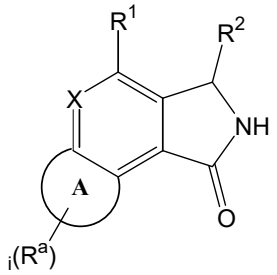
CLAIMS

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



I

or a pharmaceutically acceptable form or an isotope derivative thereof,

wherein

Ring A is a 4- to 7-membered monocyclic non-aromatic ring, substituted with 0-10 R^a's;

R^1 is Z^B-R^B;

R^2 is Z^C-R^C;

X is N, CH or CR^X;

R^X is Z^X-$R^{X'}$;

each of Z^B, Z^C and Z^X is independently a covalent bond, O, S, NR, NRC(O), C(O)NR, C(O), C(O)O, OC(O), $S(O)_2$, $NRS(O)_2$, $S(O)_2NR$, or a linking group selected from C_{1-4} saturated or unsaturated bivalent hydrocarbon radicals, wherein one or more carbons are optionally and independently substituted with a heteroatom selected from the group consisting of N, S and O;

each of R^B, R^C and R^X is independently

H, deuterium, oxo, halogen, -CN, $-NO_2$, -OR, -SR, -NRR', $-S(O)_2R$, $-S(O)_2NRR'$, -S(O)R, -S(O)NRR', -S(O)(NR)R, -C(O)R, -C(O)OR, -C(O)NRR', -C(O)N(R)OR, -OC(O)R, -OC(O)NRR', -N(R)C(O)OR, -N(R)C(O)R, -N(R)C(O)NRR', -N(R)C(NR)NRR', $-N(R)S(O)_2NRR'$, or $-N(R)S(O)_2R$; or

a C_{1-6} aliphatic chain, a 5- to 10-membered monocyclic, bicyclic or bridged carbocyclyl, heterocyclic, aryl or heteroaryl ring with 0-4 ring heteroatoms

independently selected from N, O and S, optionally substituted with one or more R^b, R^c or R^x, respectively;

each of R^a, R^b, R^c and R^x is independently

H, deuterium, oxo, halogen, -CN, -NO_2, -OR, -SR, -NRR', -$S(O)_2$R, -$S(O)_2$NRR', -S(O)R, -S(O)NRR', -S(O)(NR)R, -C(O)R, -C(O)OR, -C(O)NRR', -C(O)N(R)OR, -OC(O)R, -OC(O)NRR', -N(R)C(O)OR, -N(R)C(O)R, -N(R)C(O)NRR', -N(R)C(NR)NRR', -N(R)$S(O)_2$NRR' or -N(R)$S(O)_2$R; or

a substituted or unsubstituted group selected from C_{1-6} alkyl or 4- to 6-membered carbocyclic ring;

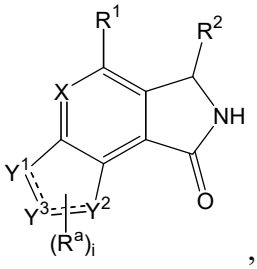
each of R and R' is independently selected from H, unsubstituted or substituted C_{1-4} alkyl, or unsubstituted or substituted 4- to 6-membered carbocyclic ring, or where R and R' are attached to the same C or N atom, together form an unsubstituted or substituted 4- to 6-membered heterocyclic ring; and

i is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10.

2. The compound of claim 1, wherein Ring A is a 4- to 7-membered carbocyclic ring with no ring heteroatoms, substituted with 0-10 R^as.

3. The compound of claim 1, wherein Ring A is a 4- to 7-membered heterocyclic ring with 1-4 ring heteroatoms selected from N, O and S, substituted with 0-10 R^as.

4. The compound of any one of claims 1-3, wherein Ring A is a 5-membered non-aromatic ring, substituted with 0-6 R^as, having the structural formula **I_b**:



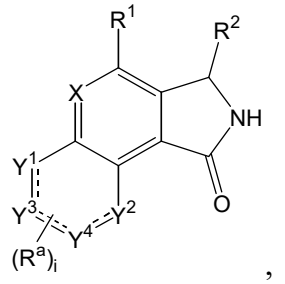
,

I_b

wherein

each of Y^1, Y^2 and Y^3 is independently CH, CH_2, N, NH, O, S or C(O), *provided that* at least one of Y^1, Y^2 and Y^3 is not N or NH and at least one of Y^1, Y^2 and Y^3 is C, CH or C(O).

