In a further aspect this description relates to a pharmaceutical composition, comprising one or more compounds of general formula **I** or one or more pharmaceutically acceptable salts thereof as defined herein, optionally together with one or more inert carriers and/or diluents.

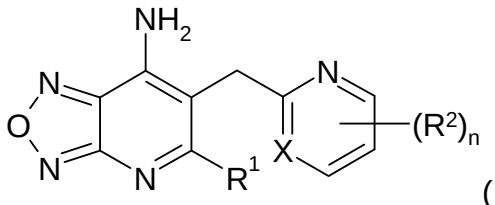
This description also relates to a method for treating diseases or conditions which are mediated by inhibiting ghrelin O-acyl transferase (GOAT) in a patient in need thereof characterized in that a compound of general formula **I** or a pharmaceutically acceptable salt thereof is administered to the patient.

There is also provided a method for treating a metabolic disease or disorder, such as obesity, including, but not limited to obesity in patients suffering from Prader-Willi-Syndrome, insulin resistance and diabetes, in particular type 2 diabetes mellitus, in a patient in need thereof characterized in that a therapeutically effective amount of a compound of general formula **I** or a pharmaceutically acceptable salt thereof is administered to the patient.

There is also provided the use of a compound of the general formula **I** or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for a therapeutic method as described hereinbefore and hereinafter. In another aspect this description relates to use of a compound as defined herein or a pharmaceutically acceptable salt thereof for the prepation of a medicament for treating obesity, including obesity in patients suffering from Prader-Willi-Syndrome, type 2 diabetes mellitus or insulin resistance.

Patent Claims

1. A compound of formula



(I),

wherein

X is CH or N;

R^1 is selected from the group consisting of CH_3, $-CH_2OH$ and Cl;

R^2 is independently of each other selected from the group consisting of H, F, Cl, Br, I, CN, C_{1-6}-alkyl, C_{3-7}-cycloalkyl, OH, -O-(C_{1-6}-alkyl), -O-(C_{3-7}-cycloalkyl), -O-(C_{1-3}-alkyl)-(C_{3-7}-cycloalkyl), -O-heterocyclyl, -O-(C_{1-3}-alkyl)-heterocyclyl, -O-aryl, -O-heteroaryl, -S-(C_{1-3}-alkyl), -SO-(C_{1-3}-alkyl), $-SO_2$-(C_{1-3}-alkyl), $-NH_2$, -NH-(C_{1-6}-alkyl), -NH-(C_{3-6}-cycloalkyl), -NH-(C_{1-3}-alkyl)-heterocyclyl, -NH-(C_{1-6}-alkyl)-C(=O)-NH_2, -C(=O)-NH_2, -C(=O)-NH-(C_{1-3}-alkyl), -C(=O)-N(C_{1-3}-alkyl)$_2$, -C(=O)OH, -C(=O)-O-(C_{1-4}-alkyl), -C(=O)-(C_{1-4}-alkyl), -C_{1-3}-alkyl-C(=O)-O-(C_{1-4}-alkyl), heterocyclyl, heteroaryl and 5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl,

wherein each alkyl or cycloalkyl group is optionally independently substituted with one or more substituents selected from the group consisting of F, CN and OH, and

wherein each heterocyclyl group is selected from a mono- or spirocyclic 4-7-membered cycloalkyl group, in which 1, 2 or 3 CH_2-groups are independently of each other replaced by O, S, NH or C=O, and

wherein each heterocyclyl group is optionally substituted with 1 or 2 substituents independently of each other selected from F, OH and C_{1-3}-alkyl,

wherein each aryl group is selected from a group conistsing of phenyl and naphthyl, and

wherein each heteroaryl group is selected from a 5-membered aromatic cycle containing 1 or 2 heteroatoms independently selected from N, O and S or from a 6-membered aromatic cycle containing 1 or 2 N, and

wherein each aryl or heteroaryl group is optionally substituted with 1 or 2 substituents independently selected from a group conisting of F, CN and C_{1-3}-alkyl, which is optionally substituted with one or more F;

or, if two groups R^2 are attached to adjacent C atoms of the pyridine or pyrimidine group, they may be linked with each other and together form a –O-CH_2-O-, -O-CH_2-CH_2-O- or –O-CH_2-CH_2-CH_2-O- bridge, in which 1 or 2 H atoms may be replaced with F or C_{1-3}-alkyl; and

n is 1, 2 or 3;

wherein each of the above-mentioned alkyl groups may be substituted with one or more F;

or a salt thereof.

