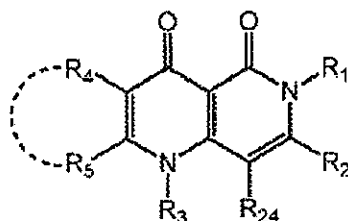


Claims

1. A compound of formula (I') in free form or in pharmaceutically acceptable salt form



(I')

wherein

- a) R_1 is a five- to seven-membered monocyclic saturated or unsaturated non-aromatic ring system, wherein said ring system may contain from 1 to 4 hetero atoms selected from nitrogen, oxygen and sulfur, and wherein said ring system may be substituted once or more than once by R_6 ;

and

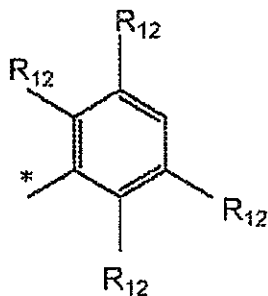
R_2 is C_{2-6} alkyl which may be substituted once or more than once by R_7 ;

or R_2 is $-X_1-R_8$; $-X_1-$ is $-O-$, $-S-$ or $-N(R_9)-$; R_9 is hydrogen or C_{1-4} alkyl; and R_8 is C_{1-6} alkyl which may be substituted once or more than once by R_{10} ;

or R_2 is a three- to seven-membered monocyclic aromatic, saturated or unsaturated non-aromatic ring system, wherein said ring system may contain from 1 to 4 hetero atoms selected from nitrogen, oxygen and sulfur, and wherein said ring system may be substituted once or more than once by R_{11} ;

or

- b) R_1 is



wherein the phenyl ring is attached via the bond marked with an asterisk;
 each R_{12} independently is hydrogen, halogen, hydroxyl, amino, cyano, nitro, C_{1-4} alkyl, C_{1-4} halogenalkyl, C_{1-4} hydroxyalkyl, C_{1-4} alkoxy- C_{1-4} alkyl, amino- C_{1-4} alkyl, C_{1-4} alkylamino- C_{1-4} alkyl, di(C_{1-4} alkyl)-amino- C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} halogenalkoxy, C_{1-4} alkylamino or di(C_{1-4} alkyl)amino; or C_{3-6} cycloalkyl, wherein one carbon atom may be replaced by an oxygen atom, wherein the C_{3-6} cycloalkyl may be attached directly or via a C_{1-2} alkylene, and wherein the C_{3-6} cycloalkyl may be substituted once or more than once by halogen;
 and

R_2 is C_{2-7} alkyl which may be substituted once or more than once by R_{13} ;

or R_2 is $-X_2-R_{14}$; $-X_2$ is $-O-$, $-S-$ or $-N(R_{15})-$; R_{15} is hydrogen or C_{1-4} alkyl; and R_{14} is C_{1-6} alkyl which may be substituted once or more than once by R_{16} ;

or R_2 is a three- to seven-membered monocyclic saturated or unsaturated non-aromatic ring system, wherein said ring system may contain from 1 to 4 hetero atoms selected from nitrogen, oxygen and sulfur, and wherein said ring system may be substituted once or more than once by R_{17} ;

or

- c) R_1 is a ring selected from pyrrolyl, pyrazolyl, thiophenyl or pyridin-2-yl, which ring may be substituted by C_{1-3} alkyl;

and

R_2 is C_{2-7} alkyl which may be substituted once or more than once by R_{13} ;

or R_2 is $-X_2-R_{14}$; $-X_2$ is $-O-$, $-S-$ or $-N(R_{15})-$; R_{15} is hydrogen or C_{1-4} alkyl; and R_{14} is C_{1-6} alkyl which may be substituted once or more than once by R_{16} ;

or R_2 is a three- to seven-membered monocyclic saturated or unsaturated nonaromatic ring system, wherein said ring system may contain from 1 to 4 hetero atoms selected from nitrogen, oxygen and sulfur, and wherein said ring system may be substituted once or more than once by R_{17} ;