5. The compound of any one of claims 1-3, wherein Ring A is a 6-membered non-aromatic ring, substituted with 0-8 R^as, having the structural formula $\mathbf{I_c}$:



,

$\mathbf{I_c}$

wherein

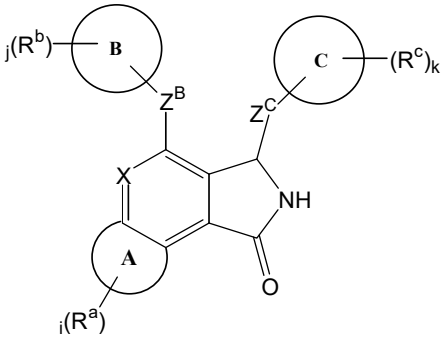
each of Y^1, Y^2, Y^3 and Y^4 is independently CH, CH_2, N, NH, O, S, $S(O)_2$, or C(O), *provided that* at least two of Y^1, Y^2, Y^3 and Y^4 is not N or NH and at least two of Y^1, Y^2, Y^3 and Y^4 is C, CH or C(O).

6. The compound of any one of claims 1-5, wherein

R^B is Ring B, a 5- to 10-membered monocyclic or bicyclic carbocyclyl, heterocyclic, aryl or heteroaryl ring with 0-4 ring heteroatoms independently selected from N, O and S, substituted with 0-6 R^bs; and

R^C is Ring C, a 5- to 10-membered monocyclic or bicyclic aryl or heteroaryl ring with 0-4 ring heteroatoms independently selected from N, O and S, substituted with 0-6 R^cs,

having the structural formula $\mathbf{I_e}$:



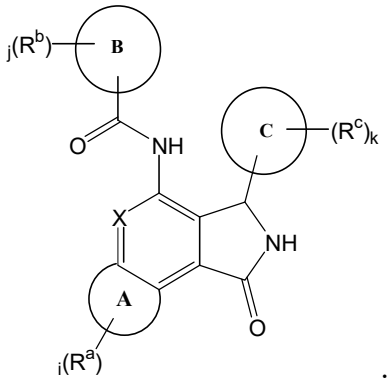
$\mathbf{I_e}$

wherein

j is 0, 1, 2, 3, 4, 5 or 6; and

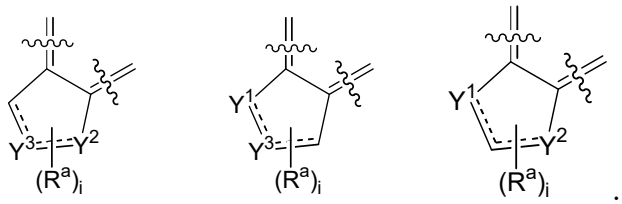
k is 0, 1, 2, 3, 4, 5 or 6.

