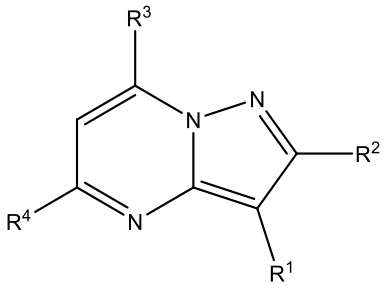
## CLAIMS

1. A compound of Formula I:



Formula I

wherein,

$R^1$ and $R^2$ are each independently selected from optionally substituted $C_{6-10}$aryl and optionally substituted $C_{5-10}$heteroaryl;

$R^3$ is selected from optionally substituted $C_{1-12}$alkyl, optionally substituted $C_{1-12}$alkoxy, optionally substituted alkylamino or dialkylamino, optionally substituted $C_{3-10}$cycloalkyl, optionally substituted $C_{3-10}$heterocycloalkyl, optionally substituted $C_{6-10}$aryl, and optionally substituted $C_{5-10}$heteroaryl, optionally substituted $-X^1-C_{3-10}$cycloalkyl, optionally substituted $-X^1-C_{3-10}$heterocycloalkyl, optionally substituted $-X^1-C_{6-10}$aryl, and optionally substituted $-X^1-C_{5-10}$heteroaryl;

$R^4$ is selected from $NH_2$, optionally substituted $C_{1-12}$alkoxy, optionally substituted alkylamino or dialkylamino, optionally substituted $C_{3-10}$cycloalkyl, optionally substituted $C_{3-10}$heterocycloalkyl, optionally substituted $-X^2-C_{3-10}$cycloalkyl, and optionally substituted $-X^2-C_{3-10}$heterocycloalkyl;

$X^1$ is selected from O and $NR^5$, wherein $R^5$ is H or an optionally substituted $C_{1-6}$alkyl; and

$X^2$ is selected from O and $NR^6$, wherein $R^6$ is H or an optionally substituted $C_{1-6}$alkyl;

or an isomer and/or a tautomer thereof, or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein $R^4$ is selected from optionally substituted $C_{1-12}$alkoxy, optionally substituted alkylamino or dialkylamino, optionally substituted $C_{3-10}$cycloalkyl, optionally substituted $C_{3-10}$heterocycloalkyl, optionally substituted $-X^2-C_{3-10}$cycloalkyl, and optionally substituted $-X^2-C_{3-10}$heterocycloalkyl, preferably $R^4$ is an optionally substituted $C_{1-12}$alkoxy, preferably optionally substituted $C_{1-6}$alkoxy, more preferably optionally substituted $C_{1-4}$alkoxy.

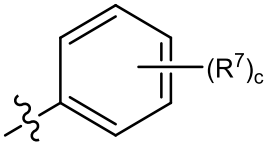
3. The compound of claim 2, wherein $R^4$ is an optionally substituted $C_{1-12}$alkyloxy, preferably optionally substituted $C_{1-5}$alkyloxy, more preferably optionally substituted $C_{1-4}$alkyloxy.

4. The compound of claim 2 or claim 3, wherein said alkyl or alkoxy is substituted with at least one group selected from OH, $CO_2H$, $CO_2NH_2$, $CO_2NHC_{1-6}$alkyl, $CO_2N(C_{1-6}alkyl)_2$, $P(O)(C_{1-6}alkyl)_2$, $NHC(O)C_{1-6}$alkyl, $N(C_{1-6}alkyl)C(O)C_{1-6}$alkyl, preferably OH.

5. The compound of any one of claims 1 to 4, wherein $R^3$ is an optionally substituted $C_{1-6}$alkyl group, optionally substituted $C_{1-6}$alkoxy, or an optionally substituted $C_{1-6}$alkylamino or di$C_{1-6}$alkylamino.

6. The compound of any one of claims 1 to 4, wherein $R^3$ is an optionally substituted $C_6$aryl, $C_{5-6}$heteroaryl, $C_{4-7}$cycloalkyl or $C_{4-7}$heterocycloalkyl group, or a $C_6$aryl, $C_{5-6}$heteroaryl, $C_{4-7}$cycloalkyl or $C_{4-7}$heterocycloalkyl linked to the pyrazolopyrimidine core through $X^1$.

