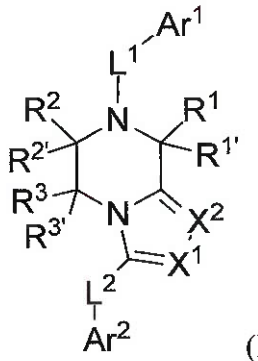
The current invention demonstrates for the first time that the use of an NK3R antagonist prevents adiposity-induced weight gain. It is also evidenced that the use of an NK3R antagonist enables weight loss by reduction of fat mass, without substantial muscle loss.

SUMMARY

This present disclosure thus relates to a NK-3 receptor antagonist for use in the therapeutic treatment of excess body weight and/or excess body fat. Especially, the present disclosure relates to a NK-3 receptor antagonist for use in the therapeutic treatment of excess body fat or in the prevention of body fat gain in patients; provided that the NK-3 receptor antagonist is not 3-Methyl-2-phenyl-N-[(1S)-1-phenylpropyl]-4-quinolinecarboxamide.

In one aspect of the present disclosure, there is provided a use of an NK-3 receptor antagonist in the manufacture of a medicament for the therapeutic treatment of excess body fat or in the prevention of body fat gain in patients; wherein the NK-3 receptor antagonist is a compound of general formula I:



(I)

or a pharmaceutically acceptable salt or solvate thereof, wherein

Ar^1 is a 5- to 6-membered aryl or heteroaryl group, 3- to 6-membered cycloalkyl group a 3- to 6-membered heterocyclyl group or a C3-C6 alkyl group, each of the aryl, heteroaryl, cycloalkyl or heterocyclyl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, aralkyl, heteroaryl, hydroxyl, alkoxy, haloalkoxy, alkoxyalkoxy, alkylamino, carboxy, alkoxycarbonyl,

alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, carbamoyl, alkylcarbamoyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or two substituents form a cycloalkyl or heterocycloalkyl moiety together with the cycloalkyl or heterocycloalkyl group they are attached to, or fused to the aryl, heteroaryl, cycloalkyl or heterocycloalkyl group may be one or more aryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, heterocyclyl, aryl, heteroaryl, aryloxy or heteroaryloxy;

$\mathbf{L^1}$ is C_1-C_2 alkylene optionally being substituted by one or more group(s) selected from halo, methyl or ethyl under the condition that $\mathbf{R^{2'}}$ together with $\mathbf{R^2}$ form an oxo substituent, or $\mathbf{L^1}$ is carbonyl or sulfonyl, or $\mathbf{L^1}$ is –(C=O)-CH_2- where the C=O is linked to the piperazine nitrogen and the CH_2 to $\mathbf{Ar^1}$;

$\mathbf{R^1}$ is H, a C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl;

$\mathbf{R^{1'}}$ is H or a C_1-C_4 alkyl group;

$\mathbf{R^2}$ is H or a C_1-C_4 alkyl group;

$\mathbf{R^{2'}}$ is H or a C_1-C_4 alkyl group, or, when $\mathbf{L^1}$ is C_1-C_2 alkylene optionally being substituted by one or more group(s) selected from halo, methyl or ethyl, $\mathbf{R^{2'}}$ together with $\mathbf{R^2}$ form an oxo substituent;

$\mathbf{R^3}$ is H or a C_1-C_4 alkyl group optionally substituted by one hydroxy;

$\mathbf{R^{3'}}$ is H or a C_1-C_4 alkyl group;

$\mathbf{X^1}$ and $\mathbf{X^2}$ are independently selected from N or C-**Z** wherein **Z** is H or C_1-C_2 alkyl under the condition that $\mathbf{X^1}$ and $\mathbf{X^2}$ cannot be both C-**Z**;

$\mathbf{L^2}$ is a single bond or carbonyl;

