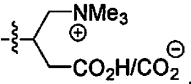
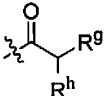


$C(=O)NH_2$, $-CO_2H$ or $-C(=O)OR^j$, and the phenyl is optionally substituted with $-OH$ or $-OR^j$, wherein R^j at each occurrence independently is linear or branched C_1 - C_4 alkyl;

R^m is hydrogen, linear or branched C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, phenyl, -

5 CH_2 -phenyl or , wherein the phenyl is optionally substituted with F, Cl, $-NO_2$, linear or branched C_1 - C_4 alkyl, $-CF_3$ or $-O$ - (linear or branched C_1 - C_4 alkyl); and

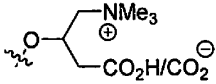
X is cis or trans $-HC=CH-$ or $-(CH_2)_n-$ optionally substituted with $-OH$ or $-OR^j$, wherein R^j is linear or branched C_1 - C_4 alkyl and n is 1, 2, 3, 4, 5 or 6;

10 R^2 at each occurrence independently is hydrogen or , wherein:

R^e is hydrogen, linear or branched C_1 - C_5 alkyl, $-CH_2$ -phenyl, $-CH_2$ -3-indole or $-CH_2$ -5-imidazole, wherein the alkyl is optionally substituted with $-OH$, $-OR^j$, $-SH$, $-SR^j$, $-NH_2$, $-NHR^j$, $-N(R^j)_2$, $-NHC(=O)R^j$, $-NHC(=NH)NH_2$, $-C(=O)NH_2$, $-CO_2H$ or $-C(=O)OR^j$, and the phenyl is optionally substituted with $-OH$ or $-OR^j$, wherein R^j at each occurrence independently is linear or branched C_1 - C_4 alkyl; and

R^h is hydrogen, methyl or $-NH_2$;

or R^e and R^h together with the carbon atom to which they are connected form a C_3 - C_6 cycloalkyl or phenyl ring, wherein the phenyl ring is optionally substituted with F, Cl, $-NO_2$, linear or branched C_1 - C_4 alkyl, $-CF_3$ or $-O$ - (linear or branched C_1 - C_4 alkyl); and

15 R^3 is $-NH_2$, $-NHR^n$, $-N(R^n)_2$, $-OH$, $-OR^o$ or , wherein:

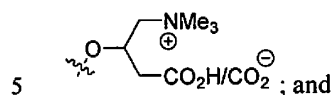
R^n at each occurrence independently is linear or branched C_1 - C_6 alkyl or allyl, wherein the alkyl is optionally substituted with $-OH$ or $-O$ - (linear or branched C_1 - C_3 alkyl), or both occurrences of R^n and the nitrogen atom to which they are connected form a 3- to 6-membered heterocyclic ring; and

25 R^o is linear or branched C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, phenyl or $-CH_2$ -phenyl, wherein the phenyl is optionally substituted with F, Cl, $-NO_2$, linear or branched C_1 - C_4 alkyl, $-CF_3$ or $-O$ - (linear or branched C_1 - C_4 alkyl);

