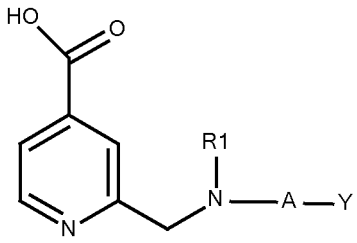
CLAIMS

1. A compound of the general Formula (I)



A is selected from -CHR^{2}C(O)-, C_{1-8} alkylene, C_{2-8} alkenylene, C_{2-8} alkynylene, C_{3-10} cycloalkylene, heterocyclylene, heteroarylene and arylene, which alkylene, alkenylene, alkynylene, cycloalkylene, heterocyclylene, heteroarylene and arylene may optionally be substituted with one or more R^3;

Y is selected from -H, -NR^{6}R^7, -OR^7, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, heteroaryl and aryl, which alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, heteroaryl and aryl may optionally be substituted with one or more R^3 and may form a cyclic structure with R^2;

R^1 is selected from -H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-10} cycloalkyl, which alkyl, alkenyl, alkynyl and cycloalkyl may be optionally substituted with one or more selected from -OH, aryl, C_{1-6} alkoxy, heteroaryl, aryloxy, heteroaryloxy, F, and C_{3-6} cycloalkyl; or more preferably is selected from -H and C_{1-4} alkyl; or with –A-Y forms a nitrogen containing optionally substituted heterocyclic group where the optional substitution may be C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, or C_{3-10} cycloalkyl, which alkyl, alkenyl, alkynyl and cycloalkyl may be optionally substituted with one or more selected from -OH, aryl, C_{1-6} alkoxy, heteroaryl, aryloxy, heteroaryloxy, F, and C_{3-6} cycloalkyl;

R^2 is selected from -H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, andC_{3-10} cycloalkyl, which alkyl, alkenyl, alkynyl and cycloalkyl may be optionally substituted with one or more selected from -OH, aryl, C_{1-6} alkoxy, heteroaryl, aryloxy, heteroaryloxy, F, and C_{3-6} cycloalkyl, and may form a cyclic structure with Y;

each R^3 is independently selected from C_{1-6} alkyl, C_{1-4} fluoroalkyl, C_{1-4} hydroxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, -Z-heterocyclyl, -Z-aryl, -Z- heteroaryl, -Z-NR^{6}R^7, -Z-C(=O)-NR^{6}R^7, -Z-NR^6-C(=O)-R^7, -Z-C(=O)-R^7, -Z-OR^7, halogen, -Z-SR^7, -Z-SOR^7, -Z-SO$_2$R^7, -Z-SO$_2$NR^{6}R^7 and -Z-COOR^7, wherein any heterocyclyl may be substituted with one or more R^4, and wherein any heteroaryl and any aryl may be substituted with one or more R^5;

Z is selected from a single bond, C_{1-4} alkylene, heterocyclylene and C_{3-6} cycloalkylene;

each R^4 is independently selected from C_{1-6} alkyl, C_{1-4} fluoroalkyl, C_{1-4} hydroxyalkyl, C_{1-4} alkoxy, C_{3-10} cycloalkyl, -N(R^1)$_2$, carbamoyl, and -OH;

each R^5 is independently selected from C_{1-6} alkyl, C_{1-4} fluoroalkyl, C_{1-4} hydroxyalkyl, C_{1-4} alkoxy, C_{3-6} cycloalkyl, -CN, -F, -Cl, -Br, carbamoyl and -OH;

each of R^6 and R^7 is independently selected from -H, C_{1-8} alkyl, C_{1-4} fluoroalkyl, C_{1-4} perfluoroalkyl, C_{1-4} hydroxyalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-10} cycloalkyl, -Z-heterocyclyl, -Z-heteroaryl and -Z-aryl, which alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, heteroaryl and aryl may optionally be substituted with one or more independently selected R^8; or, alternatively, R^6 and R^7 may together with the N-atom to which they are attached form an N-heterocyclic ring optionally substituted with one or more independently selected R^8;

