 3, or 4;

[0057] X is absent or $-(CH(R^9))_z$-and z is an integer of 1, 2, 3, or 4;

[0058] Y is absent, $-N(R^9)-$, or $-N(R^9)-CH(R^9)-$;

[0059] W_d is:  or  ;

[0060] R^1 is hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, or carbonate;

[0061] R^2 is alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, or phosphate;

[0062] R^3 is hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, alkoxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, aryl or heteroaryl;

[0063] each instance of R^9 is independently hydrogen, C_1-C_{10}alkyl, C_3-C_7cycloalkyl, heterocycloalkyl, or C_2-C_{10}heteroalkyl; and

[0064] R^{12} is H, alkyl, alkynyl, alkenyl, halo, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, cyano, amino, carboxylic acid, alkoxycarbonyl or amido.

[0065] In some embodiments, R^3 is -H, $-CH_3$, $-CH_2CH_3$, $-CF_3$, -Cl or -F. In other embodiments, R^3 is $-CH_3$, -Cl, or -F.

[0066] In some embodiments, B is a moiety of Formula II, wherein W_c is aryl, heteroaryl, heterocycloalkyl, or cycloalkyl,

and q is an integer of 0, 1, 2, 3, or 4. In some embodiments, B is heterocycloalkyl. In some embodiments, B is a monocyclic heteroaryl. In some embodiments, B is substituted phenyl. In some embodiments, B is substituted alkyl.

[0067] In some embodiments, B is $-(CH_2)_2-NR^aR^a$, wherein each R^a is independently hydrogen, alkyl, fluoroalkyl, carbocyclyl, carbocyclylalkyl, aryl, aralkyl, heterocycloalkyl, heterocycloalkylalkyl, heteroaryl or heteroarylalkyl, or $-NR^aR^a$ are combined together to form a cyclic moiety.

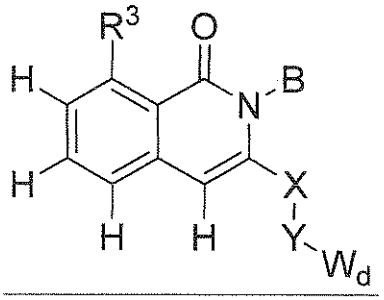
[0068] In some embodiments, R^1 is H, –F, -Cl, -CN, $-CH_3$, isopropyl, $-CF_3$, $-OCH_3$, nitro, or phosphate. In some embodiments, R^1 is phosphate.

[0069] In some embodiments, R^2 is halo, hydroxy, cyano, or nitro, and q is 1. In some embodiments, R^2 is phosphate and q is 1. In some embodiments, R^2 is alkyl or halo and q is 1 or 2.

[0070] In some embodiments, X is $-CH_2-$, $-CH(CH_2CH_3)$, or $-CH(CH_3)-$. In some embodiments, X-Y is $-CH_2-N(CH_3)$, $-CH_2-N(CH_2CH_3)$, $-CH(CH_2CH_3)-NH-$ or $-CH(CH_3)-NH-$. In some embodiments is $N(CH_2CH_3)CH_2-$ or $N(CH_3)CH_2-$.

[0071] In some embodiments,R^{12} is a monocyclic heteroaryl. In some embodiments,R^{12} is a bicyclic heteroaryl. In some embodiments, R^{12} is a heterocycloalkyl.

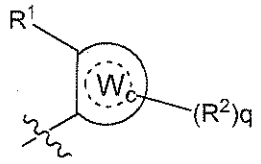
[0071a] In one aspect, there is provided a compound of Formula I:



Formula I

or a pharmaceutically acceptable salt thereof, wherein

B is a moiety of Formula II:



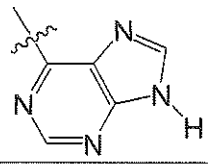
Formula II

wherein W_c is aryl, heteroaryl, heterocycloalkyl, or cycloalkyl, and

q is an integer of 0, 1, 2, 3, or 4;

X is absent or $-(CH(R^9))_z-$, and z is an integer of 1;

Y is $-N(R^9)-$;

W_d is 

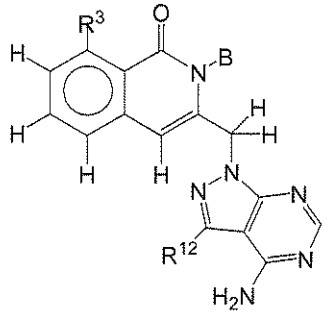
R^1 is hydrogen, alkyl, or halo;

R^2 is alkyl or halo;

R^3 is hydrogen or alkyl; and

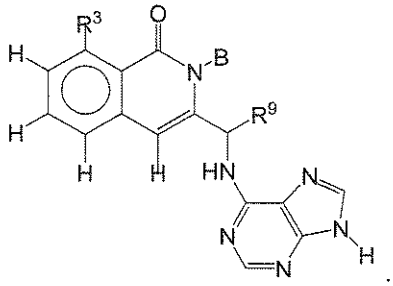
each instance of R^9 is independently hydrogen or alkyl.