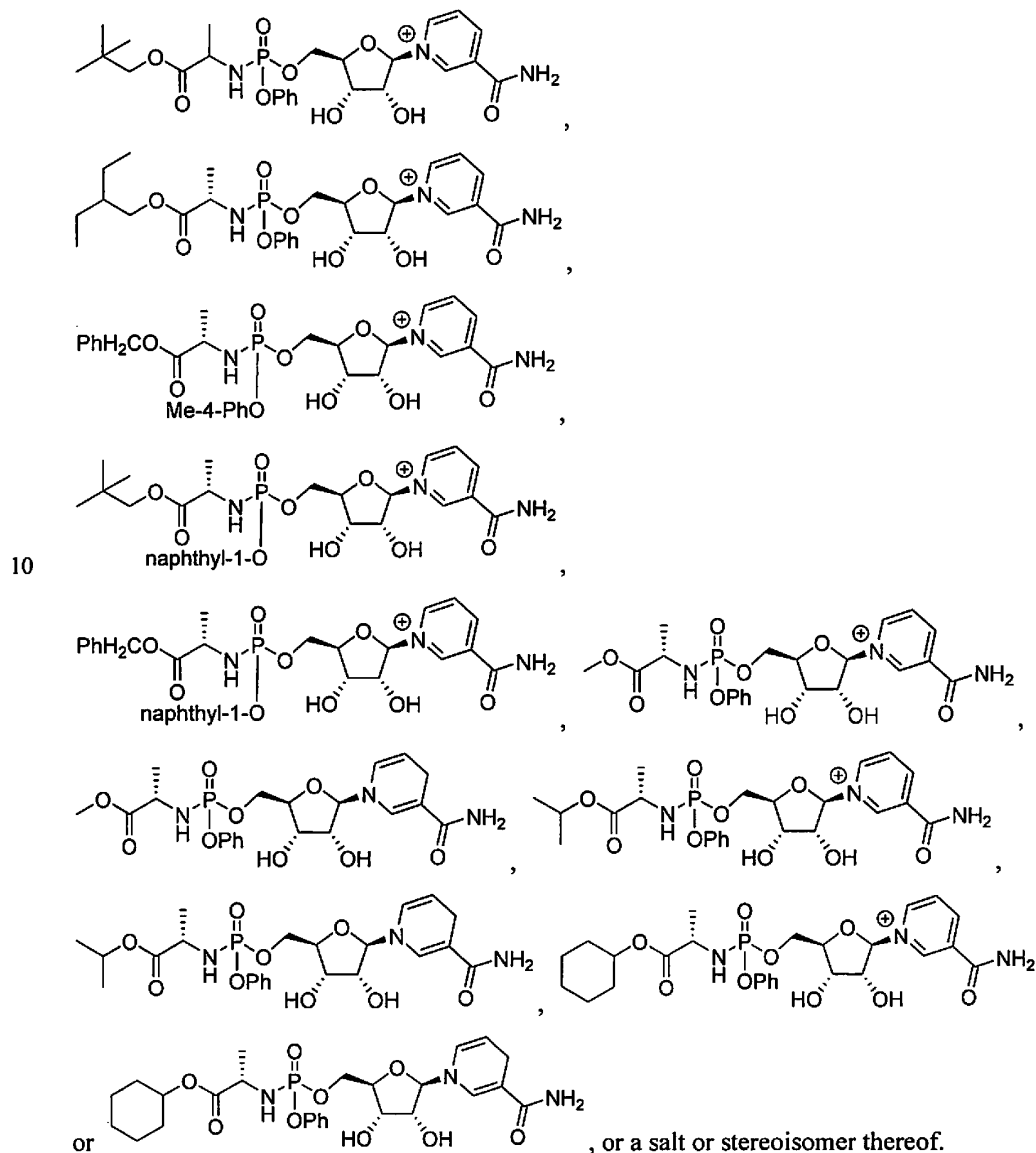
or a pharmaceutically acceptable salt, solvate, hydrate, clathrate, polymorph or stereoisomer thereof;

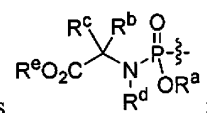
with the proviso that:

1) R^1 and both occurrences of R^2 all are not hydrogen except when R^3 is



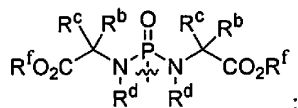
2) the compound of Formula I or II is not:





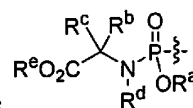
2. The compound of Formula I or II of claim 1, wherein when R¹ is
- 1) both occurrences of R² are not hydrogen; or
 - 2) R³ is not -NH₂; or
 - 3) both occurrences of R² are not hydrogen and R³ is not -NH₂.

- 5 3. The compound of Formula I or II of claim 1, wherein when R¹ is

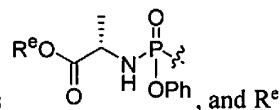


- 1) both occurrences of R² are not hydrogen; or
- 2) R³ is not -NH₂; or
- 3) both occurrences of R² are not hydrogen and R³ is not -NH₂.

- 10 4. The compound of Formula I or II of claim 1, wherein R¹ is hydrogen.

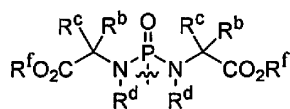


5. The compound of Formula I or II of claim 1 or 2, wherein R¹ is



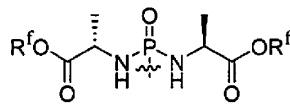
6. The compound of Formula I or II of claim 5, wherein R¹ is linear or branched C₁-C₆ alkyl, such as methyl, ethyl or isopropyl.