7. The compound of claim 6, wherein Z^B is NH-C(O) and Z^c is a single bond, having the structural formula **I_f**:

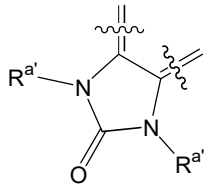


I_f

8. The compound of any one of claims 1-7, wherein Ring A is selected from:



9. The compound of any one of claims 1-7, wherein Ring A is

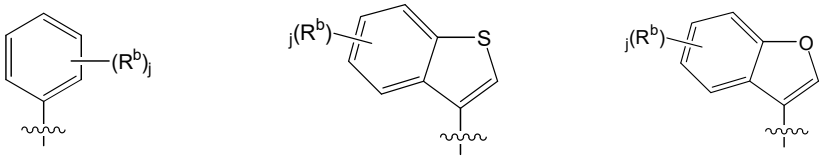


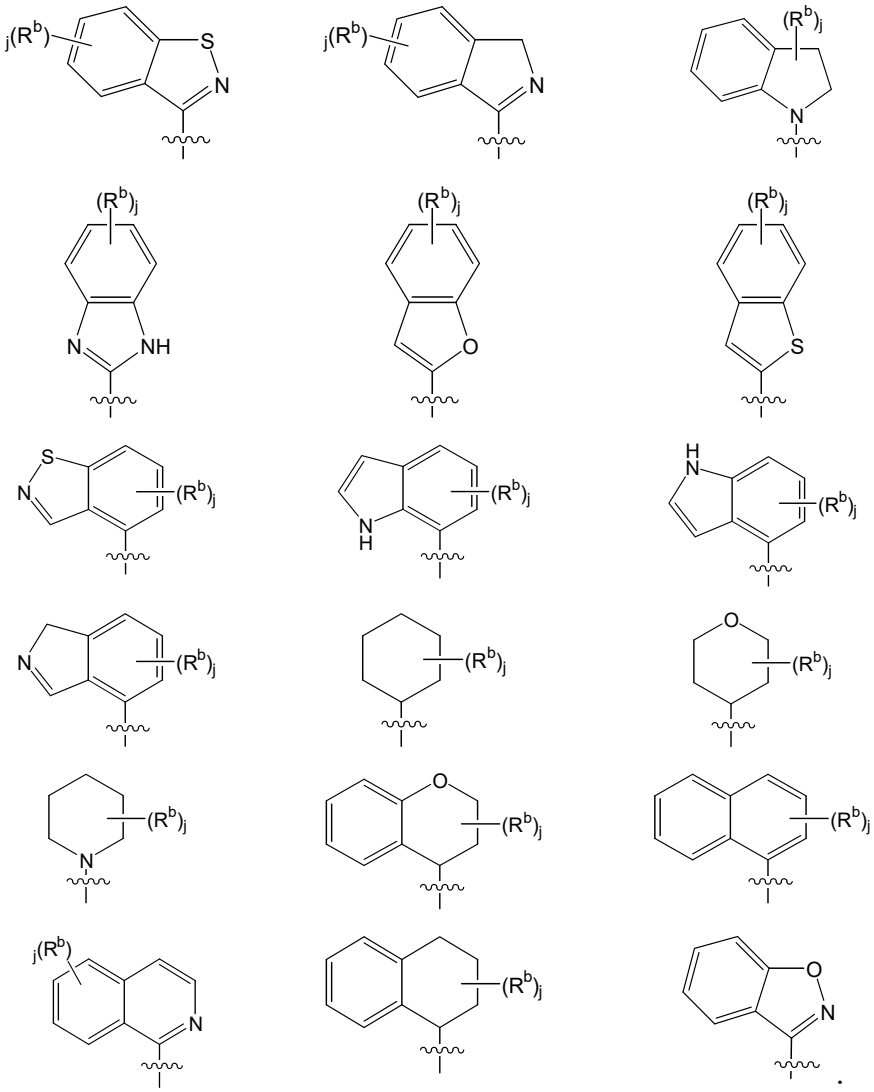
wherein one of $R^{a'}$ is CH_2CHF_2 or CH_2CF_3, and the other $R^{a'}$ is H, CH_3 or CD_3.

10. The compound of claim any one of 1-9, wherein X is N.

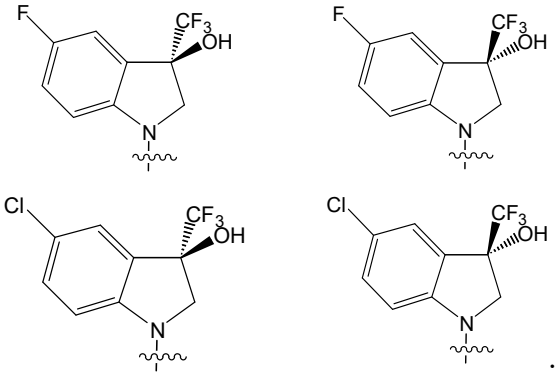
11. The compound of claim any one of 1-9, wherein X is CH or CR^X, wherein R^X is C_{1-3} alkyl.