[0072] In some embodiments, the compound of Formula I has the structure of Formula IV-A:



Formula IV-A

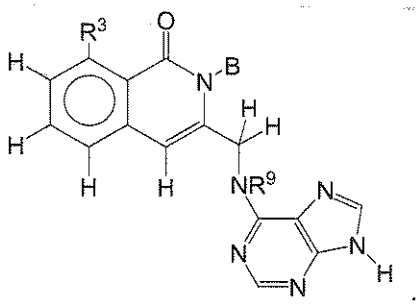
[0073] In some embodiments, the compound of Formula I has the structure of Formula V-A:



Formula V-A

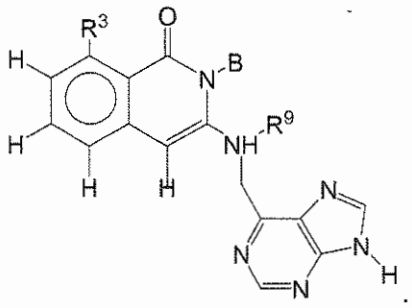
[0074] In some embodiments, the compound of Formula I has the structure of Formula IV-A or Formula V-A.

[0075] In some embodiments, the compound of Formula I has the structure of Formula V-B:



Formula V-B

[0076] In some embodiments, the compound of Formula I has the structure of Formula VI-A:



Formula VI-A

[0077] The disclosure also provides~~In another aspect of the invention,~~ a composition ~~is provided~~ which comprises a pharmaceutically acceptable excipient and one or more compounds of Formula I, Formula IV, IV-A, V, V-A, V-B, VI, and VI-A. In some embodiments, the composition is a liquid, solid, semi-solid, gel, or an aerosol form.

[0077a] In a second aspect, there is provided a pharmaceutical composition comprising a pharmaceutically acceptable excipient and a compound as defined above.

[0078] The disclosure also provides~~In another aspect of the invention,~~ a method of inhibiting a phosphatidyl inositol-3 kinase (PI3 kinase)~~, is provided~~ comprising: contacting the PI3 kinase with an effective amount of one or more compounds disclosed herein. For instance, the step of contacting involves the use of one or more compounds of Formula I, Formula IV, IV-A, V, V-A, V-B, VI, and VI-A. In some embodiments, the step of contacting comprises contacting a cell that contains said PI3 kinase. In some embodiments of the method, the inhibition takes place in a subject suffering from a disorder associated with malfunctioning of one or more types of PI3 kinase. Some exemplary diseases involving malfunctioning of one or more types of PI3 kinases are selected from the group consisting of autoimmune diseases, rheumatoid arthritis, respiratory disease, allergic reactions, and various types of cancers. Where desired, the compound used in the method has the structure of Formula IV, wherein R^{11} is amino and R^{12} is substituted phenyl.

[0079] In some embodiments of the method, the inhibition takes place in a subject suffering from rheumatoid arthritis or a respiratory disease, and wherein the compound has the structure of Formula IV, and wherein R^{11} is amino and R^{12} is bicyclic heteroaryl.

[0080] In some embodiments, the method comprises administering a second therapeutic agent to the subject.

[0081] The disclosure also~~In yet another aspect, the present invention~~ provides a method of treating a disease manifesting an undesired immune response. The method comprises the step of administering to a subject in need thereof, one or more compounds disclosed herein including compounds of Formula I, Formula IV, IV-A, V, V-A, V-B, VI, and/or VI-A, in an amount that is effective in ameliorating said undesired immune response. In some embodiments, the one or more compounds inhibit T-cell independent B-cell activation as evidenced by a reduction in production of anti-TNP IgG3 by at least about five folds when administered in an amount less than about 30mg/kg BID dose to a test animal.