7. The compound of Formula I or II of claim 1 or 3, wherein R¹ is

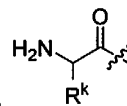


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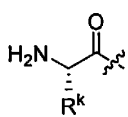
8. The compound of Formula I or II of claim 7, wherein R¹ is

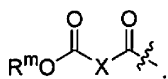


- , and both occurrences of R^f are linear or branched C₁-C₆ alkyl, such as methyl, ethyl or isopropyl.

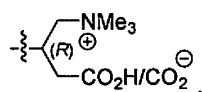


9. The compound of Formula I or II of claim 1, wherein R¹ is

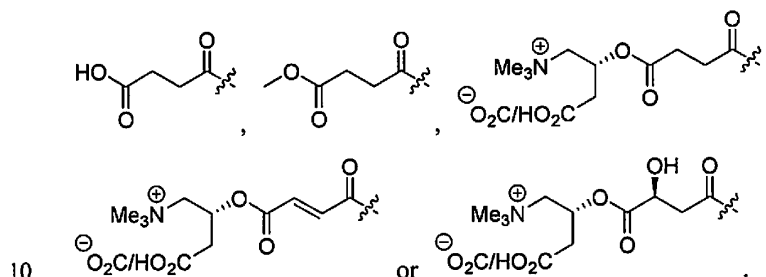
10. The compound of Formula I or II of claim 9, wherein R¹ is , and R^k is linear or branched C₁-C₆ alkyl, such as methyl, ethyl or isopropyl.

11. The compound of Formula I or II of claim 1, wherein R¹ is .

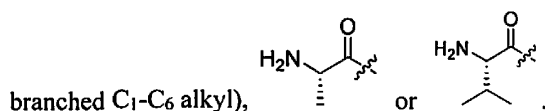
12. The compound of Formula I or II of claim 11, wherein:
 5 X is trans -HC=CH-, -CH₂CH₂- or -CH(OH)CH₂-; and
 R^m is hydrogen, linear or branched C₁-C₆ alkyl (e.g., methyl, ethyl or isopropyl) or



13. The compound of Formula I or II of claim 12, wherein R¹ is

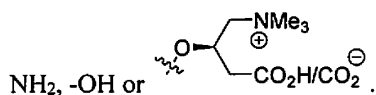


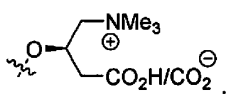
14. The compound of Formula I or II of any one of the preceding claims, wherein R² at each occurrence independently, or at both occurrences, is hydrogen, -C(=O)- (linear or



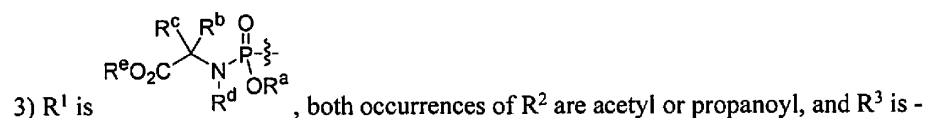
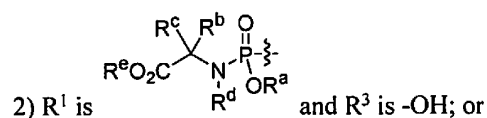
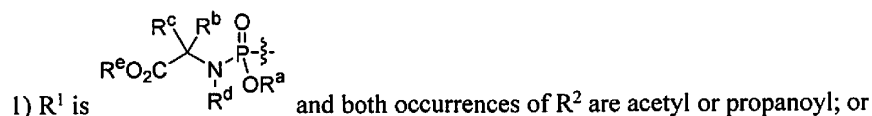
15. The compound of Formula I or II of claim 14, wherein R² at each occurrence independently, or at both occurrences, is hydrogen, acetyl or propanoyl.

16. The compound of Formula I or II of any one of the preceding claims, wherein R³ is -



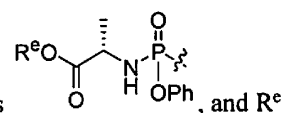
17. The compound of Formula I or II of claim 16, wherein R³ is .