2. A compound of formula (I) according to claim 1, wherein
R^1 is -CH_3; and
n is 1 or 2.

3. A compound of formula (I) according to claim 1 or 2, wherein

R^2 is independently of each other selected from the group consisting of H, F, Cl, Br, CN, C_{1-6}-alkyl, C_{3-7}-cycloalkyl, OH, -O-(C_{1-6}-alkyl), -O-(C_{1-3}-alkyl)-(C_{3-7}-cycloalkyl), -O-heterocyclyl, -O-(C_{1-3}-alkyl)-heterocyclyl, -O-aryl, -O-heteroaryl, -S-(C_{1-3}-alkyl), -SO_2-(C_{1-3}-alkyl), -NH_2, -NH-(C_{1-6}-alkyl), -NH-(C_{3-6}-cycloalkyl), -NH-(C_{1-3}-alkyl)-heterocyclyl, -NH-(C_{1-6}-alkyl)-C(=O)-NH_2, -C(=O)-NH_2, -C(=O)-NH-(C_{1-3}-alkyl), -C(=O)-(C_{1-4}-alkyl), -C_{1-3}-alkyl-C(=O)-O-(C_{1-4}-alkyl), heterocyclyl, heteroaryl and 5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl,

wherein each alkyl or cycloalkyl group is optionally independently substituted with one or more substituents selected from the group consisting of F, CN and OH, and

wherein each heterocyclyl group is selected from a mono- or spirocyclic 4-7-membered cycloalkyl group, in which 1, 2 or 3 CH_2-groups are independently of each other replaced by O, S, NH or C=O, and

wherein each heterocyclyl group is optionally substituted with 1 or 2 substituents independently of each other selected from F, OH and C_{1-3}-alkyl,

wherein each aryl group is selected from a group consisting of phenyl and naphthyl, and

wherein each heteroaryl group is selected from a 5-membered aromatic cycle containing 1 or 2 heteroatoms independently selected from N, O and S or from a 6-membered aromatic cycle containing 1 or 2 N, and

wherein each aryl or heteroaryl group is optionally substituted with 1 or 2 substituents independently selected from a group consisting of F and C_{1-3}-alkyl, which is optionally substituted with one or more F;

or, if two groups R^2 are attached to adjacent C atoms of the pyridine or pyrimidine group, they may be linked with each other and together form a –O-CH_2-O-, -O-CH_2-CH_2-O- or –O-CH_2-CH_2-CH_2-O- bridge.

4. A compound of formula (I) according to claim 3, wherein

R^2 is independently of each other selected from the group consisting of F, Cl, Br, CN, C_{1-3}-alkyl, C_{3-6}-cycloalkyl, -O-(C_{1-4}-alkyl), -O-CH_2-cyclopropyl, -O-CH_2-heterocyclyl, -O-phenyl, -O-heteroaryl, -S-CH_3, -NH_2, -NH-(C_{1-4}-alkyl), -NH-(C_{3-5}-cycloalkyl), -NH-(CH_2-heterocyclyl), -NH-(C_{1-4}-alkyl)-C(=O)-NH_2, -C(=O)-NH-(C_{1-3}-alkyl), -C(=O)-(C_{1-4}-alkyl), heterocyclyl, heteroaryl and 5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl,

wherein each alkyl or cycloalkyl group is optionally independently substituted with one to three F atoms or with one CN or one OH, and

wherein each heterocyclyl group is selected from a group consisting of oxetanyl, tetrahydrofuranyl, azetidinyl, pyrrolidinyl, morpholinyl and 1,4-diazepan-5-one, and

wherein each heterocyclyl group is optionally substituted with 1 or 2 substituents independently of each other selected from F, OH and CH_3,

wherein each heteroaryl group is selected from a group consisting of furanyl, isoxazolyl, thiazolyl and pyrazolyl, and

wherein each heteroaryl group is optionally substituted with 1 or 2 substituents independently selected from a group consisting of F, CH_3 and CF_3.