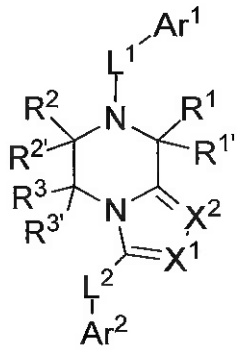
$\mathbf{Ar^2}$ is a 5- to 6-membered aryl or heteroaryl group, each of the aryl, or heteroaryl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, hydroxyl, alkoxy,

haloalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, acylamino, carbamoyl, alkylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, arylsulfonylalkyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or fused to the aryl or heteroaryl group may be one or more cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, alkoxy, haloalkoxy, cycloalkyl, heterocyclyl optionally substituted by alkyl, aryl, heteroaryl, hydroxyl, alkoxyalkyl, hydroxyalkoxy, alkylamino, alkylsulfonylamino, alkoxycarbonylamino, aminoalkoxy, or alkoxycarbonylaminoalkoxy.

In another aspect of the present disclosure, there is provided a use of an NK-3 receptor antagonist in the manufacture of a medicament for the treatment of a leptin-related disease,

wherein the leptin-related disease is selected from metabolic disorders such as diabetes, cardiovascular diseases or metabolic syndrome; lipid regulation disorders such as lipodystrophy, including congenital and acquired lipodystrophy, dyslipidemia, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis or hyperlipidemia; Congenital Leptin Deficiency; hypothalamic amenorrhea, including exercise-induced hypothalamic amenorrhea; Rabson-Mendenhall syndrome; and osteoporosis; and

wherein the NK-3 receptor antagonist is a compound of general formula I:



(I)

or a pharmaceutically acceptable salt or solvate thereof, wherein

$\mathbf{Ar^1}$ is a 5- to 6-membered aryl or heteroaryl group, 3- to 6-membered cycloalkyl group a 3- to 6-membered heterocyclyl group or a C3-C6 alkyl group, each of the aryl, heteroaryl, cycloalkyl or heterocyclyl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, aralkyl, heteroaryl, hydroxyl, alkoxy, haloalkoxy, alkoxyalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, carbamoyl, alkylcarbamoyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or two substituents form a cycloalkyl or heterocycloalkyl moiety together with the cycloalkyl or heterocycloalkyl group they are attached to, or fused to the aryl, heteroaryl, cycloalkyl or heterocycloalkyl group may be one or more aryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, heterocyclyl, aryl, heteroaryl, aryloxy or heteroaryloxy;

$\mathbf{L^1}$ is C_1-C_2 alkylene optionally being substituted by one or more group(s) selected from halo, methyl or ethyl under the condition that $\mathbf{R^{2'}}$ together with $\mathbf{R^2}$ form an oxo substituent, or $\mathbf{L^1}$ is carbonyl or sulfonyl, or $\mathbf{L^1}$ is –(C=O)-CH_2- where the C=O is linked to the piperazine nitrogen and the CH_2 to $\mathbf{Ar^1}$;

$\mathbf{R^1}$ is H, a C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl;

$\mathbf{R^{1'}}$ is H or a C_1-C_4 alkyl group;

$\mathbf{R^2}$ is H or a C_1-C_4 alkyl group;

$\mathbf{R^{2'}}$ is H or a C_1-C_4 alkyl group, or, when $\mathbf{L^1}$ is C_1-C_2 alkylene optionally being substituted by one or more group(s) selected from halo, methyl or ethyl, $\mathbf{R^{2'}}$ together with $\mathbf{R^2}$ form an oxo substituent;

$\mathbf{R^3}$ is H or a C_1-C_4 alkyl group optionally substituted by one hydroxy;

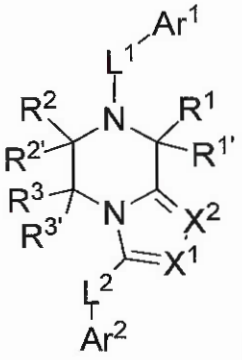
$\mathbf{R^{3'}}$ is H or a C_1-C_4 alkyl group;

