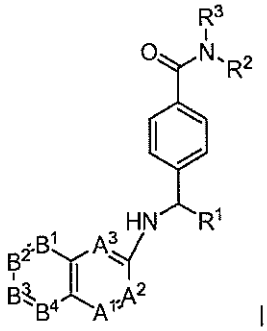
We Claim:

1. A compound of Formula I



I

or a pharmaceutically acceptable salt thereof, wherein

R^1 is (C_1-C_6)alkyl which is optionally substituted with one to three fluoro, hydroxy or methoxy; (C_3-C_7)cycloalkyl which is optionally substituted with one to two fluoro or one to two (C_1-C_3)alkyl which are each optionally substituted with one to three fluoro and wherein one carbon of the (C_3-C_7)cycloalkyl can be replaced with an O; or (C_3-C_7)cycloalkyl-(C_1-C_6)alkyl wherein the (C_3-C_7)cycloalkyl group of said (C_3-C_7)cycloalkyl-(C_1-C_6)alkyl is optionally substituted with one to two (C_1-C_3)alkyl which are each optionally substituted with one to three fluoro;

R^2 is hydrogen or (C_1-C_3)alkyl;

R^3 is tetrazolyl, -CH_2-tetrazolyl, -$(CH_2)_2SO_3H$, -$(CH_2)_2CO_2H$, -CH_2CHFCO_2H or -$CH_2CH(OH)CO_2H$;

A^1, A^2 and A^3 are each independently CR^4 or N, with the proviso that at least one but no more than two of A^1, A^2 and A^3 are N;

R^4 at each occurrence is independently hydrogen, halo, cyano, (C_1-C_3)alkyl optionally substituted with one to three fluoro, (C_1-C_3)alkoxy optionally substituted with one to three fluoro, or (C_3-C_5)cycloalkyl;

B^1, B^2, B^3 and B^4 are each independently CR^5 or N, with the proviso that no more than two of B^1, B^2, B^3 and B^4 are N; and

R^5 at each occurrence is independently hydrogen, halo, cyano, (C_1-C_3)alkyl optionally substituted with one to three fluoro, or (C_1-C_3)alkoxy optionally substituted with one to three fluoro, or (C_3-C_5)cycloalkyl.

2. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein R^2 is hydrogen and R^3 is $-(CH_2)_2CO_2H$.

3. The compound according to claim 2, or a pharmaceutically acceptable salt thereof, wherein R^1 is ethyl, propyl, isopropyl, isobutyl, t-butyl, pentyl, neopentyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cyclopropylmethyl each optionally substituted with 1 to 3 fluoro and wherein said cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl are each optionally substituted with 1 to 2 methyl.

4. The compound according to claim 3, or a pharmaceutically acceptable salt thereof, wherein B^1, B^2, B^3 and B^4 are each CR^5.

5. The compound according to claim 4, or a pharmaceutically acceptable salt thereof, wherein

A^1 and A^2 are each CR^4 and A^3 is N;

R^4 at each occurrence is independently hydrogen, fluoro, chloro, methyl or ethyl; and

R^5 at each occurrence is independently hydrogen, fluoro, chloro, methyl, trifluoromethyl or methoxy.

6. The compound according to claim 1 selected from the group consisting of

(+/-)-3-(4-(1-(3-methylquinolin-2-ylamino)butyl)benzamido)propanoic acid;

(+/-)-3-{4-[3-methyl-1-(quinolin-3-ylamino)-butyl]-benzoylamino}-propionic acid;