18. The compound of Formula I or II of claim 1 or 2, wherein:

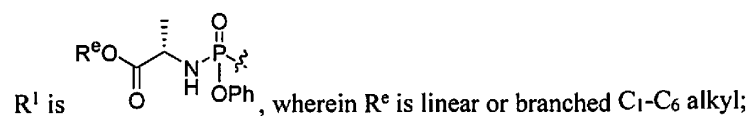


5 OH.

19. The compound of Formula I or II of claim 18, wherein R^1 is linear or branched C_1 - C_6 alkyl, such as methyl, ethyl or isopropyl.



20. The compound of Formula I or II of claim 1 or 2, wherein:

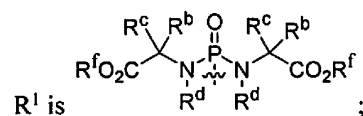


10 R^2 at both occurrences is -C(=O)-(linear or branched C_1 - C_6 alkyl); and R^3 is -NH₂ or -OH.

21. The compound of Formula I or II of claim 20, wherein:

R^e of the R^1 moiety is methyl, ethyl or isopropyl; and R^2 at both occurrences is acetyl or propanoyl.

15 22. The compound of Formula I or II of claim 1 or 3, wherein:



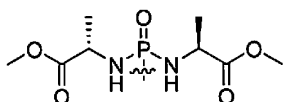
R^2 at each occurrence independently, or at both occurrences, is hydrogen, acetyl or propanoyl; and

R^3 is -NH₂ or -OH.

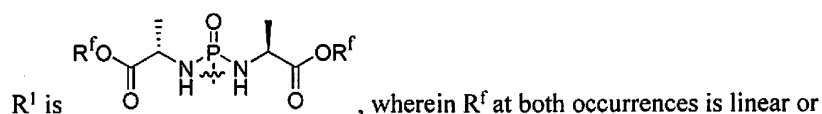
23. The compound of Formula I or II of claim 22, wherein for the R^1 moiety:
 R^b and R^c at each occurrence independently are hydrogen or linear or branched C_1 - C_5 alkyl, or each pair of R^b and R^c is hydrogen and linear or branched C_1 - C_5 alkyl;
 R^d at both occurrences is hydrogen; and

5 R^f at both occurrences is linear or branched C_1 - C_6 alkyl.

24. The compound of Formula I or II of claim 23, wherein R^1 is



25. The compound of Formula I or II of claim 1 or 3, wherein:



10 branched C_1 - C_6 alkyl;

- R^2 at each occurrence independently, or at both occurrences, is hydrogen or $-C(=O)-$ (linear or branched C_1 - C_6 alkyl); and

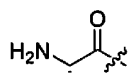
R^3 is $-NH_2$ or $-OH$.

26. The compound of Formula I or II of claim 25, wherein:

15 R^f of the R^1 moiety at both occurrences is methyl, ethyl or isopropyl; and

- R^2 at each occurrence independently, or at both occurrences, is hydrogen, acetyl or propanoyl.

27. The compound of Formula I or II of claim 1, wherein:



R^1 is $H_2N-CH_2-CH_2-C(=O)-R^k$, wherein R^k is linear or branched C_1 - C_6 alkyl;

20 R^2 at each occurrence independently, or at both occurrences, is hydrogen or $-C(=O)-$ (linear or branched C_1 - C_6 alkyl); and

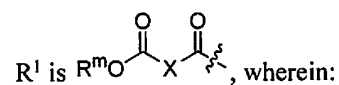
R^3 is $-NH_2$ or $-OH$.

28. The compound of Formula I or II of claim 27, wherein:

R^k of the R^1 moiety is methyl, ethyl or isopropyl; and

25 R^2 at each occurrence independently, or at both occurrences, is hydrogen, acetyl or propanoyl.

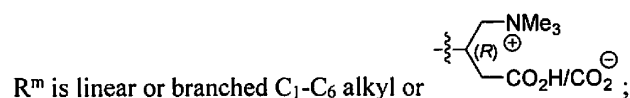
29. The compound of Formula I or II of claim 1, wherein:



X is cis or trans -HC=CH- or -(CH₂)_n- optionally substituted with -OH or -OR^j, wherein R^j is linear or branched C₁-C₄ alkyl and n is 1, 2, 3, 4, 5 or 6;

5

and

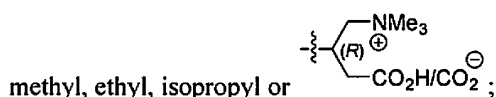


R² at each occurrence independently, or at both occurrences, is hydrogen or -C(=O)- (linear or branched C₁-C₆ alkyl); and

R³ is -NH₂ or -OH.