5. A compound of formula (I) according to claim 4, wherein

R^2 is independently of each other selected from the group consisting of F, Cl, Br, CN, CH_3, C_{3-5}-cycloalkyl, -O-(C_{1-4}-alkyl), -O-CH_2-heterocyclyl, -O-phenyl, -S-CH_3, -NH_2, -NH-(C_{1-4}-alkyl), -NH-(C_{3-5}-cycloalkyl), -NH-(CH_2-heterocyclyl), -NH-(C_{1-4}-alkyl)-C(=O)-NH_2, heterocyclyl, heteroaryl and 5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl,

wherein each alkyl or cycloalkyl group is optionally independently substituted with one to three F atoms or with one CN or one OH, and

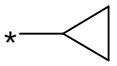
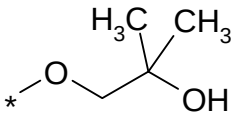
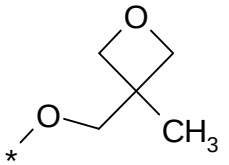
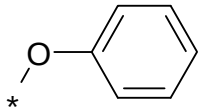
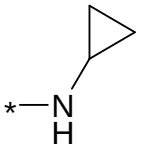
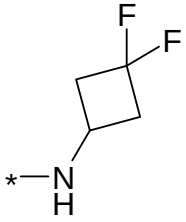
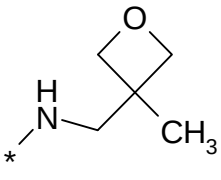
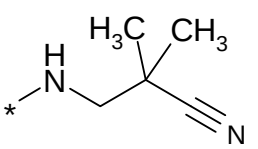
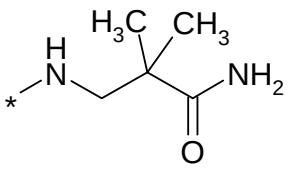
wherein each heterocyclyl group is selected from a group consisting of oxetanyl, azetidinyl, pyrrolidinyl, morpholinyl and 1,4-diazepan-5-one, and

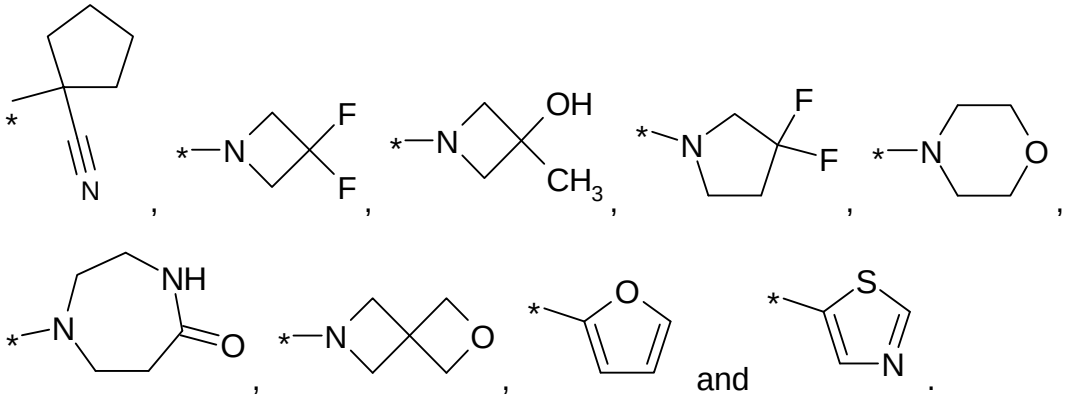
wherein each heterocyclyl group is optionally substituted with 1 or 2 substituents independently selected from F, OH and CH_3, and

wherein each heteroaryl group is selected from a group consisting of furanyl and thiazolyl.