(+/-)-3-{4-[1-(7-fluoro-quinazolin-2-ylamino)-3-methyl-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[3-methyl-1-(quinolin-2-ylamino)-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[1-(8-methoxy-quinolin-2-ylamino)-3-methyl-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[3-methyl-1-(3-methyl-quinoxalin-2-ylamino)-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[3-methyl-1-(quinoxalin-2-ylamino)-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[3-methyl-1-(4-methyl-quinolin-2-ylamino)-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[3-methyl-1-(3-methyl-quinolin-2-ylamino)-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[1-(7-fluoro-4-methyl-quinolin-2-ylamino)-3-methyl-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[1-(8-chloro-quinolin-2-ylamino)-3-methyl-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[3-methyl-1-(quinazolin-2-ylamino)-butyl]-benzoylamino}-propionic acid;
(+/-) 3-(4-(3-methyl-1-(7-(trifluoromethyl)quinolin-2-ylamino)butyl)benzamido) propanoic acid;
(+/-)-3-(4-(3-methyl-1-(6-(trifluoromethyl)quinolin-2-ylamino)butyl)benzamido) propanoic acid;
(+\-)-3-(4-(3-methyl-1-(2-methylquinolin-3-ylamino)butyl)benzamido)propanoic acid;
(+\-)-3-(4-(3-methyl-1-(4-methylquinolin-3-ylamino)butyl)benzamido)propanoic acid;
(+/-)-3-{4-[(3,3-dimethyl-cyclobutyl)-(3-methyl-quinolin-2-ylamino)-methyl]-benzoylamino}-propionic acid;

(+/-)-3-{4-[(3,3-dimethyl-cyclobutyl)-(6-fluoro-3-methyl-quinolin-2-ylamino)-methyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[(3,3-dimethyl-cyclobutyl)-(7-fluoro-3-methyl-quinolin-2-ylamino)-methyl]-benzoylamino}-propionic acid;
(+/-) 3-(4-((3,3-dimethylcyclobutyl)(6-fluoroquinolin-3-ylamino)methyl)benzamido) propanoic acid;
(+/-)-3-(4-((3,3-dimethylcyclobutyl)(7-fluoroquinolin-3-ylamino)methyl)benzamido) propanoic acid;
(+/-)-3-(4-(4,4,4-trifluoro-1-(quinolin-3-ylamino)butyl)benzamido)propanoic acid;
(+/-)-3-(4-((6,7-difluoroquinolin-3-ylamino)(3,3-dimethylcyclobutyl)methyl) benzamido)propanoic acid;
(+/-)-3-(4-(3-methyl-1-(7-methylquinolin-3-ylamino)butyl)benzamido)propanoic acid;
(+/-)-3-(4-(3-methyl-1-(8-methylquinolin-3-ylamino)butyl)benzamido)propanoic acid;
(+/-)-3-(4-(3-methyl-1-(6-methylquinolin-3-ylamino)butyl)benzamido)propanoic acid; and
(+/-)-3-(4-(3-methyl-1-(5-methylquinolin-3-ylamino)butyl)benzamido)propanoic acid;
or a pharmaceutically acceptable salt thereof.

7. The compound according to claim 1 selected from the group consisting of
(+)-3-(4-(1-(3-methylquinolin-2-ylamino)butyl)benzamido)propanoic acid;
(-)-3-(4-(1-(3-methylquinolin-2-ylamino)butyl)benzamido)propanoic acid;
(+)-3-(4-(3-methyl-1-(3-methylquinolin-2-ylamino)butyl)benzamido)propanoic acid; and
(-)-3-(4-(3-methyl-1-(3-methylquinolin-2-ylamino)butyl)benzamido)propanoic acid;
or a pharmaceutically acceptable salt thereof.

8. 3-{4-[(3,3-dimethyl-cyclobutyl)-(3-methyl-quinolin-2-ylamino)-methyl]-benzoylamino}-propionic acid, isomer 1, or a pharmaceutically acceptable salt thereof.

9. 3-{4-[(3,3-dimethyl-cyclobutyl)-(3-methyl-quinolin-2-ylamino)-methyl]-benzoylamino}-propionic acid, isomer 2, or a pharmaceutically acceptable salt thereof.

10. 3-{4-[(3,3-dimethyl-cyclobutyl)-(6-fluoro-3-methyl-quinolin-2-ylamino)-methyl]-benzoylamino}-propionic acid, isomer 1, or a pharmaceutically acceptable salt thereof.

11. 3-{4-[(3,3-dimethyl-cyclobutyl)-(6-fluoro-3-methyl-quinolin-2-ylamino)-methyl]-benzoylamino}-propionic acid, isomer 2, or a pharmaceutically acceptable salt thereof.