10 30. The compound of Formula I or II of claim 29, wherein:

for the R¹ moiety, X is trans -HC=CH-, -CH₂CH₂- or -CH(OH)CH₂-, and R^m is

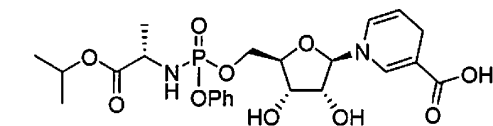
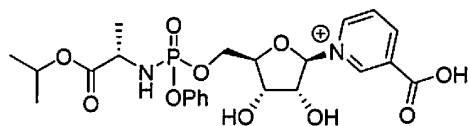
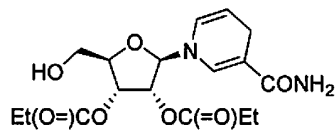
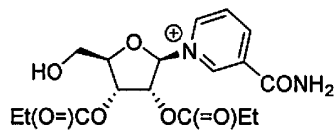
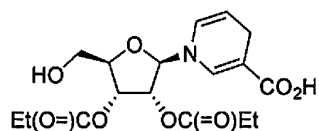
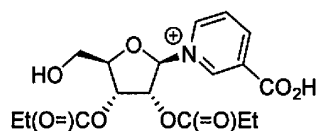
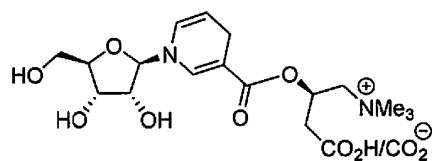
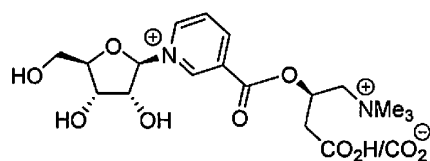


R² at each occurrence independently, or at both occurrences, is hydrogen, acetyl or propanoyl; and