6. A compound of formula (I) according to claim 5, wherein

R^2 is independently selected from the group consisting of:

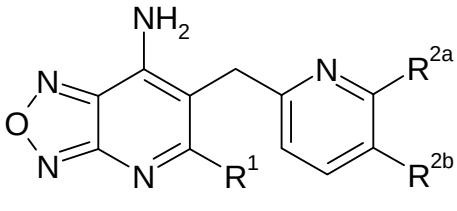
F, Cl, Br, -CN, $-CF_3$, , $-O-CH_3$, $-O-CHF_2$, $-O-CH_2-CH_2-F$, $-O-CH_2-CHF_2$, $-O-CH_2-CF_3$, $-O-CH_2-CH_2-CH_2-F$, $-O-CH_2-CF_2-CH_3$, , , , $-S-CH_3$, $-NH_2$, $-NH-CH_2-CH_2-CH_2-F$, $-NH-CH_2-CH_2-CHF_2$, , , , , ,



7. A compound of formula (I) according to any one of the previous claims, wherein X is CH.

8. A compound of formula (I) according to any one of the previous claims, wherein X is N.

9. A compound according to claim 1 having the formula

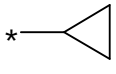
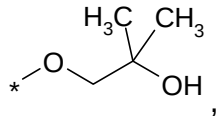
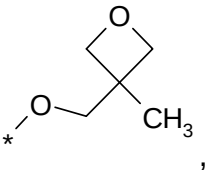


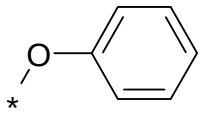
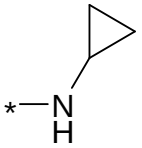
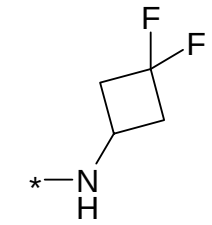
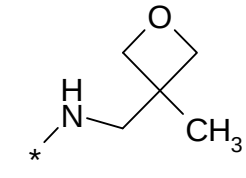
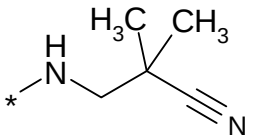
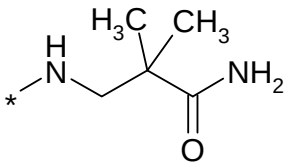
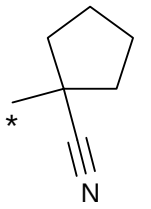
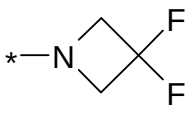
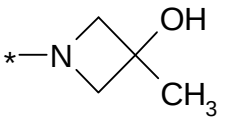
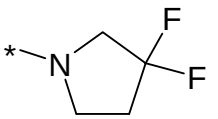
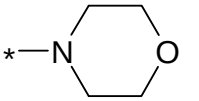
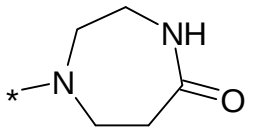
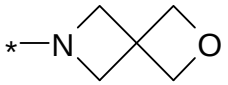
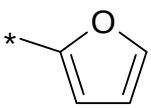
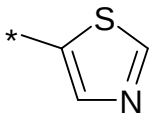
(I.2)

wherein

R^1 is CH_3;

R^{2a} and R^{2b} are each independently selected from the group consisting of:

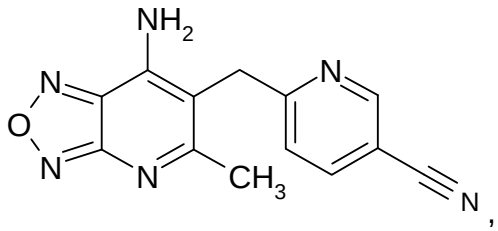
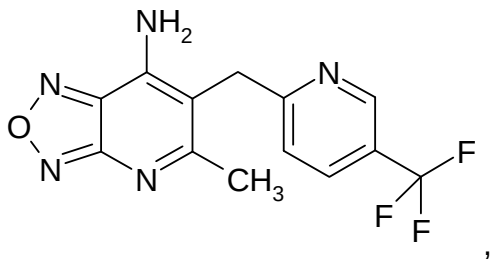
H, F, Cl, Br, -CN, $-CF_3$, , $-O-CH_3$, $-O-CHF_2$, $-O-CH_2-CH_2-F$, $-O-CH_2-CHF_2$, $-O-CH_2-CF_3$, $-O-CH_2-CH_2-CH_2-F$, $-O-CH_2-CF_2-CH_3$, , ,