12. The compound of any one of claims 1-11, wherein Ring B is selected from:

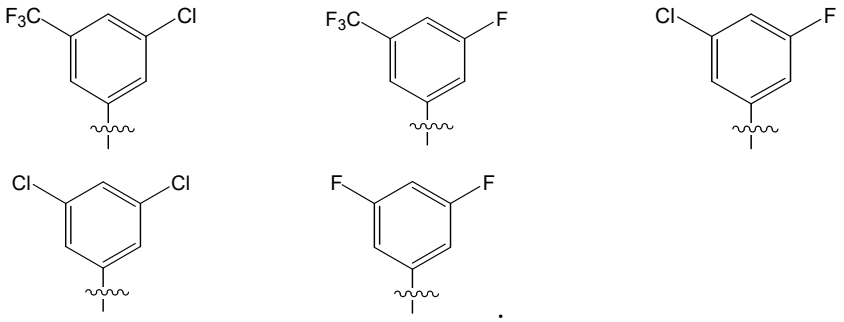




13. The compound of any one of claims 1-11, wherein Ring B is selected from:



14. The compound of any one of claims 1-11, wherein Ring B is selected from:

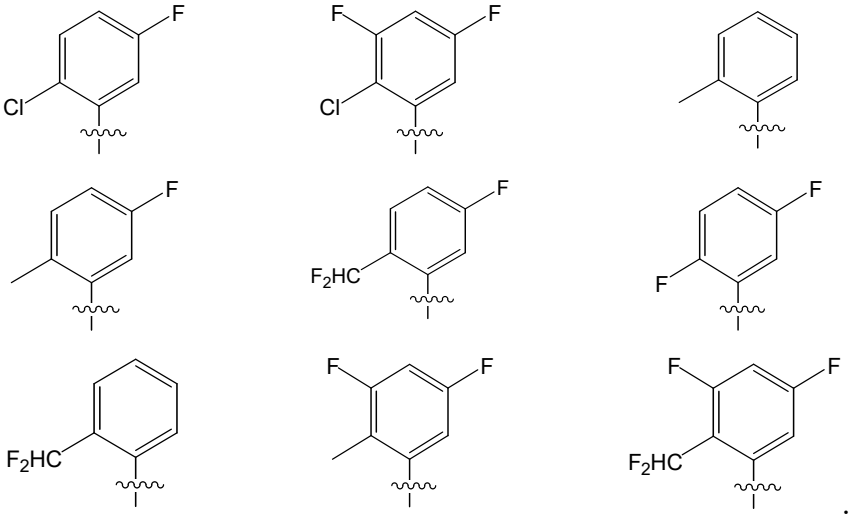


15. The compound of any one of claims 1-11, wherein Ring B is a substituted or unsubstituted phenyl, pyridyl, pyridazinyl or pyrazinyl.

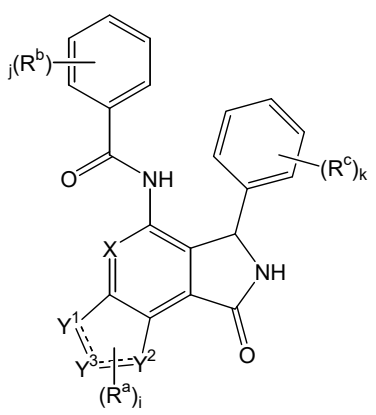
16. The compound of any one of claims 1-15, wherein Ring C is a substituted or unsubstituted phenyl, pyridyl, pyridazinyl or pyrazinyl.

17. The compound of claim 15 or 16, wherein each of Ring B and Ring C is independently a substituted or unsubstituted phenyl.

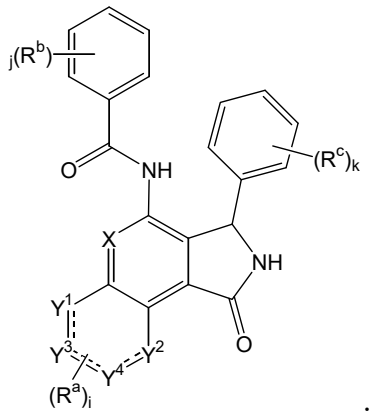
18. The compound of any one of claims 1-17, wherein Ring C is selected from:



19. The compound of claim 1, having the structural formula $\mathbf{I_h}$ or $\mathbf{I_i}$:

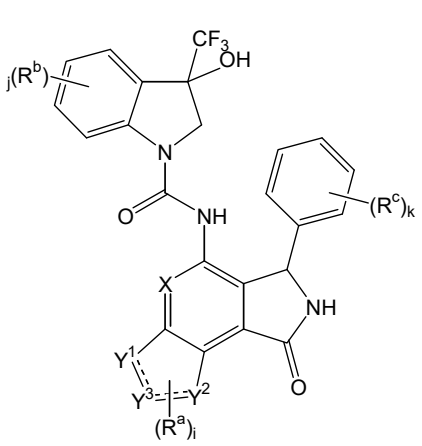


or

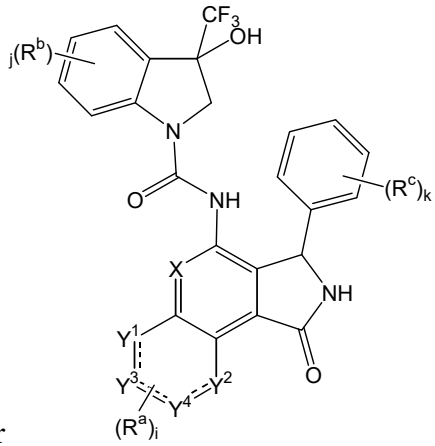


$\mathbf{I_h}$ $\mathbf{I_i}$

20. The compound of claim 1, having the structural formula $\mathbf{I_l}$ or $\mathbf{I_m}$:



or



$\mathbf{I_l}$ $\mathbf{I_m}$

21. The compound of claim 1 selected from **Table 1**, or a pharmaceutically acceptable form or an isotope derivative thereof.

22. A pharmaceutical composition comprising a compound according to any one of claims 1-21 and a pharmaceutically acceptable excipient, carrier, or diluent.

23. Use of the compound according to any one of claims 1-21, and a pharmaceutically acceptable excipient, carrier, or diluent, in preparation of a medicament for treating a disease or disorder mediated by phosphoinositide 3-kinase α (PI3Kα).

24. The use of claim 23, wherein the disease or disorder is cancer.