7. The compound of claim 6, wherein the aryl group is of the formula:



wherein,

$R^7$ is independently in each occurrence selected from halogen, OH, $OR^9$, CN, $NO_2$, $C(O)R^9$, $C(O)N(R^8)_2$, $C(R^{10})=NR^{10}$, $SO_2R^9$, $SO_2N(R^8)_2$, $N(R^{10})C(O)R^9$, $N(R^{10})SO_2R^9$, $N(R^{10})C(O)N(R^8)_2$, $N(R^{10})SO_2N(R^8)_2$, $N(R^8)_2$, $P(O)(R^8)_2$, $P(O)(OR^8)_2$, $B(OR^8)_2$, $C_{1-6}$alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, $C_{6-10}$aryl, $C_{5-10}$heteroaryl, $C_{3-10}$cycloalkyl, and $C_{4-10}$heterocycloalkyl;

$R^8$ is independently in each occurrence selected from H, $C_{1-6}$alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, $C_{3-10}$cycloalkyl, $C_{4-10}$heterocycloalkyl, $C_6$aryl, and $C_{5-10}$heteroaryl, or two $R^8$ are taken together with their adjacent atom(s) to form a $C_{4-10}$heterocycloalkyl group;

$R^9$ is independently in each occurrence selected from $C_{1-6}$alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, $C_{3-7}$cycloalkyl, $C_{3-7}$heterocycloalkyl, $C_6$aryl, and $C_{5-6}$heteroaryl;

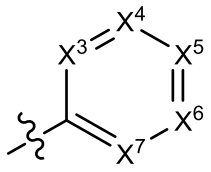
$R^{10}$ is independently in each occurrence selected from H, $C_{1-6}$alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, $C_{3-7}$cycloalkyl, $C_{3-7}$heterocycloalkyl, $C_6$aryl, and $C_{5-6}$heteroaryl; and

c is 0, 1, 2, 3, 4 or 5;

wherein said alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl group is optionally further substituted;

or

wherein the aryl or heteroaryl group is of the formula:



wherein,

$X^3$, $X^4$, $X^5$, $X^6$, and $X^7$ are each independently selected from N and $CR^{11}$, wherein at most three of $X^3$, $X^4$, $X^5$, $X^6$, and $X^7$ are N, or wherein one of two adjacent $X^3$, $X^4$, $X^5$, $X^6$, and $X^7$ is absent and the other is O, S or $NR^{10}$;

$R^8$ is independently in each occurrence selected from H, $C_{1-6}$alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, $C_{3-10}$cycloalkyl, $C_{4-10}$heterocycloalkyl, $C_6$aryl, and $C_{5-10}$heteroaryl, or two $R^8$ are taken together with their adjacent atom(s) to form a $C_{4-10}$heterocycloalkyl group;

$R^9$ is independently in each occurrence selected from $C_{1-6}$alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, $C_{3-7}$cycloalkyl, $C_{3-7}$heterocycloalkyl, $C_6$aryl, and $C_{5-6}$heteroaryl;

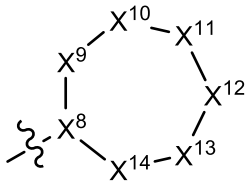
$R^{10}$ is independently in each occurrence selected from H, $C_{1-6}$alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, $C_{3-7}$cycloalkyl, $C_{3-7}$heterocycloalkyl, $C_6$aryl, and $C_{5-6}$heteroaryl; and

$R^{11}$ is independently in each occurrence selected from hydrogen, halogen, OH, $OR^9$, CN, $NO_2$, $C(O)R^9$, $C(O)N(R^8)_2$, $C(R^{10})=NR^{10}$, $SO_2R^9$, $SO_2N(R^8)_2$, $N(R^{10})C(O)R^9$, $N(R^{10})SO_2R^9$, $N(R^{10})C(O)N(R^8)_2$, $N(R^{10})SO_2N(R^8)_2$, $N(R^8)_2$, $P(O)(R^8)_2$, $P(O)(OR^8)_2$, $B(OR^8)_2$, $C_{1-6}$alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, $C_{6-10}$aryl, $C_{5-10}$heteroaryl, $C_{3-10}$cycloalkyl, and $C_{4-10}$heterocycloalkyl;

wherein said alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl group is optionally further substituted;

or

wherein the cycloalkyl or heterocycloalkyl group is of the formula:



wherein,

$X^8$ is selected from N and $CR^{11}$;