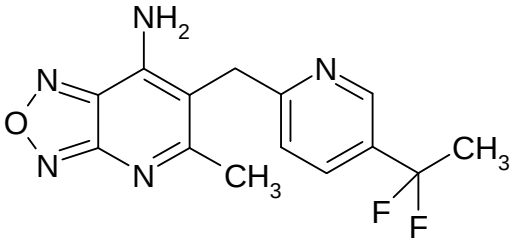
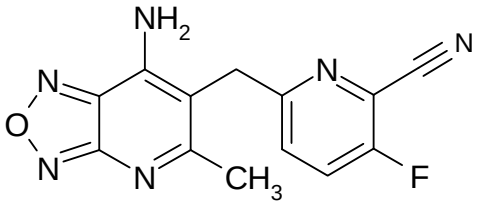
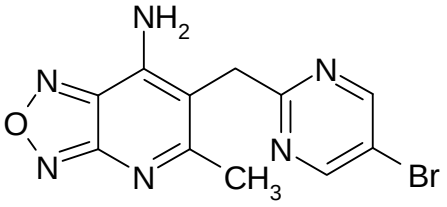
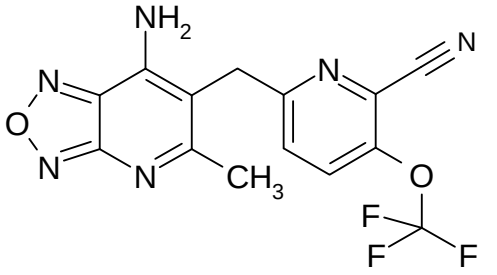
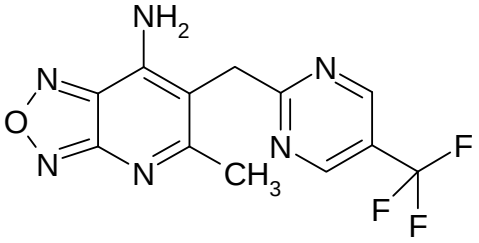
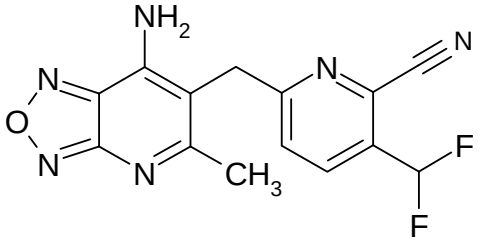
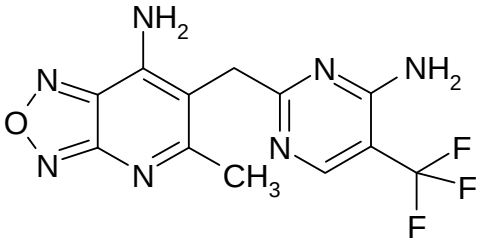
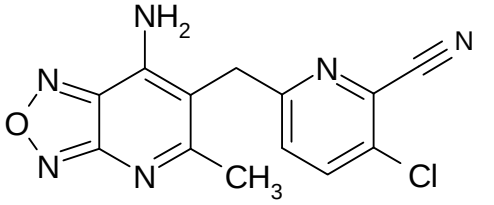
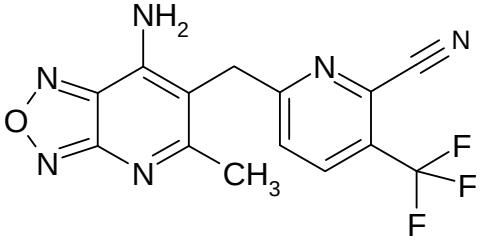
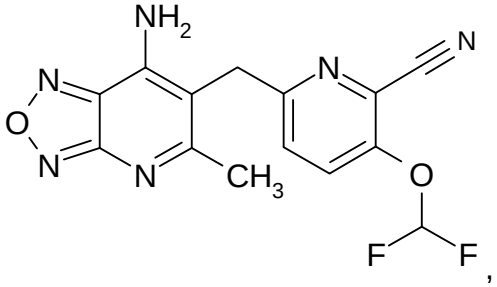
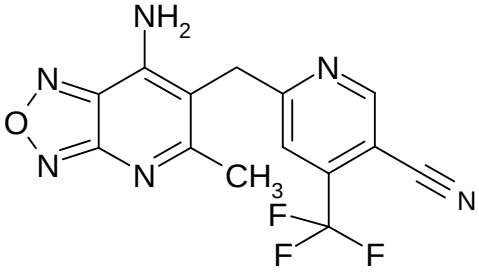
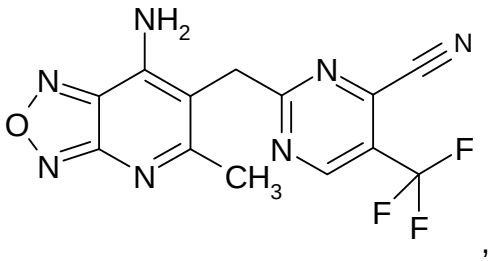