R_3 is hydrogen or $-CH_2R_{18}$;

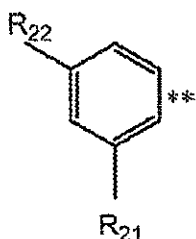
R_{18} is hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{3-6} cycloalkyl, C_{1-3} alkoxy C_{1-3} alkyl, hydroxy C_{1-3} alkyl or amino C_{1-3} alkyl;

R_4 and R_5 are independently selected from hydrogen, C_1 - C_3 alkyl;

or

R_4 and R_5 together with the bond to which they are attached form a ring which is selected from

- 5- to 7-membered monocyclic non-aromatic carbocyclic ring which may be substituted once or more than once by R_{19} ;
- a thiophene ring, which may be substituted once by R_{20} ;



which is fused to the rest of the molecule by the bond marked with two asterisks;

R_{19} and R_{20} are independently selected from halogen, C_1 - C_3 alkyl;

R_{21} is hydrogen, halogen, hydroxyl, amino, cyano, C_{1-4} alkyl, C_{1-4} halogenalkyl, C_{1-4} hydroxyalkyl, C_{1-4} alkoxy- C_{1-4} alkyl, amino- C_{1-4} alkyl, C_{1-4} alkyl-amino- C_{1-4} alkyl, di(C_{1-4} alkyl)amino- C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} halogenalkoxy, C_{1-4} alkylamino or di(C_{1-4} alkyl)amino;

or a three- to seven-membered monocyclic aromatic, saturated or unsaturated non-aromatic ring system, wherein said ring system may contain from 1 to 4 hetero atoms selected from nitrogen, oxygen and sulfur, wherein said ring system may be attached directly or via a C_{1-2} alkylene, and wherein said ring system may be substituted once or more than once by R_{23} ;

or

R_3 and R_{21} taken together are $-\text{CH}_2-\text{CH}_2-$;

R_{22} is hydrogen, halogen, hydroxyl, cyano, C_{1-4} alkyl, C_{1-4} halogenalkyl, C_{1-4} hydroxyalkyl, C_{1-4} alkoxy- C_{1-4} alkyl, amino- C_{1-4} alkyl, C_{1-4} alkyl-amino- C_{1-4} alkyl, di(C_{1-4} alkyl)-amino- C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkinyl, C_{1-4} alkoxy or C_{1-4} halogenalkoxy; or C_{3-4} cycloalkyl, wherein one carbon atom may be replaced by an oxygen atom, wherein the C_{3-4} cycloalkyl may be attached directly or via a C_{1-2} alkylene, and wherein the C_{3-4} cycloalkyl may be substituted once or more than once by halogen;

R_6 , R_{11} , R_{17} and R_{23} each independently is halogen, hydroxyl, amino, cyano, nitro, C_{1-4} alkyl, C_{1-4} halogenalkyl, C_{1-4} hydroxyalkyl, C_{1-4} alkoxy- C_{1-4} alkyl, amino- C_{1-4} alkyl, C_{1-4} alkyl-amino- C_{1-4} alkyl, di(C_{1-4} alkyl)-amino- C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} halogenalkoxy, C_{1-4} alkylamino or di(C_{1-4} alkyl)amino;

or C₃₋₆cycloalkyl, wherein one carbon atom may be replaced by an oxygen atom, wherein the C₃₋₆cycloalkyl may be attached directly or via a C₁₋₂alkylene, and wherein the C₃₋₆cycloalkyl may be substituted once or more than once by halogen;

or two R₆, R₁₁, R₁₇ and R₂₃ at the same ring atom together are oxo;

or two R₆, R₁₁, R₁₇ and R₂₃ at the same ring carbon atom together with said carbon atom form a C₃₋₆cycloalkyl;

R₇, R₁₀, R₁₃ and R₁₆ each independently is halogen, hydroxyl, amino, cyano, nitro, C₁₋₄alkoxy, C₁₋₄halogenalkoxy, C₁₋₄alkylamino or di(C₁₋₄alkyl)amino;