[0082] In some embodiments, the disease treated is associated with swelling or pain of a joint of a subject. The method can be effective in ameliorating one or more rheumatoid arthritis symptoms as evidenced by reduction in mean joint diameter by at least about 10% after 17 days and/or reduction in ankle diameter by at least 5-10% or more after several days to weeks of treatment, including for example reduction in ankle diameter by at least 5% after 7 days of treatment. In another embodiment, the undesired immune response is evidenced by enhanced production of anti-type II collagen antibodies, and the use of one or more subject compounds reduces the serum anti-type II collagen level at an ED50 of less than about 10 mg/kg.

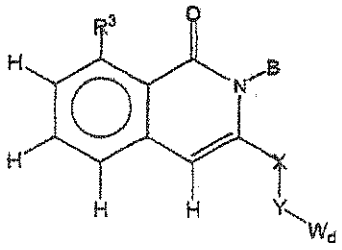
INCORPORATION BY REFERENCE

[0083] 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.

CLAIMS

WHAT IS CLAIMED IS:

1. A compound of Formula I:



Formula I

or its pharmaceutically acceptable salt thereof, wherein

B is a moiety of Formula II;



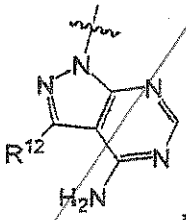
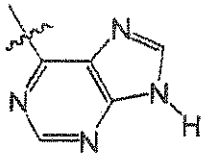
Formula II

wherein W_c is aryl, heteroaryl, heterocycloalkyl, or cycloalkyl, and

q is an integer of 0, 1, 2, 3, or 4;

X is absent or $-(CH(R^9))_z-$, and z is an integer of 1;

Y is absent or $-N(R^9)-$;

when Y is absent, Wd is:  , or when Y is present, Wd is: 

R^1 is hydrogen, alkyl, alkenyl, alkynyl, alkoxy, amido, alkoxycarbonyl, sulfonamido, halo, cyano, or nitro;

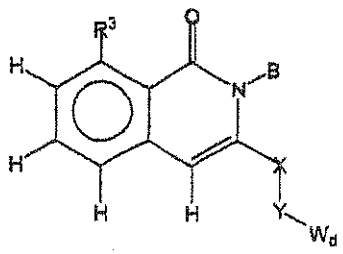
R^2 is alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, heteroarylalkyl, alkoxy, amino, halo, cyano, hydroxy or nitro;

R^3 is hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, alkoxy, amido, amino, alkoxycarbonyl sulfonamido, halo, cyano, hydroxy or nitro;

each instance of R^9 is independently hydrogen, alkyl, or heterocycloalkyl; and

R^{12} is H, alkyl, alkynyl, alkenyl, halo, aryl, heteroaryl, heterocycloalkyl, or cycloalkyl.

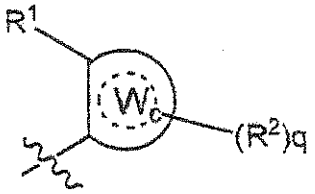
2. A compound of Formula I:



Formula I

or its pharmaceutically acceptable salt thereof, wherein

B is alkyl, amino, heteroalkyl, or a moiety of Formula II;



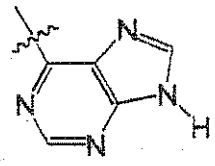
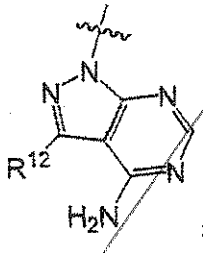
Formula II

wherein W_c is aryl, heteroaryl, heterocycloalkyl, or cycloalkyl, and

q is an integer of 0, 1, 2, 3, or 4;

X is absent or $-(CH(R^9))_z-$ and z is an integer of 1, 2, 3, or 4;

Y is absent, $-N(R^9)-$, or $-N(R^9)-CH(R^9)-$;

Wd is:  or ;

R^1 is hydrogen, alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, phosphate, urea, or carbonate;

R^2 is alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, or phosphate;

R^3 is hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, alkoxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, sulfonamido, halo, cyano, hydroxy, nitro, aryl or heteroaryl;

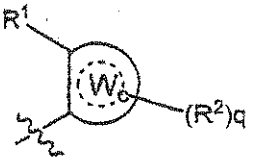
each instance of R^9 is independently hydrogen, C_1-C_{10}alkyl, C_3-C_7cycloalkyl, heterocycloalkyl, or C_2-C_{10}heteroalkyl; and

R^{12} is H, alkyl, alkynyl, alkenyl, halo, aryl, heteroaryl, heterocycloalkyl, cycloalkyl, cyano, amino, carboxylic acid, alkoxycarbonyl or amido.