$\mathbf{X^1}$ and $\mathbf{X^2}$ are independently selected from N or C-**Z** wherein **Z** is H or C_1-C_2 alkyl under the condition that $\mathbf{X^1}$ and $\mathbf{X^2}$ cannot be both C-**Z**;

$\mathbf{L^2}$ is a single bond or carbonyl;

$\mathbf{Ar^2}$ is a 5- to 6-membered aryl or heteroaryl group, each of the aryl, or heteroaryl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, hydroxyl, alkoxy, haloalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, acylamino, carbamoyl, alkylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, arylsulfonylalkyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or fused to the aryl or heteroaryl group may be one or more cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, alkoxy, haloalkoxy, cycloalkyl, heterocyclyl optionally substituted by alkyl, aryl, heteroaryl, hydroxyl, alkoxyalkyl, hydroxyalkoxy, alkylamino, alkylsulfonylamino, alkoxycarbonylamino, aminoalkoxy, or alkoxycarbonylaminoalkoxy.

In yet another aspect of the present disclosure, there is provided a cosmetic treatment method for improving the bodily appearance by stimulating the loss of body fat in a subject, comprising the administration to said subject of a NK-3 receptor antagonist, and optionally the renewal of said administration until the expected cosmetic effect is obtained, wherein the NK-3 receptor antagonist is a compound of general formula I:



(I)

or a pharmaceutically acceptable salt or solvate thereof, wherein

Ar^1 is a 5- to 6-membered aryl or heteroaryl group, 3- to 6-membered cycloalkyl group a 3- to 6-membered heterocyclyl group or a C3-C6 alkyl group, each of the aryl, heteroaryl, cycloalkyl or heterocyclyl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, aralkyl, heteroaryl, hydroxyl, alkoxy, haloalkoxy, alkoxyalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, carbamoyl, alkylcarbamoyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or two substituents form a cycloalkyl or heterocycloalkyl moiety together with the cycloalkyl or heterocycloalkyl group they are attached to, or fused to the aryl, heteroaryl, cycloalkyl or heterocycloalkyl group may be one or more aryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, heterocyclyl, aryl, heteroaryl, aryloxy or heteroaryloxy;

L^1 is C_1-C_2 alkylene optionally being substituted by one or more group(s) selected from halo, methyl or ethyl under the condition that **R**$^{2'}$ together with **R**^{2} form an oxo substituent, or **L**^{1} is carbonyl or sulfonyl, or **L**^{1} is –(C=O)-CH_2- where the C=O is linked to the piperazine nitrogen and the CH_2 to **Ar**^{1};

$\mathbf{R^1}$ is H, a C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl;

$\mathbf{R^{1'}}$ is H or a C_1-C_4 alkyl group;

$\mathbf{R^2}$ is H or a C_1-C_4 alkyl group;

$\mathbf{R^{2'}}$ is H or a C_1-C_4 alkyl group, or, when $\mathbf{L^1}$ is C_1-C_2 alkylene optionally being substituted by one or more group(s) selected from halo, methyl or ethyl, $\mathbf{R^{2'}}$ together with $\mathbf{R^2}$ form an oxo substituent;

$\mathbf{R^3}$ is H or a C_1-C_4 alkyl group optionally substituted by one hydroxy;

$\mathbf{R^{3'}}$ is H or a C_1-C_4 alkyl group;

$\mathbf{X^1}$ and $\mathbf{X^2}$ are independently selected from N or C-**Z** wherein **Z** is H or C_1-C_2 alkyl under the condition that $\mathbf{X^1}$ and $\mathbf{X^2}$ cannot be both C-**Z**;

$\mathbf{L^2}$ is a single bond or carbonyl;

$\mathbf{Ar^2}$ is a 5- to 6-membered aryl or heteroaryl group, each of the aryl, or heteroaryl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, hydroxyl, alkoxy, haloalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, acylamino, carbamoyl, alkylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, arylsulfonylalkyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or fused to the aryl or heteroaryl group may be one or more cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, alkoxy, haloalkoxy, cycloalkyl, heterocyclyl optionally substituted by alkyl, aryl, heteroaryl, hydroxyl, alkoxyalkyl, hydroxyalkoxy, alkylamino, alkylsulfonylamino, alkoxycarbonylamino, aminoalkoxy, or alkoxycarbonylaminoalkoxy.