$X^9$, $X^{10}$, $X^{11}$, $X^{12}$, $X^{13}$, and $X^{14}$ are each independently selected from O, $NR^{12}$, $SO_2$, and $C(R^{13})_2$, wherein at most two of $X^8$, $X^9$, $X^{10}$, $X^{11}$, $X^{12}$, $X^{13}$, and $X^{14}$ are or comprise O, N or S, and/or wherein up to 3 of $X^9$, $X^{10}$, $X^{11}$, $X^{12}$, $X^{13}$, and $X^{14}$ are absent to form a 4, 5, or 6-membered ring, and/or two or three of $X^8$, $X^9$, $X^{10}$, $X^{11}$, $X^{12}$, $X^{13}$, and $X^{14}$ are taken together to form a bridge through one to three additional bridging atoms, e.g. carbon atoms;

$R^8$ is independently in each occurrence selected from H, $C_{1\text{-}6}$alkyl, $C_{2\text{-}6}$alkenyl, $C_{2\text{-}6}$alkynyl, $C_{3\text{-}10}$cycloalkyl, $C_{4\text{-}10}$heterocycloalkyl, $C_6$aryl, and $C_{5\text{-}10}$heteroaryl, or two $R^8$ are taken together with their adjacent atom(s) to form a $C_{4\text{-}10}$heterocycloalkyl group;

$R^9$ is independently in each occurrence selected from $C_{1\text{-}6}$alkyl, $C_{2\text{-}6}$alkenyl, $C_{2\text{-}6}$alkynyl, $C_{3\text{-}7}$cycloalkyl, $C_{3\text{-}7}$heterocycloalkyl, $C_6$aryl, and $C_{5\text{-}6}$heteroaryl;

$R^{10}$ is independently in each occurrence selected from H, $C_{1\text{-}6}$alkyl, $C_{2\text{-}6}$alkenyl, $C_{2\text{-}6}$alkynyl, $C_{3\text{-}7}$cycloalkyl, $C_{3\text{-}7}$heterocycloalkyl, $C_6$aryl, and $C_{5\text{-}6}$heteroaryl;

$R^{11}$ is independently in each occurrence selected from hydrogen, halogen, OH, $OR^9$, CN, $NO_2$, $C(O)R^9$, $C(O)N(R^8)_2$, $C(R^{10})=NR^{10}$, $SO_2R^9$, $SO_2N(R^8)_2$, $N(R^{10})C(O)R^9$, $N(R^{10})SO_2R^9$, $N(R^{10})C(O)N(R^8)_2$, $N(R^{10})SO_2N(R^8)_2$, $N(R^8)_2$, $P(O)(R^8)_2$, $P(O)(OR^8)_2$, $B(OR^8)_2$, $C_{1\text{-}6}$alkyl, $C_{2\text{-}6}$alkenyl, $C_{2\text{-}6}$alkynyl, $C_{6\text{-}10}$aryl, $C_{5\text{-}10}$heteroaryl, $C_{3\text{-}10}$cycloalkyl, and $C_{4\text{-}10}$heterocycloalkyl;

$R^{12}$ is selected from is independently in each occurrence selected from hydrogen, $C(O)R^9$, $C(O)N(R^8)_2$, $SO_2R^9$, $SO_2N(R^8)_2$, $P(O)(R^8)_2$, $P(O)(OR^8)_2$, $B(OR^8)_2$, $C_{1\text{-}6}$alkyl, $C_{2\text{-}6}$alkenyl, $C_{2\text{-}6}$alkynyl, $C_{6\text{-}10}$aryl, $C_{5\text{-}10}$heteroaryl, $C_{3\text{-}10}$cycloalkyl, and $C_{4\text{-}10}$heterocycloalkyl; and