each R^8 is independently selected from C_{1-6} alkyl, C_{1-4} fluoroalkyl, C_{1-4} hydroxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, -Z-heterocyclyl, -Z-heteroaryl, -Z-aryl, -Z-$NR^{10}R^{11}$, -Z-C(=O)-$NR^{10}R^{11}$, -Z-OR^9, halogen, -CN, -Z-SR^9, -Z-SOR^9, -Z-SO_2R^9 and -Z-$COOR^9$, which alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclics, heteroaryl and aryl may optionally be substituted with one or more selected from C_{1-4} alkyl, C_{1-4} fluoroalkyl, C_{1-4} hydroxyalkyl, C_{3-6} cycloalkyl, -Z-heterocyclyl, -Z-heteroaryl, -Z-aryl, -Z-$NR^{10}R^{11}$, -Z-C(=O)-$NR^{10}R^{11}$, -Z-OR^9, halogen, -CN, -Z-SR^9, -Z-SOR^9, -Z-SO_2R^9 and -Z-$COOR^9$; wherein any heterocyclyl may be further substituted with one or more R^4 as defined above, and wherein any heteroaryl and any aryl may be further substituted with one or more R^5 as defined above, and

each R^9 is independently selected from -H, C_{1-8} alkyl, C_{1-4} fluoroalkyl, C_{1-4} hydroxyalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-10} cycloalkyl, -Z-heterocyclyl, -Z-aryl, and -Z- heteroaryl, wherein any heterocyclyl may be substituted with one or more R^4 as defined above, and wherein any heteroaryl and any aryl may be substituted with one or more R^5 as defined above;

each of R^{10} and R^{11} is independently selected from -H, C_{1-6} alkyl, C_{1-4} fluoroalkyl, C_{1-4} hydroxyalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, heteroaryl, and aryl, wherein any heterocyclyl may be substituted with one or more R^4 as defined above, and wherein any heteroaryl and any aryl may be substituted with one or more R^5 as defined above, or, alternatively, R^{10} and R^{11} may together with the N-atom to which they are attached form an N-heterocyclic ring optionally substituted with one or more R^4 as defined above;

with the proviso that Y is not H when A is $-CH_2-$;

or an isomer or a mixture of isomers thereof, or a pharmaceutically acceptable salt, solvate or prodrug thereof.

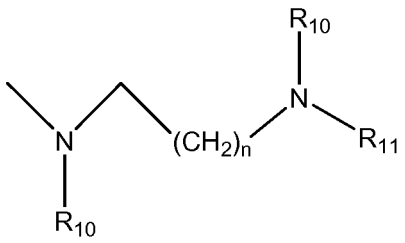
2. A compound according to claim 1, wherein A is selected from -CHR^2C(O)-, or C_{1-8} alkylene, or heterocyclylene.

3. A compound according to claim 1 or claim 2, wherein Y is $-NR^6R^7$.

4. A compound according to claim 3, wherein A is -CHR^{2}C(O)-.

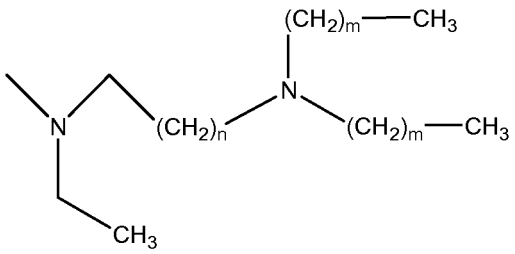
5. A compound according to claim 4, wherein A is –CH_2-C(O)-.

6. A compound according to any one of claims 2 to 5, wherein Y is



wherein n is from 1 to 3 and each of R_{10} and R_{11} independently is as defined in claim 1.

7. A compound according to claim 6, wherein Y is



wherein n is from 1 to 3 and each m independently is from 0 to 2.