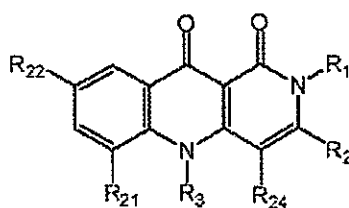
or C₃₋₆cycloalkyl, wherein one carbon atom may be replaced by an oxygen atom, wherein the C₃₋₆cycloalkyl may be attached directly or via a C₁₋₂alkylene, and wherein the C₃₋₆cycloalkyl may be substituted once or more than once by halogen;

or two R₇, R₁₀, R₁₃ or R₁₆ at the same carbon atom together are oxo;

or two R₇, R₁₀, R₁₃ or R₁₆ at the same carbon atom together with said carbon atom form a C₃₋₆cycloalkyl;

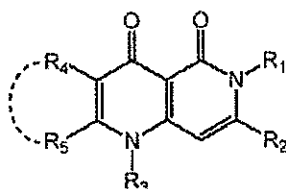
R₂₄ is hydrogen or halogen.

2. A compound of formula (Ia') in free form or in a pharmaceutically acceptable salt form according to claim 1 which is



(Ia').

3. A compound of formula (Ib) in free form or in a pharmaceutically acceptable salt form according to claim 1 which is



(Ib).

4. A compound of formula (I') in free form or in a pharmaceutically acceptable salt form according to any of claims 1 to 3 wherein

R₁ is phenyl;

R₁₂ for each occurrence is hydrogen;

R₂ is C₂₋₇alkyl which may be substituted once or more than once by R₁₃;

or R₂ is a three- to seven-membered monocyclic saturated or unsaturated nonaromatic ring system, wherein said ring system may contain from 1 to 4 hetero atoms selected from nitrogen, oxygen and sulfur, and wherein said ring system may be substituted once or more than once by R₁₇.

5. A compound of formula (I') in free form or in a pharmaceutically acceptable salt form according to any of claims 1 to 3 wherein

R₁ is a ring selected from pyrazolyl, thiophenyl or pyridin-2-yl, which ring may be substituted by C₁₋₃alkyl;

R₂ is C₂₋₇alkyl which may be substituted once or more than once by R₁₃;

or R₂ is a three- to seven-membered monocyclic saturated or unsaturated nonaromatic ring system, wherein said ring system may contain from 1 to 4 hetero atoms selected from nitrogen, oxygen and sulfur, and wherein said ring system may be substituted once or more than once by R₁₇.

6. A compound of formula (I') in free form or in a pharmaceutically acceptable salt form according to any of claims 1 to 3 wherein

R₁ is a five- to seven-membered monocyclic saturated or unsaturated non-aromatic ring system, wherein said ring system may contain from 1 to 4 hetero atoms selected from nitrogen, oxygen and sulfur, and wherein said ring system may be substituted once or more than once by R₆;
and

R₂ is C₂₋₆alkyl which may be substituted once or more than once by R₇;

or R₂ is a three- to seven-membered monocyclic aromatic, saturated or unsaturated non-aromatic ring system, wherein said ring system may contain from 1 to 4 hetero atoms selected from nitrogen, oxygen and sulfur, and wherein said ring system may be substituted once or more than once by R₁₁.