$R^{13}$ is independently in each occurrence selected from hydrogen, halogen, OH, $OR^9$, CN, $NO_2$, $C(O)R^9$, $C(O)N(R^8)_2$, $C(R^{10})=NR^{10}$, $SO_2R^9$, $SO_2N(R^8)_2$, $N(R^{10})C(O)R^9$, $N(R^{10})SO_2R^9$, $N(R^{10})C(O)N(R^8)_2$, $N(R^{10})SO_2N(R^8)_2$, $N(R^8)_2$, $P(O)(R^8)_2$, $P(O)(OR^8)_2$, $B(OR^8)_2$, $C_{1\text{-}6}$alkyl, $C_{2\text{-}6}$alkenyl, $C_{2\text{-}6}$alkynyl, $C_{6\text{-}10}$aryl, $C_{5\text{-}10}$heteroaryl, $C_{3\text{-}10}$cycloalkyl, and $C_{4\text{-}10}$heterocycloalkyl or two $R^{13}$ are taken together with their adjacent atom(s) to form a $C_{4\text{-}10}$cycloalkyl or $C_{4\text{-}10}$heterocycloalkyl group;

wherein said alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl group is optionally further substituted.

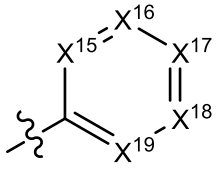
8. The compound of claim 7, wherein $X^3$, $X^4$, $X^5$, $X^6$, and $X^7$ is N, preferably one of $X^4$ and $X^6$.

9. The compound of claim 8, wherein $X^4$ is N and $X^3$, $X^6$, and $X^7$ are each CH.

10. The compound of any one of claims 7 to 9, wherein $X^5$ is $CR^{11}$ and $R^{11}$ is selected from CN, an optionally substituted $C_{1-6}$alkyl group (e.g., $CH_3$, $CF_3$, etc.), and $OR^9$, wherein $R^9$ is an optionally substituted $C_{1-6}$alkyl group.

11. The compound of any one of claims 1 to 10, wherein $R^2$ is an optionally substituted $C_6$aryl or optionally substituted $C_{5-6}$heteroaryl.

12. The compound of claim 11, wherein $R^2$ is of the formula:




wherein,

$X^{15}$, $X^{16}$, $X^{17}$, $X^{18}$, and $X^{19}$ are each independently selected from N and $CR^{11}$, wherein at most three of $X^{15}$, $X^{16}$, $X^{17}$, $X^{18}$, and $X^{19}$ are N, or wherein one of two adjacent $X^{15}$, $X^{16}$, $X^{17}$, $X^{18}$, and $X^{19}$ is absent and the other is O, S or $NR^{10}$;

$R^{10}$ is independently in each occurrence selected from H, $C_{1-6}$alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, $C_{3-7}$cycloalkyl, $C_{3-7}$heterocycloalkyl, $C_6$aryl, and $C_{5-6}$heteroaryl;

$R^{11}$ is independently in each occurrence selected from hydrogen, halogen, OH, $OR^9$, CN, $NO_2$, $C(O)R^9$, $C(O)N(R^8)_2$, $C(R^{10})=NR^{10}$, $SO_2R^9$, $SO_2N(R^8)_2$, $N(R^{10})C(O)R^9$, $N(R^{10})SO_2R^9$, $N(R^{10})C(O)N(R^8)_2$, $N(R^{10})SO_2N(R^8)_2$, $N(R^8)_2$, $P(O)(R^8)_2$, $P(O)(OR^8)_2$, $B(OR^8)_2$, $C_{1-6}$alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, $C_{6-10}$aryl, $C_{5-10}$heteroaryl, $C_{3-10}$cycloalkyl, and $C_{4-10}$heterocycloalkyl; and

wherein said alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl group is optionally further substituted.

13. The compound of claim 12, wherein $X^{15}$, $X^{16}$, $X^{17}$, $X^{18}$, and $X^{19}$ are each $CR^{11}$.

14. The compound of claim 12 or claim 13, wherein $X^{15}$ is $CR^{11}$, wherein $R^{11}$ is selected from halogen and $OR^{9}$.