According to one embodiment, the NK-3 receptor antagonist is selected from the group consisting of:

(a) 3-Methyl-2-phenyl-N-[(1S)-1-phenylpropyl]-4-quinolinecarboxamide

(b) (R)-N-(1-(3-(1-benzoyl-3-(3,4-dichlorophenyl)piperidin-3-yl)propyl)-4-phenyl piperidin-4-yl)-N-methylacetamide

(c) (R)-[[2-Phenyl-4-quinolinyl)carbonyl]amino]-methyl ester benzeneacetic acid

(d) N1-[1-3-[(3R)-1-Benzoyl-3-(3-(3,4-dichlorophenyl)-3-piperidinyl]propyl]-4-phenyl-piperidinyl]-N,N-dimethylurea hydrochloride

(e) 3-methanesulfonamido-2-phenyl-N-[(1S)-1-phenylpropyl]quinoline-4-carbox amide

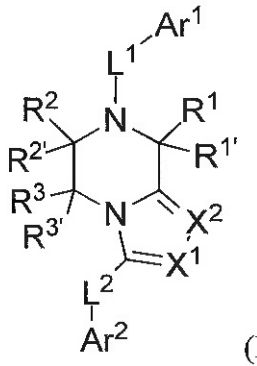
(f) 3-Hydroxy-2-phenyl-N-[(1S)-1-phenylpropyl]-4-quinolinecarboxamide

(g) methyl 2-(3-((4-(tert-butyl)piperazin-1-yl)methyl)-8-fluoro-2-phenylquinoline-4-carbonyl)-1-phenylhydrazinecarboxylate

(h) compounds of general formula A:

CLAIMS

1. Use of an NK-3 receptor antagonist in the manufacture of a medicament for the therapeutic treatment of excess body fat or in the prevention of body fat gain in patients; wherein the NK-3 receptor antagonist is a compound of general formula I:



(I)

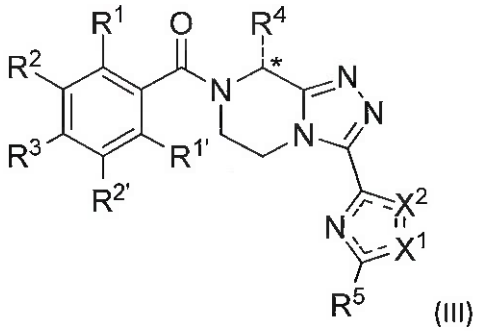
or a pharmaceutically acceptable salt or solvate thereof, wherein

Ar^1 is a 5- to 6-membered aryl or heteroaryl group, 3- to 6-membered cycloalkyl group a 3- to 6-membered heterocyclyl group or a C3-C6 alkyl group, each of the aryl, heteroaryl, cycloalkyl or heterocyclyl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, aralkyl, heteroaryl, hydroxyl, alkoxy, haloalkoxy, alkoxyalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, carbamoyl, alkylcarbamoyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or two substituents form a cycloalkyl or heterocycloalkyl moiety together with the cycloalkyl or heterocycloalkyl group they are attached to, or fused to the aryl, heteroaryl, cycloalkyl or heterocycloalkyl group may be one or more aryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, heterocyclyl, aryl, heteroaryl, aryloxy or heteroaryloxy;

L^1 is C_1-C_2 alkylene optionally being substituted by one or more group(s) selected from halo, methyl or ethyl under the condition that **R$^{2'}$** together with **R^2** form an oxo substituent, or **L^1** is carbonyl or sulfonyl, or **L^1** is –

alkylamino, alkylsulfonylamino, alkoxycarbonylamino, aminoalkoxy, or alkoxycarbonylaminoalkoxy.