3. The compound of claim 1 or 2 wherein R^3 is -H, $-CH_3$, $-CH_2CH_3$, $-CF_3$, -Cl or -F.

4. The compound of claim 1 or 2 wherein R^3 is -CH_3, -Cl, or -F.

5. The compound of claim 2 wherein B is a moiety of Formula II;



Formula II

wherein W_c is aryl, heteroaryl, heterocycloalkyl, or cycloalkyl,

and q is an integer of 0, 1, 2, 3, or 4.

6. The compound of claim 1 or 2 wherein B is heterocycloalkyl.

7. The compound of claim 1 or 2 wherein B is a monocyclic heteroaryl.

8. The compound of claim 1 or 2 wherein B is substituted phenyl.

9. The compound of claim 2 wherein B is a substituted alkyl.

10. The compound of claim 9 wherein B is–$(CH_2)_2$-NR^aR^a ,wherein each R^a is independently hydrogen, alkyl, fluoroalkyl, carbocyclyl, carbocyclylalkyl, aryl, aralkyl, heterocycloalkyl, heterocycloalkylalkyl, heteroaryl or heteroarylalkyl, or -NR^aR^a are combined together to form a cyclic moiety.

11. The compound of claim 1 or 2 wherein R^1 is H, –F, -Cl, -CN, -CH_3, isopropyl, -CF_3, -OCH_3, nitro, or phosphate.

12. The compound of claim 2 wherein R^1 is phosphate.

13. The compound of claim 1 or 2 wherein R^2 is halo, hydroxy, cyano, or nitro, and q is 1.

14. The compound of claim 2 wherein R^2 is phosphate and q is 1.

15. The compound of claim 1 or 2 wherein R^2 is alkyl or halo and q is 1 or 2.

16. The compound of claim 1 or 2 wherein X is -CH_2-, -$CH(CH_2CH_3)$, or -$CH(CH_3)$-.

17. The compound of claim 1 or 2 wherein X-Y is -CH_2-$N(CH_3)$, -CH_2-$N(CH_2CH_3)$, -$CH(CH_2CH_3)$-NH- or -$CH(CH_3)$-NH-.

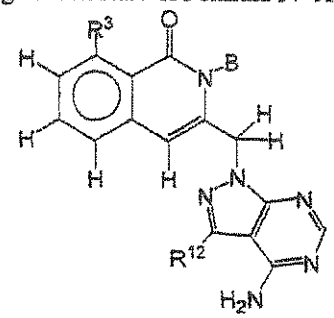
18. The compound of claim 2 wherein Y is $N(CH_2CH_3)CH_2$- or $N(CH_3)CH_2$-.

19. The compound of claim 1 or 2 wherein R^{12} is a monocyclic heteroaryl.

20. The compound of claim 1 or 2 wherein R^{12} is a bicyclic heteroaryl.

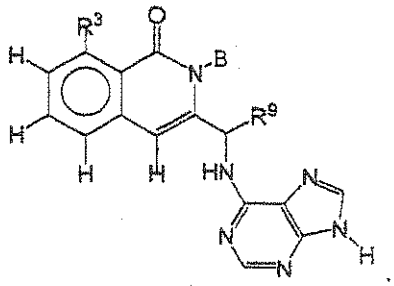
21. The compound of claim 1 or 2 wherein R^{12} is a heterocycloalkyl.