7. A compound according to claim 1 in free form or in pharmaceutically acceptable salt form which is selected from

3-cyclobutyl-2-phenylbenzo[b][1,6]naphthyridine-1, 10(2H, 5H)-dione;
 3-cyclobutyl-5-methyl-2-phenylbenzo[b][1,6]naphthyridine-1, 10(2H,5H)-dione;
 3-isopropyl-2-phenylbenzo[b][1,6]naphthyridine-1, 10(2H, 5H)-dione;
 3-isopropyl-5-methyl-2-phenylbenzo[b][1,6]naphthyridine-1, 10(2H,5H)-dione;
 8-fluoro-3-isopropyl-2-phenylbenzo[b][1,6]naphthyridine-1, 10(2H,5H)-dione;
 8-fluoro-3-isopropyl-5-methyl-2-phenylbenzo[b][1,6]naphthyridine-1, 10(2H, 5H)-dione;
 8-chloro-3-isopropyl-2-phenylbenzo[b][1,6]naphthyridine-1, 10(2H, 5H)-dione;
 8-chloro-3-isopropyl-5-methyl-2-phenylbenzo[b][1,6]naphthyridine-1, 10(2H, 5H)-dione;
 3-isopropyl-8-methyl-2-phenylbenzo[b][1,6]naphthyridine-1, 10(2H,5H)-dione;
 3-isopropyl-5,8-dimethyl-2-phenylbenzo[b][1,6]naphthyridine-1, 10(2H, 5H)-dione;
 9-isopropyl-8-phenyl-1H-indolo[1,7-ab][1,6]naphthyridine-6, 7(2H,8H)-dione;
 7-isopropyl-6-phenylthieno[2,3-b][1,6]naphthyridine-4,5(6H, 9H)-dione;
 7-isopropyl-9-methyl-6-phenylthieno[2,3-b][1,6]naphthyridine-4,5(6H, 9H)-dione;
 7-isopropyl-2-methyl-6-phenylthieno[2,3-b][1,6]naphthyridine-4,5(6H, 9H)-dione;
 7-isopropyl-2,9-dimethyl-6-phenylthieno[2,3-b][1,6]naphthyridine-4,5(6H, 9H)-dione;
 6-isopropyl-7-phenylthieno[3,2-b][1,6]naphthyridine-8,9(4H, 7H)-dione;
 6-isopropyl-4-methyl-7-phenylthieno[3,2-b][1,6]naphthyridine-8,9(4H, 7H)-dione;
 6-isopropyl-2-methyl-7-phenylthieno[3,2-b][1,6]naphthyridine-8,9(4H, 7H)-dione;
 6-isopropyl-2,4-dimethyl-7-phenylthieno[3,2-b][1,6]naphthyridine-8,9(4H, 7H)-dione;
 6-isopropyl-3-methyl-7-phenylthieno[3,2-b][1,6]naphthyridine-8,9(4H, 7H)-dione;
 6-isopropyl-3,4-dimethyl-7-phenylthieno[3,2-b][1,6]naphthyridine-8,9(4H, 7H)-dione;
 3-isopropyl-2-phenyl-6,7,8,9-tetrahydrobenzo[b][1,6]naphthyridine-1,10(2H, 5H)-dione;
 3-isopropyl-2-phenyl-5,6,7,8-tetrahydro-1H-cyclopenta[b][1,6]naphthyridine-1,9(2H)-dione;
 3-cyclobutyl-5-methyl-2-phenyl-5,6,7,8-tetrahydro-1H-cyclopenta[b][1,6]naphthyridine-1,9(2H)-dione;
 7-cyclobutyl-1,2,3-trimethyl-6-phenyl-1,6-naphthyridine-4,5(1H,6H)-dione;
 3-cyclobutyl-2-phenyl-5,6,7,8-tetrahydro-1H-cyclopenta[b][1,6]naphthyridine-1,9(2H)dione;
 7-cyclobutyl-2,3-dimethyl-6-phenyl-1,6-naphthyridine-4,5(1H,6H)-dione;
 3-cyclobutyl-5-methyl-2-phenyl-6,7,8,9-tetrahydrobenzo[b][1,6]naphthyridine-1,10(2H, 5H)-dione;
 7-cyclobutyl-9-methyl-6-phenylthieno[2,3-b][1,6]naphthyridine-4,5(6H, 9H)-dione;
 3-cyclobutyl-2-phenyl-6,7,8,9-tetrahydrobenzo[b][1,6]naphthyridine-1,10(2H,5H)-dione;