2. The use according to claim **1**, wherein the NK-3 receptor antagonist is of formula III



(III)

and pharmaceutically acceptable solvates thereof, wherein:

$\mathbf{R^1}$ is H, F or methyl;

$\mathbf{R^{1'}}$ is H;

$\mathbf{R^2}$ is H, F, Cl or methoxy;

$\mathbf{R^{2'}}$ is H or F;

$\mathbf{R^3}$ is H, F, Cl, methyl, trifluoromethyl, nitrile or $\mathbf{R^3}$ is thiophen-2-yl under the condition that $\mathbf{R^5}$ is not methyl;

$\mathbf{R^4}$ is methyl, ethyl, *n*-propyl, hydroxyethyl, methoxyethyl, trifluoromethyl, difluoromethyl or fluoromethyl;

$\mathbf{R^5}$ is methyl, ethyl, methoxymethyl, trifluoromethyl, difluoromethyl, fluoromethyl, 1-fluoroethyl, 1,1-difluoroethyl or 2,2,2-trifluoroethyl;

$\mathbf{X^1}$ is N and $\mathbf{X^2}$ is S or O; or $\mathbf{X^1}$ is S and $\mathbf{X^2}$ is N;

--- represents a single or a double bound depending on $\mathbf{X^1}$ and $\mathbf{X^2}$;

*---stands for the (*R*)-enantiomer or for the racemate of compound of formula III.

3. The use according to claim **1** or claim 2, under the form of a pharmaceutical composition comprising the NK-3 receptor antagonist and at least one pharmaceutically acceptable vehicle.

4. The use according to anyone of claims **1** to **3**, for the treatment of patients suffering from pathological excess of body fat or for the prevention of body fat gain in patients prone to suffer from pathological excess body fat.

5. The use according to claim **4**, wherein patients suffering from pathological excess of body fat or patients prone to suffer from pathological excess body fat are selected from individuals suffering from hormonal imbalance; individuals suffering from genetic susceptibility to excess body weight; and individuals where an adipose-specific decrease in weight is deemed to be of therapeutic benefit.

6. The use according to claim **5**, wherein the individuals suffering from hormonal imbalance are selected from women subjected to estrogen-lowering therapies; and women experiencing natural, age-related decreases in estrogen.

7. The use according to claim **5**, wherein the individuals suffering from hormonal imbalance are selected from women that undergo changes in ovarian hormone levels.

8. The use according to claim **5**, wherein the individuals suffering from hormonal imbalance are selected from men subjected to androgen-lowering therapies; and men experiencing natural, age-related decreases in circulating testosterone.

9. The use according to claim **5**, wherein the individuals where an adipose-specific decrease in weight is deemed to be of

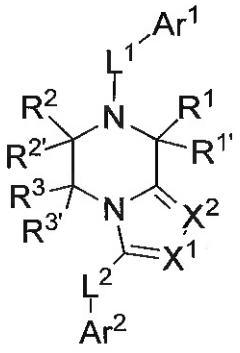
therapeutic benefit are selected from overweight individuals; individuals receiving medical treatments that are accompanied with weight gain comprising but not limited to hormonal treatment as well as steroids, pain or antipsychotic medications; individuals having inappropriate eating behaviors.

10. The use according to claim **4**, wherein patients are leptin-sensitive patients, preferably leptin sensitive women patients.

11. Use of an NK-3 receptor antagonist in the manufacture of a medicament for the treatment of a leptin-related disease,

wherein the leptin-related disease is selected from metabolic disorders such as diabetes, cardiovascular diseases or metabolic syndrome; lipid regulation disorders such as lipodystrophy, including congenital and acquired lipodystrophy, dyslipidemia, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis or hyperlipidemia; Congenital Leptin Deficiency; hypothalamic amenorrhea, including exercise-induced hypothalamic amenorrhea; Rabson-Mendenhall syndrome; and osteoporosis; and

wherein the NK-3 receptor antagonist is a compound of general formula I:



(I)

or a pharmaceutically acceptable salt or solvate thereof, wherein

Ar^1 is a 5- to 6-membered aryl or heteroaryl group, 3- to 6-membered cycloalkyl group a 3- to 6-membered heterocyclyl group or a C3-C6 alkyl group, each of the aryl, heteroaryl, cycloalkyl or heterocyclyl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, aralkyl, heteroaryl, hydroxyl, alkoxy, haloalkoxy, alkoxyalkoxy, alkylamino, carboxy, alkoxycarbonyl,

alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, carbamoyl, alkylcarbamoyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or two substituents form a cycloalkyl or heterocycloalkyl moiety together with the cycloalkyl or heterocycloalkyl group they are attached to, or fused to the aryl, heteroaryl, cycloalkyl or heterocycloalkyl group may be one or more aryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, heterocyclyl, aryl, heteroaryl, aryloxy or heteroaryloxy;

$\mathbf{L^1}$ is C_1-C_2 alkylene optionally being substituted by one or more group(s) selected from halo, methyl or ethyl under the condition that $\mathbf{R^{2'}}$ together with $\mathbf{R^2}$ form an oxo substituent, or $\mathbf{L^1}$ is carbonyl or sulfonyl, or $\mathbf{L^1}$ is –(C=O)-CH_2- where the C=O is linked to the piperazine nitrogen and the CH_2 to $\mathbf{Ar^1}$;

$\mathbf{R^1}$ is H, a C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl;

$\mathbf{R^{1'}}$ is H or a C_1-C_4 alkyl group;

$\mathbf{R^2}$ is H or a C_1-C_4 alkyl group;

$\mathbf{R^{2'}}$ is H or a C_1-C_4 alkyl group, or, when $\mathbf{L^1}$ is C_1-C_2 alkylene optionally being substituted by one or more group(s) selected from halo, methyl or ethyl, $\mathbf{R^{2'}}$ together with $\mathbf{R^2}$ form an oxo substituent;

$\mathbf{R^3}$ is H or a C_1-C_4 alkyl group optionally substituted by one hydroxy;

$\mathbf{R^{3'}}$ is H or a C_1-C_4 alkyl group;

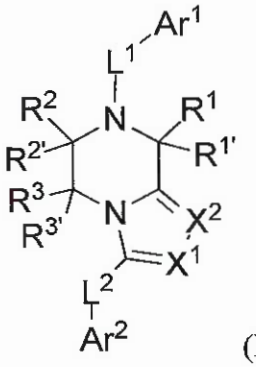
$\mathbf{X^1}$ and $\mathbf{X^2}$ are independently selected from N or C-**Z** wherein **Z** is H or C_1-C_2 alkyl under the condition that $\mathbf{X^1}$ and $\mathbf{X^2}$ cannot be both C-**Z**;

$\mathbf{L^2}$ is a single bond or carbonyl;

$\mathbf{Ar^2}$ is a 5- to 6-membered aryl or heteroaryl group, each of the aryl, or heteroaryl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, hydroxyl, alkoxy, haloalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy,

alkylcarbonylamino, haloalkylcarbonylamino, acylamino, carbamoyl, alkylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, arylsulfonylalkyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or fused to the aryl or heteroaryl group may be one or more cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, alkoxy, haloalkoxy, cycloalkyl, heterocyclyl optionally substituted by alkyl, aryl, heteroaryl, hydroxyl, alkoxyalkyl, hydroxyalkoxy, alkylamino, alkylsulfonylamino, alkoxycarbonylamino, aminoalkoxy, or alkoxycarbonylaminoalkoxy.