12. A pharmaceutical composition comprising (i) a compound of any one of claims 1 to 11; or a pharmaceutically acceptable salt thereof and (ii) a pharmaceutically acceptable excipient, diluent, or carrier.

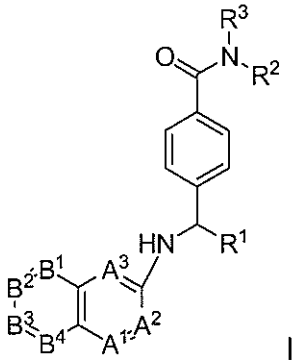
13. Use of a compound of any one of claims 1 through 11, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating obesity and obesity-related disorders.

14. Use of a compound of any one of claims 1 through 11, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating or delaying the progression or onset of type 2 diabetes, type 1 diabetes and diabetes-related disorders.

15. Use of a compound of any one of claims 1 through 11, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease, condition or disorder that is modulated by the deactivation of a glucagon receptor.

We claim:

1. A compound of Formula I



I

or a pharmaceutically acceptable salt thereof, wherein

R^1 is ethyl, propyl, isopropyl, isobutyl, t-butyl, pentyl, neopentyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cyclopropylmethyl each optionally substituted with 1 to 3 fluoro and wherein said cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl are each optionally substituted with 1 to 2 methyl;

R^2 is hydrogen ;

R^3 is $-(CH_2)_2CO_2H$;

A^1, A^2 and A^3 are each independently CR^4 or N, with the proviso that at least one but no more than two of A^1, A^2 and A^3 are N;

R^4 at each occurrence is independently hydrogen, halo, cyano, $(C_1\text{-}C_3)$alkyl optionally substituted with one to three fluoro, $(C_1\text{-}C_3)$alkoxy optionally substituted with one to three fluoro, or $(C_3\text{-}C_5)$cycloalkyl;

B^1, B^2, B^3 and B^4 are each independently CR^5 ; and

R^5 at each occurrence is independently hydrogen, halo, cyano, $(C_1\text{-}C_3)$alkyl optionally substituted with one to three fluoro, or $(C_1\text{-}C_3)$alkoxy optionally substituted with one to three fluoro, or $(C_3\text{-}C_5)$cycloalkyl.

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

A^1 and A^2 are each CR^4 and A^3 is N;

R^4 at each occurrence is independently hydrogen, fluoro, chloro, methyl or ethyl; and

R^5 at each occurrence is independently hydrogen, fluoro, chloro, methyl, trifluoromethyl or methoxy.

3. The compound according to claim 1 selected from the group consisting of
(+/-)-3-(4-(1-(3-methylquinolin-2-ylamino)butyl)benzamido)propanoic acid;
(+/-)-3-{4-[3-methyl-1-(quinolin-3-ylamino)-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[1-(7-fluoro-quinazolin-2-ylamino)-3-methyl-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[3-methyl-1-(quinolin-2-ylamino)-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[1-(8-methoxy-quinolin-2-ylamino)-3-methyl-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[3-methyl-1-(3-methyl-quinoxalin-2-ylamino)-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[3-methyl-1-(quinoxalin-2-ylamino)-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[3-methyl-1-(4-methyl-quinolin-2-ylamino)-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[3-methyl-1-(3-methyl-quinolin-2-ylamino)-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[1-(7-fluoro-4-methyl-quinolin-2-ylamino)-3-methyl-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[1-(8-chloro-quinolin-2-ylamino)-3-methyl-butyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[3-methyl-1-(quinazolin-2-ylamino)-butyl]-benzoylamino}-propionic acid;
(+/-) 3-(4-(3-methyl-1-(7-(trifluoromethyl)quinolin-2-ylamino)butyl)benzamido) propanoic acid;
(+/-)-3-(4-(3-methyl-1-(6-(trifluoromethyl)quinolin-2-ylamino)butyl)benzamido) propanoic acid;
(+\-)-3-(4-(3-methyl-1-(2-methylquinolin-3-ylamino)butyl)benzamido)propanoic acid;
(+\-)-3-(4-(3-methyl-1-(4-methylquinolin-3-ylamino)butyl)benzamido)propanoic acid;
(+/-)-3-{4-[(3,3-dimethyl-cyclobutyl)-(3-methyl-quinolin-2-ylamino)-methyl]-benzoylamino}-propionic acid;
(+/-)-3-{4-[(3,3-dimethyl-cyclobutyl)-(6-fluoro-3-methyl-quinolin-2-ylamino)-methyl]-benzoylamino}-propionic acid;