7-cyclobutyl-2, 9-dimethyl-6-phenylthieno[2,3-b][1, 6]naphthyridine-4,5(6H, 9H)-dione;
 7-cyclobutyl-6-phenylthieno[2,3-b][1, 6]naphthyridine-4,5(6H, 9H)-dione;
 7-cyclobutyl-2-methyl-6-phenylthieno[2, 3-b][1, 6]naphthyridine-4,5 (6H, 9H)-dione;
 6-cyclobutyl-4-methyl-7 -phenylthieno[3, 2-b][1, 6]naphthyridine-8 , 9(4H, 7H)-dione;
 6-cyclobutyl-7 -phenylthieno[3,2-b][1, 6]naphthyridine-8, 9(4H, 7H)-dione;
 6-cyclobutyl-2,4-dimethyl-7 -phenylthieno[3,2-b][1, 6]naphthyridine-8, 9(4H, 7H)-dione;
 6-cyclobutyl-2-methyl-7 -phenylthieno[3, 2-b][1, 6]naphthyridine-8, 9(4H, 7H)-dione;
 3-cyclobutyl-5, 8-dimethyl-2-phenylbenzo[b][1, 6]naphthyridine-1, 10(2H, 5H)-dione;
 3-cyclobutyl-8-fluoro-5-methyl-2-phenylbenzo[b][1, 6]naphthyridine-1, 10(2H, 5H)-dione;
 8-chloro-3-cyclobutyl-2-phenylbenzo[b][1, 6]naphthyridine-1, 10(2H, 5H)-dione;
 3-cyclobutyl-8-methyl-2-phenylbenzo[b][1, 6]naphthyridine-1, 10(2H,5H)-dione;
 8-chloro-3-cyclobutyl-5-methyl-2-phenylbenzo[b][1, 6]naphthyridine-1, 10(2H,5H)-dione;
 3-isopropyl-6-methoxy-5-methyl-2-phenylbenzo[b][1, 6]naphthyridine-1, 10(2H, 5H)-dione;
 3-cyclobutyl-8-fluoro-2-phenylbenzo[b][1, 6]naphthyridine-1, 10(2H, 5H)-dione;
 9-cyclobutyl-8-phenyl-1H-indolo[1, 7-ab][1, 6]naphthyridine-6, 7 (2H, 8H)-dione;
 3-cyclobutyl-6-methoxy-5-methyl-2-phenylbenzo[b][1, 6]naphthyridine-1, 10(2H, 5H)-dione;
 3-isopropyl-6-methoxy-2-phenylbenzo[b][1, 6]naphthyridine-1, 10(2H, 5H)-dione;
 3-cyclobutyl-6-methoxy-2-phenylbenzo[b][1, 6]naphthyridine-1, 10(2H,5H)-dione;
 3-isopropyl-8-methoxy-5-methyl-2-phenylbenzo[b][1, 6]naphthyridine-1, 10(2H, 5H)-dione;
 3-isopropyl-8-methoxy-2-phenylbenzo[b][1, 6]naphthyridine-1, 10(2H, 5H)-dione;
 8-hydroxy-3-isopropyl-5-methyl-2-phenylbenzo[b][1, 6]naphthyridine-1, 10(2H,5H)dione;
 6-hydroxy-3-isopropyl-5-methyl-2-phenylbenzo[b][1, 6]naphthyridine-1, 10(2H,5H)dione;
 3-cyclobutyl-2-cyclopentylbenzo[b][1, 6]naphthyridine-1, 10(2H,5H)-dione;
 3-cyclobutyl-2-cyclopentyl-5-methylbenzo[b][1, 6]naphthyridine-1, 10(2H, 5H)-dione;
 2-cyclopentyl-3-isopropylbenzo[b][1, 6]naphthyridine-1, 10(2H, 5H)-dione;
 2-cyclopentyl-3-isopropyl-5-methylbenzo[b][1, 6]naphthyridine-1, 10(2H, 5H)-dione;
 3-cyclobutyl-2-(pyridin-2-yl)benzo[b][1, 6]naphthyridine-1, 10(2H, 5H)-dione;
 3-cyclobutyl-5-methyl-2-(pyridin-2-yl)benzo[b][1, 6]naphthyridine-1, 10(2H, 5H)-dione;
 3-cyclobutyl-2-(pyrrolidin-1-yl)benzo[b][1, 6]naphthyridine-1, 10(2H,5H)-dione;
 3-cyclobutyl-5-methyl-2-(pyrrolidin-1-yl)benzo[b][1, 6]naphthyridine-1, 10(2H,5H)-dione;
 4-chloro-3-isopropyl-2-phenylbenzo[b][1, 6]naphthyridine-1, 10(2H, 5H)-dione;
 4-chloro-3-isopropyl-5-methyl-2-phenylbenzo[b][1, 6]naphthyridine-1, 10(2H, 5H)-dione;
 and
 4-bromo-3-isopropyl-5-methyl-2-phenylbenzo[b][1, 6]naphthyridine-1, 10(2H, 5H)-dione.