8. A compound according to claim 1 or claim 2, wherein Y is selected from heterocyclyl, heteroaryl and aryl, which may be optionally substituted with one or more R^3.

9. A compound according to any one of the preceding claims, which has a molecular weight of 130-1,000 g/mol, such as 180-800 g/mol, e.g. 225-600 g/mol or 250-500 g/mol.

10. A compound according to any one of the preceding claims, wherein the moiety -A-Y includes 1-3 cyclic moieties selected from monocylic cycloalkyl, monocyclic heterocyclyl, monocylic heteroaryl, dicyclic heteroaryl and monocyclic aryl.

11. A pharmaceutical composition comprising at least one compound of Formula (I) as defined in any one of the claims 1-10 and optionally one or more pharmaceutically acceptable excipients, diluents or carriers.

12. A pharmaceutical composition according to claim 7, which comprises one or more further active substances.

13. A compound according to any one of the claims 1-10 for use as a medicament.

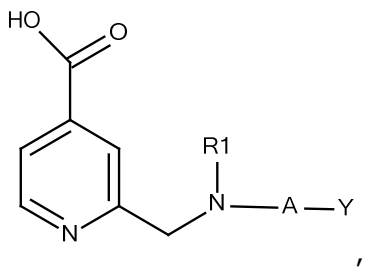
14. A compound according to any one of the claims 1-10 for use in the treatment of a HDME dependent disease.

15. Use of a compound according to any one of the claims 1-10 for the preparation of a pharmaceutical composition for the treatment of a HDME dependent disease.

16. A method of treating a HDME dependent disease in a subject, said method comprises administering to said subject a therapeutically effective amount of at least one compound of Formula (I) as defined in any one of the claims 1-10.

CLAIMS

1. A compound of the general Formula (I)



,

A is $–CH_2C(O)-$;

Y is $-NR^6R^7$;

R^1 is –H;

Z is selected from a single bond, C_{1-4} alkylene, heterocyclylene and C_{3-6} cycloalkylene;

each R^4 is independently selected from C_{1-6} alkyl, C_{1-4} fluoroalkyl, C_{1-4} hydroxyalkyl, C_{1-4} alkoxy, C_{3-10} cycloalkyl, $-N(R^{10})_2$, carbamoyl, and -OH;

each R^5 is independently selected from C_{1-6} alkyl, C_{1-4} fluoroalkyl, C_{1-4} hydroxyalkyl, C_{1-4} alkoxy, C_{3-6} cycloalkyl, -CN, -F, -Cl, -Br, carbamoyl and -OH;

each of R^6 and R^7 is independently selected from -H, C_{1-8} alkyl, C_{1-4} fluoroalkyl, C_{1-4} hydroxyalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-10} cycloalkyl, -Z-heterocyclyl, -Z-heteroaryl and -Z-aryl, wherein alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, heteroaryl and aryl may optionally be substituted with one or more independently selected R^8;

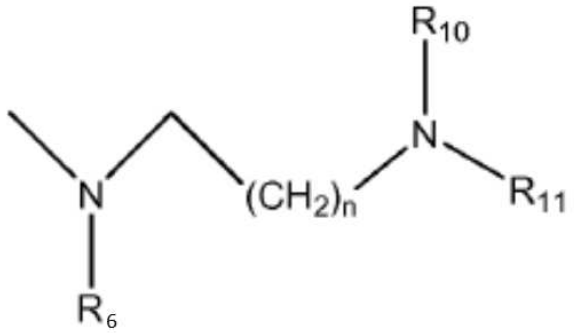
each R^8 is independently selected from C_{1-6} alkyl, C_{1-4} fluoroalkyl, C_{1-4} hydroxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, -Z-heterocyclyl, -Z-heteroaryl, -Z-aryl, -Z-$NR^{10}R^{11}$, -Z-C(=O)-$NR^{10}R^{11}$, -Z-OR^9, halogen, -CN, -Z-SR^9, -Z-SOR^9, -Z-SO_2R^9 and -Z-$COOR^9$, wherein alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, heteroaryl and aryl may optionally be substituted with one or more selected from C_{1-4} alkyl, C_{1-4} fluoroalkyl, C_{1-4} hydroxyalkyl, C_{3-6} cycloalkyl, -Z-heterocyclyl, -Z-heteroaryl, -Z-aryl, -Z-$NR^{10}R^{11}$, -Z-C(=O)-$NR^{10}R^{11}$, -Z-OR^9, halogen, -CN, -Z-SR^9, -Z-SOR^9, -Z-SO_2R^9 and -Z-$COOR^9$; wherein any heterocyclyl may be further substituted with one or more R^4 as defined above, and wherein any heteroaryl and any aryl may be further substituted with one or more R^5 as defined above;