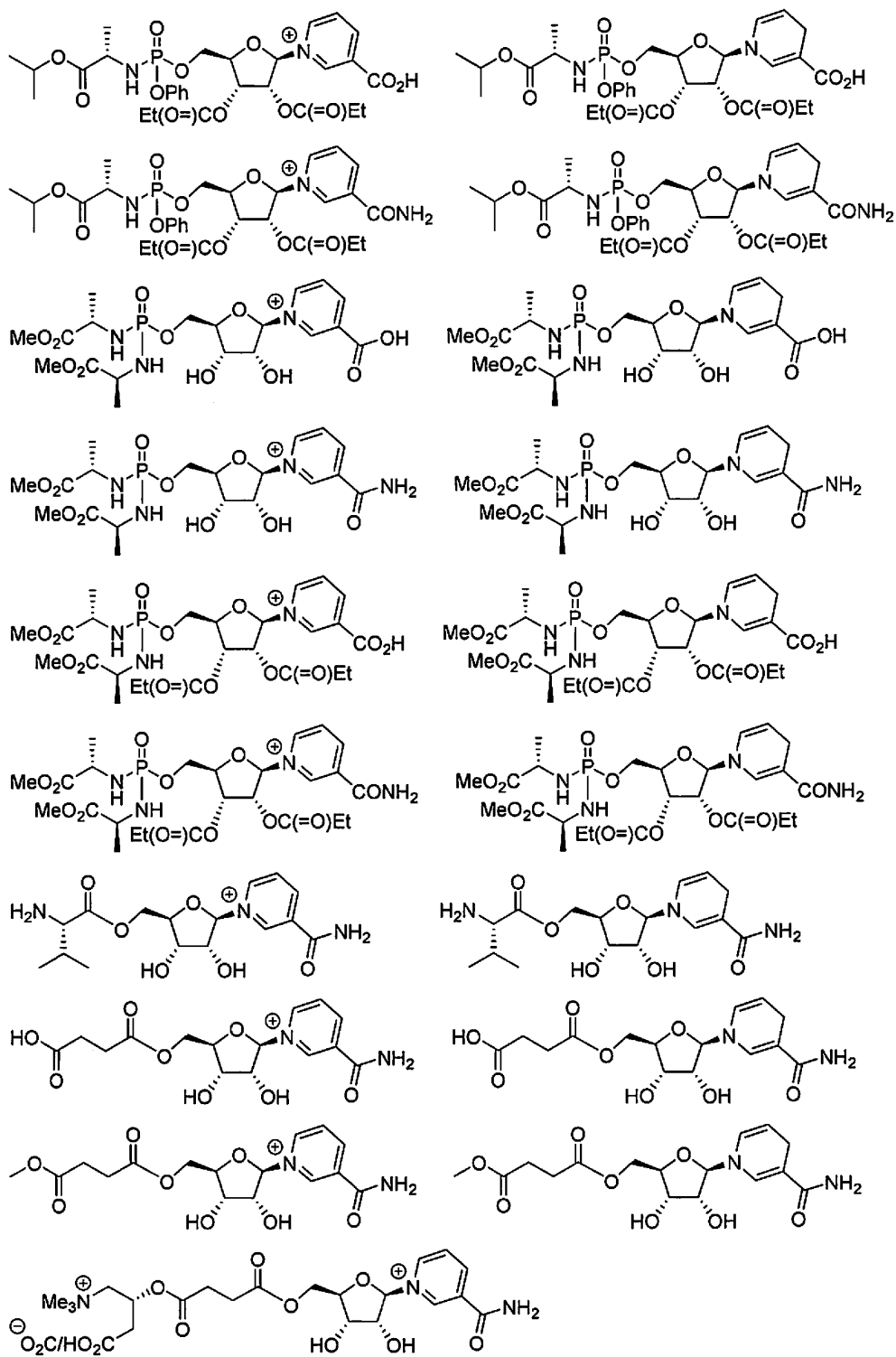
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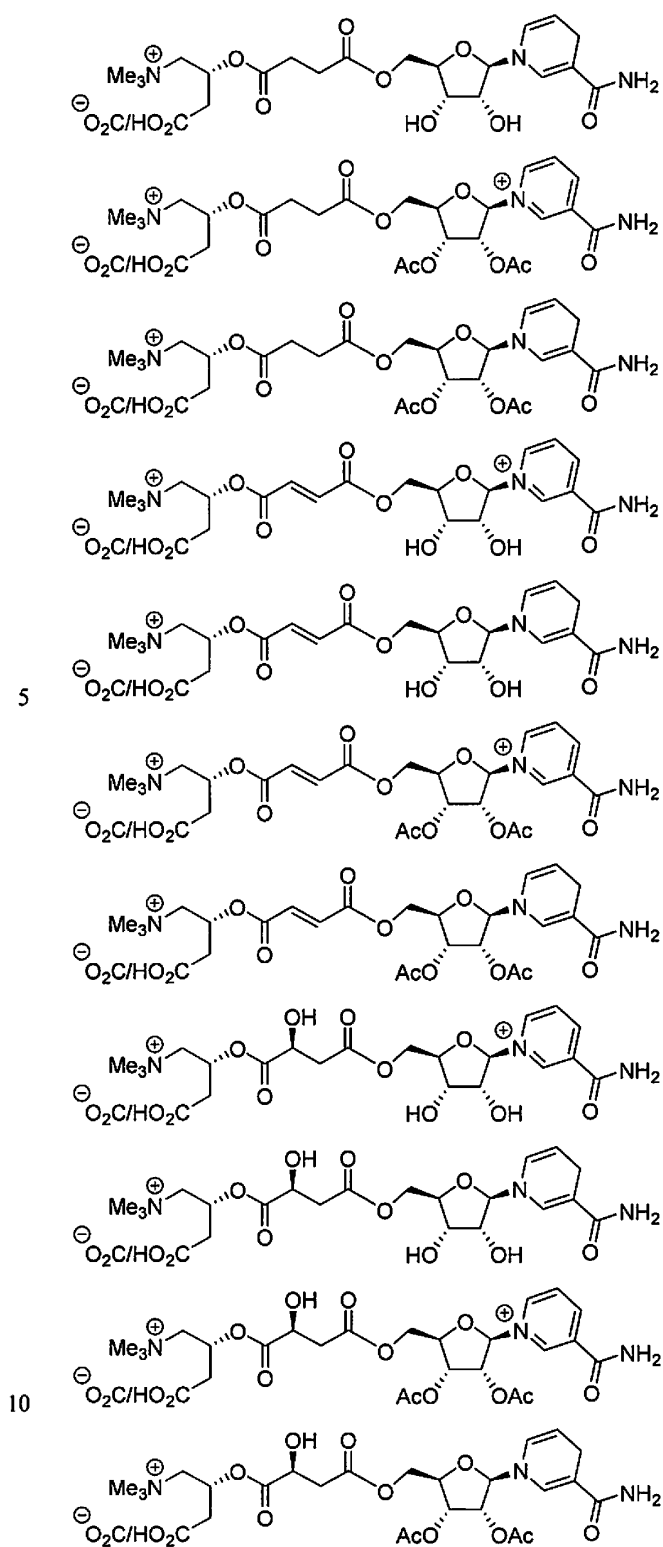
R³ is -NH₂.