22. The compound of claim 1 having the structure of Formula IV-A:



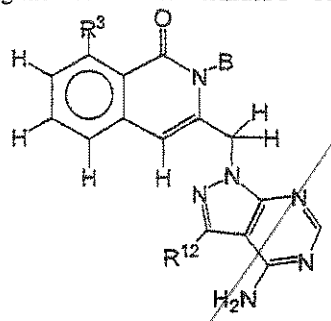
Formula IV-A

23. The compound of claim 1 having the structure of Formula V-A:



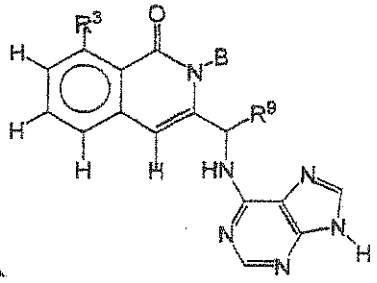
Formula V-A

24. The compound of claim 2 having the structure of Formula IV-A:



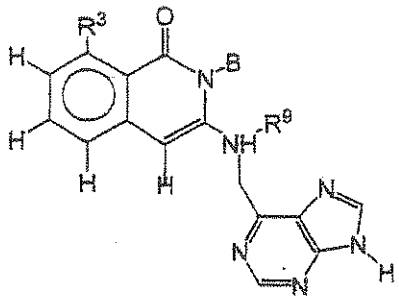
Formula IV-A

25. The compound of claim 2 having the structure of Formula V-A



Formula V-A

26. The compound of claim 2 having the structure of Formula VI-A:



Formula VI-A

27. A composition comprising a pharmaceutically acceptable excipient and a compound of claim 1.

28. The composition of claim 27 wherein the composition is a liquid, solid, semi-solid, gel, or an aerosol form.

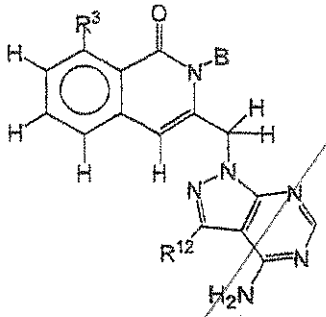
29. A composition comprising a pharmaceutically acceptable excipient and a compound of claim 2.

30. The composition of claim 29 wherein the composition is a liquid, solid, semi-solid, gel, or an aerosol form.

31. A method of inhibiting a phosphatidyl inositol-3 kinase (PI3 kinase), comprising: contacting the PI3 kinase with an effective amount of a compound of claim 1 or 2.

32. The method of claim 31 wherein said step of contacting comprising contacting a cell that contains said PI3 kinase.

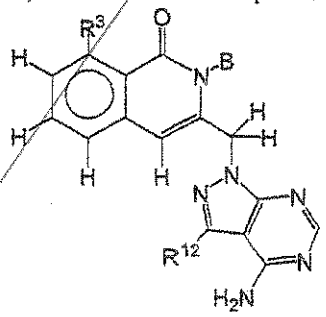
33. The method of claim 31, wherein the inhibition takes place in a subject suffering from a respiratory disease, and wherein the compound has the structure of Formula IV-A:



Formula IV-A

wherein R^{12} is substituted phenyl.

34. The method of claim 31 wherein the inhibition takes place in a subject suffering from rheumatoid arthritis or a respiratory disease, and wherein the compound has the structure of Formula IV-A:



Formula IV-A

wherein R^{12} is bicyclic heteroaryl.

35. The method of claim 31 comprising administering a second therapeutic agent to the subject.

36. A method of treating a disease manifesting an undesired immune response, comprising administering to a subject in need thereof, one or more compounds of claim 1 or 2 in an amount that is effective in ameliorating said undesired immune response.

37. The method of claim 36 wherein the one or more compounds inhibit T-cell independent B-cell activation as evidenced by a reduction in production of anti-TNP IgG3 by at least about five folds when administered in an amount less than about 30mg/kg BID dose to a test animal.

38. The method of claim 36, wherein the disease is associated with swelling or pain of a joint of a subject.

39. The method of claim 36, wherein the administration is effective in ameliorating one or more rheumatoid arthritis symptoms as evidenced by reduction in mean joint diameter by at least about 10% after 17 days and/or reduction in ankle diameter by at least 5% after 7 days of treatment.

40. A method of claim 36, wherein the undesired immune response is evidenced by enhanced production anti-type II collagen antibodies.

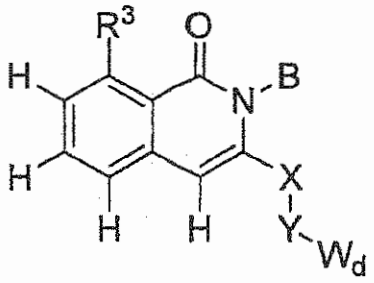
41. The method of claim 40 wherein the one or more compounds reduce the serum anti-type II collagen level with an ED50 value of less than about 10 mg/kg.