each R^9 is independently selected from -H, C_{1-8} alkyl, C_{1-4} fluoroalkyl, C_{1-4} hydroxyalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-10} cycloalkyl, -Z-heterocyclyl, -Z-aryl, and -Z- heteroaryl, wherein any heterocyclyl may be substituted with one or more R^4 as defined above, and wherein any heteroaryl and any aryl may be substituted with one or more R^5 as defined above;

each of R^{10} and R^{11} is independently selected from -H, C_{1-6} alkyl, C_{1-4} fluoroalkyl, C_{1-4} hydroxyalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, heteroaryl, and aryl, wherein any heterocyclyl may be substituted with one or more R^4 as defined above, and wherein any heteroaryl and any aryl may be substituted with one or more R^5 as defined above;

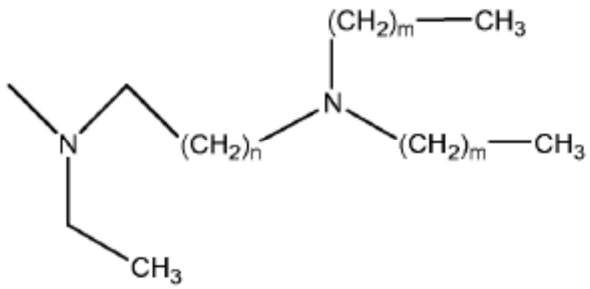
or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein Y is



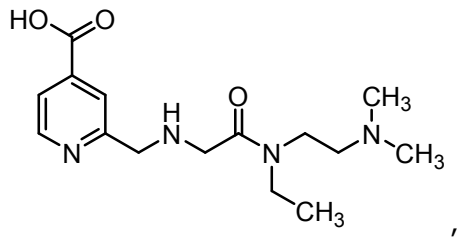
wherein n is from 1 to 3.

3. A compound of claim 1, wherein Y is



wherein n is from 1 to 3 and each m independently is from 0 to 2.

4. The compound of claim 1, wherein the compound is



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or a pharmaceutically acceptable salt thereof.

5. The pharmaceutically acceptable salt of the compound of claim 1, wherein the pharmaceutically acceptable salt is selected from succinic, maleic, acetic, fumaric, citric, tartaric, benzoic, trifluoroacetic, malic, lactic, formic, propionic, glycolic, gluconic, camphorsulfuric, isothionic, mucic, gentisic, isonicotinic, saccharic, glucuronic, furoic, glutamic, ascorbic, anthranilic, salicylic, phenylacetic, mandelic, embonic (pamoic), ethanesulfonic, pantothenic, stearic, sulfinilic, alginic, galacturonic, benzenesulfonic, p-toluenesulfonic, oxalic, methanesulfonic and naphthalenesulfonic acid salt.

6. A pharmaceutical composition comprising a compound of claim 1 and one or more pharmaceutically acceptable excipients, diluents or carriers.

7. The pharmaceutical composition according to claim 6, further comprising one or more active substances.

8. The pharmaceutically acceptable salt of claim 5, wherein the pharmaceutically acceptable salt is the oxalic acid salt.