31. The compound of Formula I or II of claim 1, which is selected from:



20





and pharmaceutically acceptable salts, solvates, hydrates, clathrates, polymorphs and stereoisomers thereof.

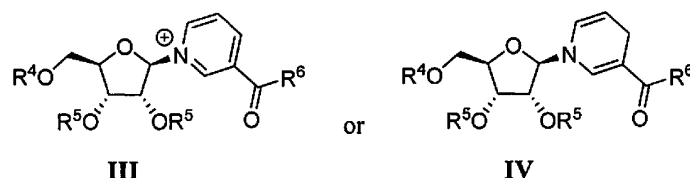
32. The compound of Formula I or II of any one of the preceding claims, which is a trifluoromethanesulfonate (triflate or ^{-}OTf) salt, an acetate (^{-}OAc) salt, a trifluoroacetate ($^{-}\text{OTFA}$) salt or a chloride (Cl^{-}) salt.

33. The compound of Formula I or II of any one of the preceding claims, which has the beta-D-ribose configuration.

34. The compound of Formula I or II of any one of the preceding claims, which is stereoisomerically pure (e.g., at least about 90%, 95%, 98% or 99% of the compound is the indicated stereoisomer).

35. The compound of Formula I or II of any one of claims 1 to 32, which is a racemic mixture.

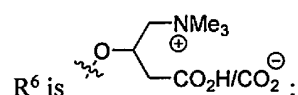
36. A compound of Formula III or IV:



wherein:

R^4 is hydrogen or $-\text{C}(=\text{O})\text{R}^7$, wherein R^7 is linear or branched C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, or phenyl optionally substituted with F, Cl, $-\text{NO}_2$, linear or branched C_1 - C_4 alkyl, $-\text{CF}_3$ or $-\text{O}$ -(linear or branched C_1 - C_4 alkyl);

R^5 at each occurrence independently is hydrogen or $-\text{C}(=\text{O})\text{R}^8$, wherein R^8 has the same definition as R^7 ; and



or a pharmaceutically acceptable salt, solvate, hydrate, clathrate, polymorph or stereoisomer thereof.

37. The compound of Formula III or IV of claim 36, wherein:

R^4 is hydrogen or $-\text{C}(=\text{O})\text{R}^7$, wherein R^7 is linear or branched C_1 - C_6 alkyl; and

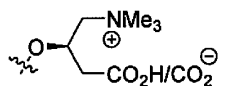
R^5 at each occurrence independently, or at both occurrences, is hydrogen or $-\text{C}(=\text{O})\text{R}^8$, wherein R^8 is linear or branched C_1 - C_6 alkyl.

38. The compound of Formula III or IV of claim 37, wherein:

R^4 is hydrogen, acetyl or propanoyl; and

R^5 at each occurrence independently, or at both occurrences, is hydrogen, acetyl or propanoyl.

39. The compound of Formula III or IV of any one of claims 36 to 38, wherein R^6 is



40. A pharmaceutical or cosmetic composition comprising one or more compounds of any one of the preceding claims or a pharmaceutically acceptable salt, solvate, hydrate, clathrate, polymorph or stereoisomer thereof, and one or more pharmaceutically acceptable carriers or excipients.