(+/-)-3-{4-[(3,3-dimethyl-cyclobutyl)-(7-fluoro-3-methyl-quinolin-2-ylamino)-methyl]-benzoylamino}-propionic acid;
(+/-) 3-(4-((3,3-dimethylcyclobutyl)(6-fluoroquinolin-3-ylamino)methyl)benzamido) propanoic acid;
(+/-)-3-(4-((3,3-dimethylcyclobutyl)(7-fluoroquinolin-3-ylamino)methyl)benzamido) propanoic acid;
(+/-)-3-(4-(4,4,4-trifluoro-1-(quinolin-3-ylamino)butyl)benzamido)propanoic acid;
(+/-)-3-(4-((6,7-difluoroquinolin-3-ylamino)(3,3-dimethylcyclobutyl)methyl) benzamido)propanoic acid;
(+/-)-3-(4-(3-methyl-1-(7-methylquinolin-3-ylamino)butyl)benzamido)propanoic acid;
(+/-)-3-(4-(3-methyl-1-(8-methylquinolin-3-ylamino)butyl)benzamido)propanoic acid;
(+/-)-3-(4-(3-methyl-1-(6-methylquinolin-3-ylamino)butyl)benzamido)propanoic acid; and
(+/-)-3-(4-(3-methyl-1-(5-methylquinolin-3-ylamino)butyl)benzamido)propanoic acid;
or a pharmaceutically acceptable salt thereof.

4. The compound according to claim 1 selected from the group consisting of
(+)-3-(4-(1-(3-methylquinolin-2-ylamino)butyl)benzamido)propanoic acid;
(-)-3-(4-(1-(3-methylquinolin-2-ylamino)butyl)benzamido)propanoic acid;
(+)-3-(4-(3-methyl-1-(3-methylquinolin-2-ylamino)butyl)benzamido)propanoic acid; and
(-)-3-(4-(3-methyl-1-(3-methylquinolin-2-ylamino)butyl)benzamido)propanoic acid;
or a pharmaceutically acceptable salt thereof.

5. (R) 3-{4-[(3,3-dimethyl-cyclobutyl)-(3-methyl-quinolin-2-ylamino)-methyl]-benzoylamino}-propionic acid or a pharmaceutically acceptable salt thereof.

6. (S) 3-{4-[(3,3-dimethyl-cyclobutyl)-(3-methyl-quinolin-2-ylamino)-methyl]-benzoylamino}-propionic acid or a pharmaceutically acceptable salt thereof.

7. (R) 3-{4-[(3,3-dimethyl-cyclobutyl)-(6-fluoro-3-methyl-quinolin-2-ylamino)-methyl]-benzoylamino}-propionic acid or a pharmaceutically acceptable salt thereof.

8. (S) 3-{4-[(3,3-dimethyl-cyclobutyl)-(6-fluoro-3-methyl-quinolin-2-ylamino)-methyl]-benzoylamino}-propionic acid or a pharmaceutically acceptable salt thereof.

9. A pharmaceutical composition comprising (i) a compound of any one of claims 1 to 8; or a pharmaceutically acceptable salt thereof and (ii) a pharmaceutically acceptable excipient, diluent, or carrier.

10. Use of a compound of any one of claims 1 through 8, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating obesity and obesity-related disorders.

11. Use of a compound of any one of claims 1 through 8, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating or delaying the progression or onset of type 2 diabetes, type 1 diabetes and diabetes-related disorders.

12. Use of a compound of any one of claims 1 through 8, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease, condition or disorder that is modulated by the deactivation of a glucagon receptor.