8. The compound 3-cyclobutyl-5-methyl-2-phenylbenzo[b][1,6]naphthyridine-1, 10(2H,5H)-dione in free form or in pharmaceutically acceptable salt form.
9. The compound 3-isopropyl-2-phenylbenzo[b][1,6]naphthyridine-1, 10(2H, 5H)-dione in free form or in pharmaceutically acceptable salt form.
10. The compound 3-isopropyl-5-methyl-2-phenylbenzo[b][1,6]naphthyridine-1, 10(2H,5H)-dione in free form or in pharmaceutically acceptable salt form.
11. The compound 3-cyclobutyl-2-cyclopentyl-5-methylbenzo[b][1,6]naphthyridine-1, 10(2H, 5H)-dione in free form or in pharmaceutically acceptable salt form.
12. The compound 2-cyclopentyl-3-isopropylbenzo[b][1,6]naphthyridine-1, 10(2H, 5H)-dione in free form or in pharmaceutically acceptable salt form.
13. The compound 2-cyclopentyl-3-isopropyl-5-methylbenzo[b][1,6]naphthyridine-1, 10(2H, 5H)-dione in free form or in pharmaceutically acceptable salt form.
14. A pharmaceutical composition comprising a therapeutically effective amount of a compound in free form or in pharmaceutically acceptable salt form according to any of claims 1 to 13 and one or more pharmaceutically acceptable carriers.
15. A combination comprising a therapeutically effective amount of the compound in free form or in pharmaceutically acceptable salt form according to any of claims 1 to 13 and one or more therapeutically active agents.
16. A compound in free form or in pharmaceutically acceptable salt form according to any of claims 1 to 13 for use as a medicament.
17. A compound according to any of claims 1 to 13 in free form or in pharmaceutically acceptable salt form for use in the treatment of a disease caused by a nonsense mutation except for when the compound in free form or in pharmaceutically acceptable salt form is either 7-isopropyl-3-methyl-6-phenylthieno[2,3-b][1,6]naphthyridine-4,5(6H,9H)-dione or 7-isopropyl-3,9-dimethyl-6-phenylthieno[2,3-b][1,6]naphthyridine-4,5(6H,9H)-dione.

18. Use of a therapeutically effective amount of the compound according to any of claims 1 to 13 in free form or in pharmaceutically acceptable salt form in the manufacture of a medicament for suppressing or treating the effect of nonsense mutations in a subject, wherein the disease is selected from the group consisting of hemophilia A, hemophilia B, cystic fibrosis, mucopolysaccharidosis I, Duchenne Muscle Dystrophy, Becker Muscle Dystrophy, loss of APC caused cancer and loss of p53 caused cancer; except for when the compound in free form or in pharmaceutically acceptable salt form is either 7-isopropyl-3-methyl-6-phenylthieno[2,3-b][1,6]naphthyridine-4,5(6H,9H)-dione or 7-iso-propyl-3, 9-dimethyl-6-phenylthieno[2,3-b][1,6]naphthyridine-4,5(6H,9H)-dione.