42. The method of claim 36 wherein the disease is an autoimmue inflammatory disease.

43. The method of claim 36 comprising administering to said subject an agent that inhibits IgE production.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

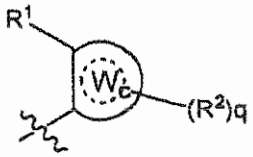
1. A compound of Formula I:



Formula I

or a pharmaceutically acceptable salt thereof, wherein

B is a moiety of Formula II;



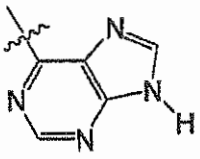
Formula II

wherein W_c is aryl, heteroaryl, heterocycloalkyl, or cycloalkyl, and

q is an integer of 0, 1, 2, 3, or 4;

X is absent or $-(CH(R^9))_z-$, and z is an integer of 1;

Y is $-N(R^9)-$;

W_d is: 

R^1 is hydrogen, alkyl, or halo;

R^2 is alkyl or halo;

R^3 is hydrogen or alkyl; and

each instance of R^9 is independently hydrogen or alkyl.

2. The compound of claim 1, wherein q is 0.

3. The compound of claim 1 or 2, wherein R^1 is halo.

4. The compound of claim 1 or 2, wherein R^1 is C_1-C_6alkyl.

5. The compound of claim 4, wherein R^1 is methyl.

6. The compound of any one of claims 1 to 5, wherein R^3 is C_1-C_6alkyl.

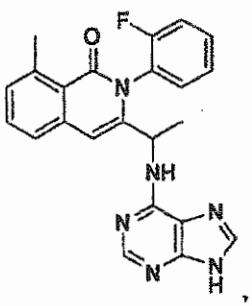
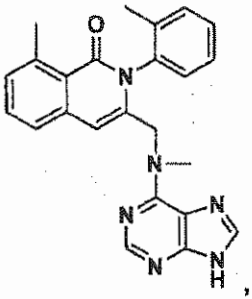
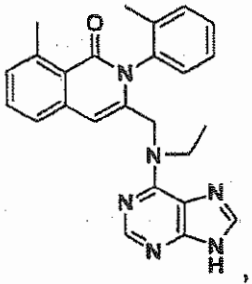
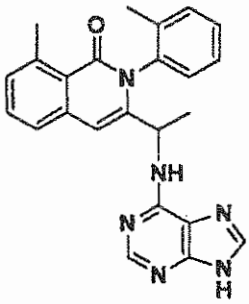
7. The compound of claim 6, wherein R^3 is methyl.

8. The compound of any one of claims 1 to 7, wherein R^9 is hydrogen.

9. The compound of any one of claims 1 to 8, wherein X is $-CH_2-$, $-CH(CH_2CH_3)-$, or $-CH(CH_3)-$.

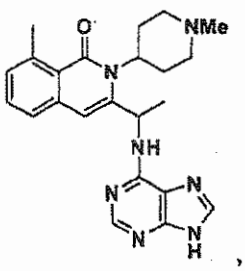
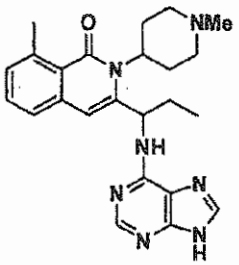
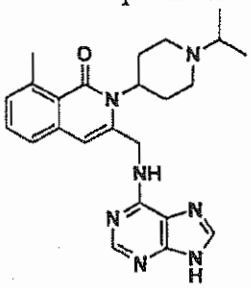
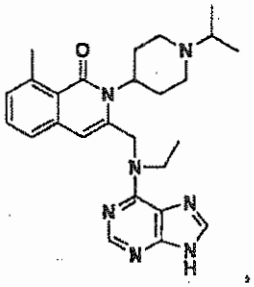
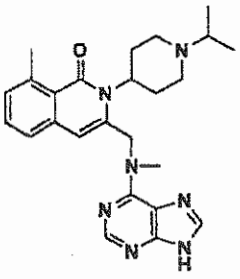
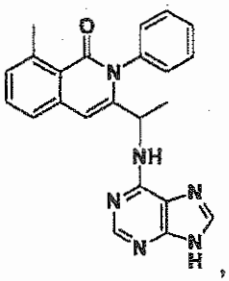
10. The compound of any one of claims 1 to 8, wherein X-Y is $-CH_2-N(CH_3)-$, $-CH_2-N(CH_2CH_3)-$, $-CH(CH_2CH_3)$ NH-, or $-CH(CH_3)$ -NH-.

11. The compound of claim 1, wherein the compound is:


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or a pharmaceutically acceptable salt thereof.

12. The compound of claim 1, wherein the compound is:


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, or

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or a pharmaceutically acceptable salt thereof.

13. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a compound of any one of claims 1-12.

14. The composition of claim 13, wherein the composition is a liquid, solid, semi-solid, gel, or an aerosol form.