12. A cosmetic treatment method for improving the bodily appearance by stimulating the loss of body fat in a subject, comprising the administration to said subject of a NK-3 receptor antagonist, and optionally the renewal of said administration until the expected cosmetic effect is obtained, wherein the NK-3 receptor antagonist is a compound of general formula I:



(I)

or a pharmaceutically acceptable salt or solvate thereof, wherein

Ar^1 is a 5- to 6-membered aryl or heteroaryl group, 3- to 6-membered cycloalkyl group a 3- to 6-membered heterocyclyl group or a C3-C6 alkyl group, each of the aryl, heteroaryl, cycloalkyl or heterocyclyl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, aralkyl, heteroaryl, hydroxyl, alkoxy, haloalkoxy, alkoxyalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, carbamoyl, alkylcarbamoyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl,

haloalkylsulfonyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or two substituents form a cycloalkyl or heterocycloalkyl moiety together with the cycloalkyl or heterocycloalkyl group they are attached to, or fused to the aryl, heteroaryl, cycloalkyl or heterocycloalkyl group may be one or more aryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, cyclopropyl, alkoxy, haloalkoxy, heterocyclyl, aryl, heteroaryl, aryloxy or heteroaryloxy;

$\mathbf{L^1}$ is C_1-C_2 alkylene optionally being substituted by one or more group(s) selected from halo, methyl or ethyl under the condition that $\mathbf{R^{2'}}$ together with $\mathbf{R^2}$ form an oxo substituent, or $\mathbf{L^1}$ is carbonyl or sulfonyl, or $\mathbf{L^1}$ is –(C=O)-CH_2- where the C=O is linked to the piperazine nitrogen and the CH_2 to $\mathbf{Ar^1}$;

$\mathbf{R^1}$ is H, a C_1-C_4 alkyl, aryl or aralkyl group, each of said alkyl, aryl or aralkyl groups being optionally substituted by one or more group(s) selected from halo or hydroxyl;

$\mathbf{R^{1'}}$ is H or a C_1-C_4 alkyl group;

$\mathbf{R^2}$ is H or a C_1-C_4 alkyl group;

$\mathbf{R^{2'}}$ is H or a C_1-C_4 alkyl group, or, when $\mathbf{L^1}$ is C_1-C_2 alkylene optionally being substituted by one or more group(s) selected from halo, methyl or ethyl, $\mathbf{R^{2'}}$ together with $\mathbf{R^2}$ form an oxo substituent;

$\mathbf{R^3}$ is H or a C_1-C_4 alkyl group optionally substituted by one hydroxy;

$\mathbf{R^{3'}}$ is H or a C_1-C_4 alkyl group;

$\mathbf{X^1}$ and $\mathbf{X^2}$ are independently selected from N or C-**Z** wherein **Z** is H or C_1-C_2 alkyl under the condition that $\mathbf{X^1}$ and $\mathbf{X^2}$ cannot be both C-**Z**;

$\mathbf{L^2}$ is a single bond or carbonyl;

$\mathbf{Ar^2}$ is a 5- to 6-membered aryl or heteroaryl group, each of the aryl, or heteroaryl groups being optionally substituted by one or more group(s) selected from halo, cyano, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, hydroxyl, alkoxy,

haloalkoxy, alkylamino, carboxy, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, haloalkylcarbonylamino, acylamino, carbamoyl, alkylcarbamoyl, carbamoylalkyl, carbamoylamino, alkylcarbamoylamino, alkylsulfonyl, haloalkylsulfonyl, arylsulfonylalkyl, sulfamoyl, alkylsulfamoyl, alkylsulfonylamino, haloalkylsulfonylamino, or two substituents form an alkylenedioxy group or a haloalkylenedioxy group, or fused to the aryl or heteroaryl group may be one or more cycloalkyl, aryl, heterocyclyl or heteroaryl moiety, each of said substituents being optionally substituted by one or more further substituent(s) selected from halo, cyano, alkyl, haloalkyl, alkoxy, haloalkoxy, cycloalkyl, heterocyclyl optionally substituted by alkyl, aryl, heteroaryl, hydroxyl, alkoxyalkyl, hydroxyalkoxy, alkylamino, alkylsulfonylamino, alkoxycarbonylamino, aminoalkoxy, or alkoxycarbonylaminoalkoxy.