, -S-CH_3, -NH_2, -NH-CH_2-CH_2-CH_2-F, -NH-CH_2-CH_2-CHF_2,


,

,

,

,

,

,

,

,

,

,

,

and

; and

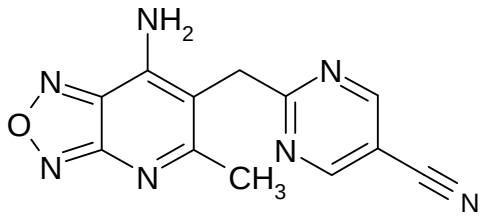
with the proviso that only one of R^{2a} and R^{2b} is H;

or a salt thereof.

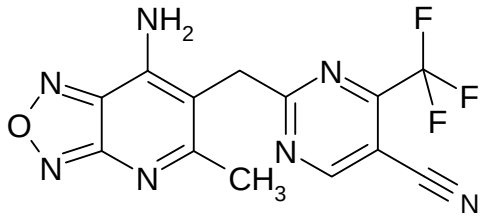
10. A compound according to claim 1 selected from:


,

,

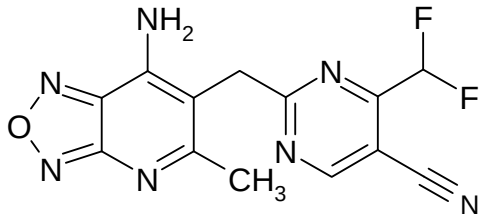

,

,

,

,

,

,

,

,

,

,

,

,



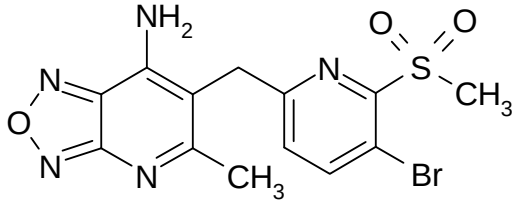
,



,



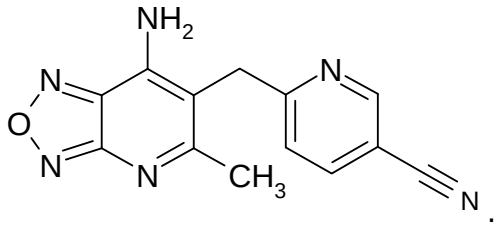
and



,

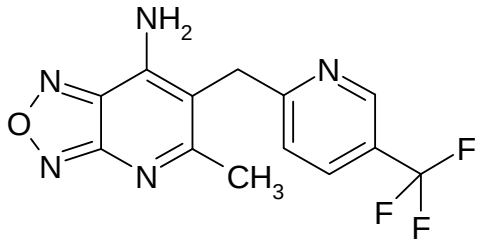
or a salt thereof.

11. The compound according to claim 10, wherein said compound is:



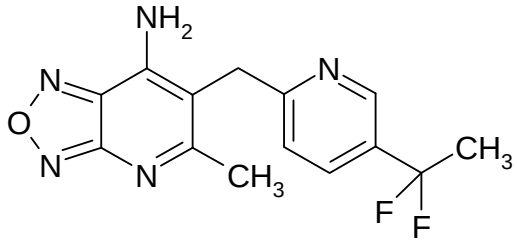
.