15. The compound of any one of claims 12 to 14, wherein $X^{16}$, $X^{17}$, $X^{18}$, and $X^{19}$ are each $CR^{11}$, wherein $R^{11}$ is hydrogen.

16. The compound of claim 14 or claim 15, wherein $R^{2}$ is a 2-methoxyphenyl or 2-chlorophenyl group.

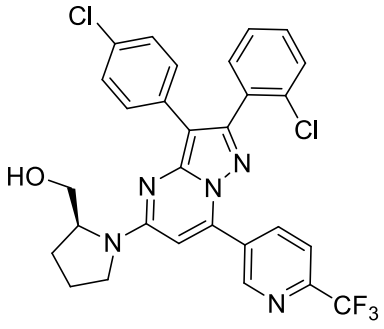
17. The compound of any one of claims 1 to 16, wherein $R^{1}$ is an optionally substituted $C_6$aryl, preferably $R^{1}$ is a 4-chlorophenyl group.

18. The compound of claim 1, wherein the compound is selected from Compounds 1 to 78 as defined herein, or an isomer or a tautomer thereof, or a pharmaceutically acceptable salt thereof.

19. The compound of claim 18, wherein the compound is selected from Compounds 1, 2, 4, 7-9, 11, 13, 15, 21, 27, 43, 45, 50-53, 56-58, 60, 61, 63, 64, 70(R), 71(S), 72(R), 72(S), as defined herein, or an isomer or a tautomer thereof, or a pharmaceutically acceptable salt thereof.

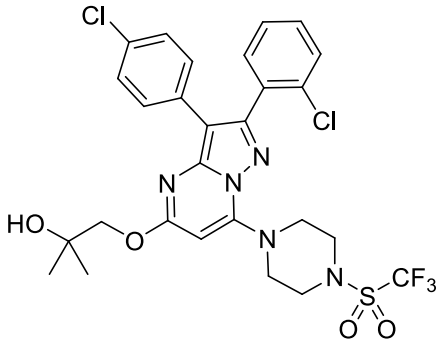
20. The compound of claim 19, wherein the compound is selected from Compound 8, Compound 15, or Compound 45, as defined herein, or an isomer or a tautomer thereof, or a pharmaceutically acceptable salt thereof.

21. A compound which is selected from



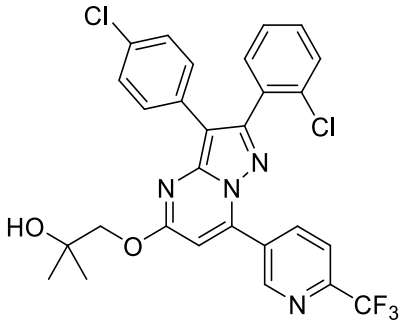

Compound 8;

or



Compound 15;

or



Compound 45,

or a tautomer thereof, or a pharmaceutically acceptable salt thereof.

22. A pharmaceutical composition comprising a compound as defined in any one of claims 1 to 21, together with a pharmaceutically acceptable carrier, diluent or excipient.

23. Use of a compound as defined in any one of claims 1 to 21 or a pharmaceutical composition as defined in claim 22 in the manufacture of a medicament for the treatment of a disorder related to appetite or one of its complications, a disorder related to glucose regulation or one of its complications, a fibrosis related disorder or one of its complications, a disorder related to metabolism or one of its complications, a disorder related to skin and hair growth and healing, a disorder related to the GI tract, a disorder related to obesity or one of its complications, or a combination thereof.

24. The use of claim 23 in the treatment of a disorder selected from diabetes Type I, diabetes Type II, obesity and chronic kidney disease.

25. A compound as defined in any one of claims 1 to 21 or a pharmaceutical composition as defined in claim 22 for use in the treatment of a disorder related to appetite or one of its complications, a disorder related to glucose regulation or one of its complications, a fibrosis related disorder or one of its complications, a disorder related to metabolism or one of its complications, a disorder related to skin and hair growth and healing, a disorder related to the GI tract, a disorder related to obesity or one of its complications, or a combination thereof.

26. Use of claim 25 in the treatment of a disorder selected from diabetes Type I and diabetes Type II, obesity and chronic kidney disease.