12. The compound according to claim 10, wherein said compound is:



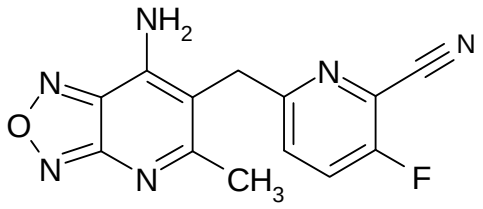
.

13. The compound according to claim 10, wherein said compound is:



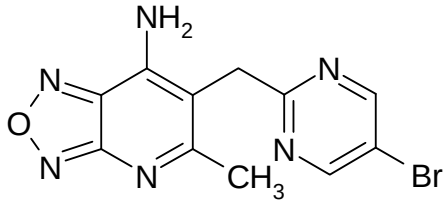
.

14. The compound according to claim 10, wherein said compound is:



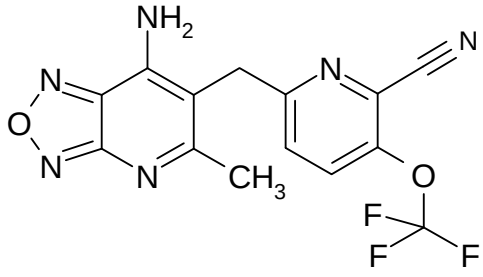
.

15. The compound according to claim 10, wherein said compound is:



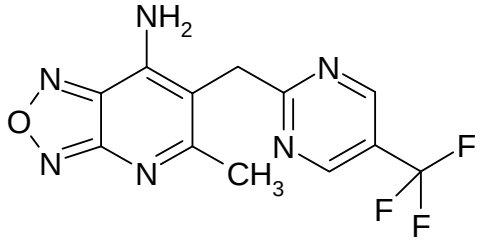
.

16. The compound according to claim 10, wherein said compound is:



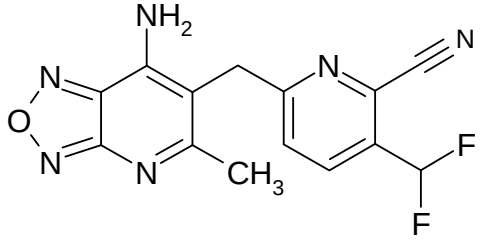
.

17. The compound according to claim 10, wherein said compound is:



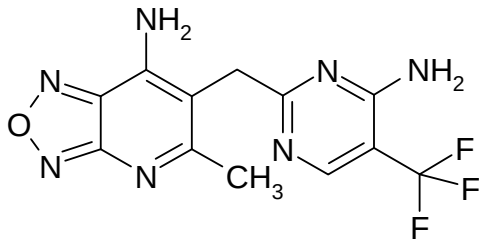
.

18. The compound according to claim 10, wherein said compound is:



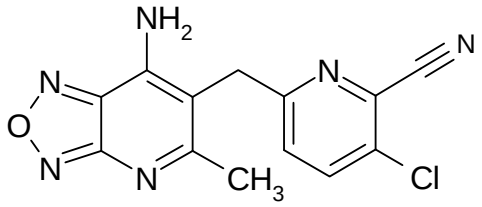
.

19. The compound according to claim 10, wherein said compound is:



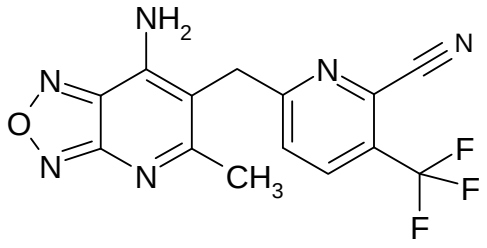
.

20. The compound according to claim 10, wherein said compound is:



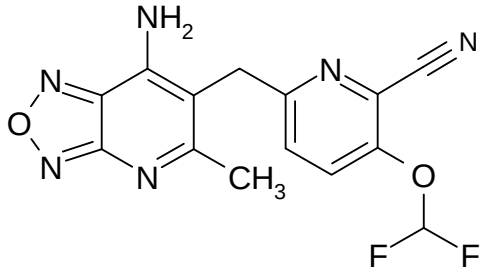
.

21. The compound according to claim 10, wherein said compound is:



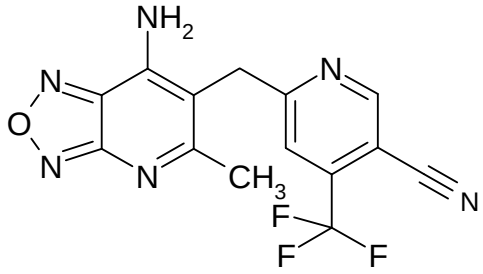
.

22. The compound according to claim 10, wherein said compound is:



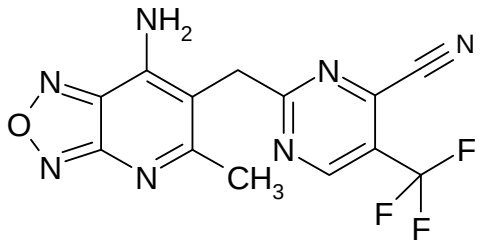
.

23. The compound according to claim 10, wherein said compound is:



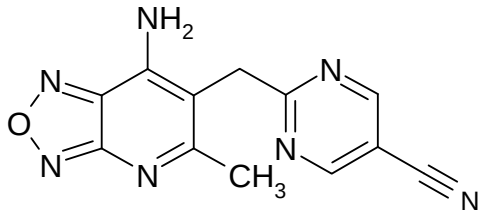
.

24. The compound according to claim 10, wherein said compound is:



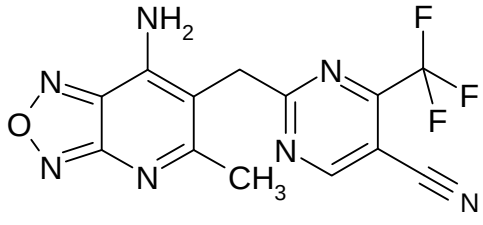
.

25. The compound according to claim 10, wherein said compound is:



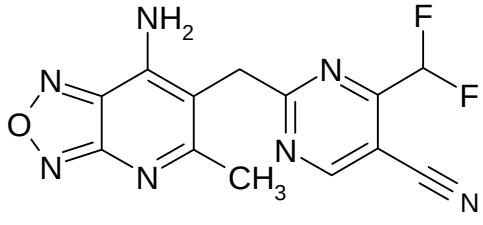
.

26. The compound according to claim 10, wherein said compound is:



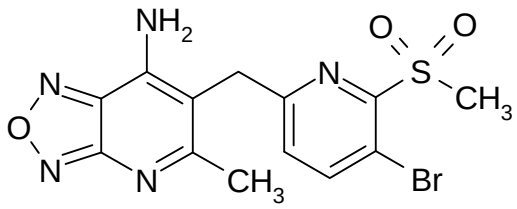
.

27. The compound according to claim 10, wherein said compound is:



.

28. The compound according to claim 10, wherein said compound is:



.

29. A pharmaceutically acceptable salt of a compound according to any one of claims 1 to 28.

30. A compound according to any one of claims 1 to 28 or a pharmaceutically acceptable salt thereof for use as a medicament.

31. A compound according to any one of claims 1 to 28 or a pharmaceutically acceptable salt thereof for use in treating obesity, type 2 diabetes mellitus, insulin resistance and/or obsesity in patients suffering from Prader-Willi-Syndrome.

32. A pharmaceutical composition comprising a compound according to any one of claims 1 to 28 or a pharmaceutically acceptable salt thereof, optionally together with one or more inert carriers and/or diluents.

33. A pharmaceutical composition comprising one or more compounds according to one or more of the claims 1 to 28 or a pharmaceutically acceptable salt thereof and one or more additional therapeutic agents, optionally together with one or more inert carriers and/or diluents.

34. Use of a compound according to any one of claims 1 to 28 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating obesity, including obesity in patients suffering from Prader-Willi-Syndrome, type 2 diabetes mellitus or insulin resistance.