41. The pharmaceutical or cosmetic composition of claim 40, which comprises a compound of Formula I and a compound of Formula II, or a compound of Formula III and a compound of Formula IV.

42. One or more compounds of any one of claims 1 to 39 or a pharmaceutically acceptable salt, solvate, hydrate, clathrate, polymorph or stereoisomer thereof for use as a medicament.

43. The one or more compounds for use according to claim 42, wherein the medicament is for use in treating a mitochondrial disease, a mitochondria-related disease or condition, or a disease or condition characterized by acute NAD^+ depletion due to DNA damage.

44. The one or more compounds for use according to claim 43, wherein the mitochondrial disease is selected from mitochondrial myopathies; Kearns-Sayre syndrome (KSS); Pearson syndrome; Leigh syndrome; neuropathy, ataxia, retinitis pigmentosa and ptosis (NARP); mitochondrial DNA depletion syndrome (Alper's disease); mitochondrial neurogastrointestinal encephalopathy (MNGIE) syndrome; mitochondrial encephalopathy, lactic acidosis and stroke-like episodes (MELAS) syndrome; myoclonic epilepsy with ragged red fibers (MERRF); chronic progressive external ophthalmoplegia (CPEO); Leber's hereditary optic neuropathy (LHON); and diabetes mellitus and deafness.

45. The one or more compounds for use according to claim 43, wherein the mitochondria-related disease or condition is a neurodegenerative disorder, a neuronal activation disorder, a muscle disorder, a beta oxidation disorder, a metabolic disorder, an inflammatory disorder, a

vascular disorder, a kidney disorder, a liver disorder, a tumor or cancer, or male or female infertility.

46. The one or more compounds for use according to claim 43 or 45, wherein the mitochondria-related disease or condition is selected from lipodystrophy, metabolic syndrome, obesity, types 1 and 2 diabetes, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), alcoholic liver disease, autoimmune hepatitis, cholestatic liver disease, hemochromatosis and alpha-1 antitrypsin deficiency.
47. The one or more compounds for use according to claim 43, wherein the disease or condition characterized by acute NAD⁺ depletion due to DNA damage is selected from exposure to radiation (e.g., UV and ionizing radiation such as X-ray), radiation or chemotherapy-induced disorders (e.g., dermatitis, myositis, myocarditis, colitis, prostatitis, hepatitis, pneumonitis, neuropathies and bone marrow failure), burn injuries (including first-degree burns, second-degree burns and third-degree burns), chemical exposure with manifestation of exfoliative dermatitis, exposure to chemical warfare agents, Stevens-Johnson syndrome, acute respiratory distress syndrome, inhalational lung injury due to smoke or chemical toxins, trauma-related crush injuries (including those with bone fractures), peripheral nerve injuries, spinal cord injuries, and contusion to internal organs (such as the heart, lung, liver, and kidneys).
48. The one or more compounds for use according to any one of claims 42 to 47, wherein the one or more compounds comprise a compound of Formula I and a compound of Formula II, or a compound of Formula III and a compound of Formula IV.
49. The one or more compounds for use according to any one of claims 42 to 48, wherein the one or more compounds is/are administered orally, parenterally (e.g., intravenously, intradermally, subcutaneously, intramuscularly or intrathecally), or topically (e.g., transdermally, transmucosally, intranasally, pulmonarily [e.g., by oral inhalation], sublingually or rectally [e.g., by suppository]).
50. The one or more compounds for use according to any one of claims 42 to 48, wherein the one or more compounds is/are used in culture medium for preparation of *ex vivo* therapy.
51. The one or more compounds for use according to claim 50, wherein the *ex vivo* therapy is a chimeric antigen receptor T-cell (CAR-T) therapy, a stem cell therapy, *in vitro* fertilization, organ transplantation or for attachment to a carrier molecule such as a dendrimer or an antibody conjugate.

52. The one or more compounds for use according to any one of claims 42 to 51, which is in combination with the use of at least one other therapeutic agent selected from sirtuin-activating agents, PARP inhibitors, NMDA receptor antagonists, acetylcholinesterase inhibitors, antidiabetics, antihyperlipidemic agents, antiplatelet agents, anticoagulants, antihypertensive agents, antioxidants, anti-inflammatory agents, analgesics, anesthetics, anticancer agents, antivirals, antibiotics, antifungals, natural compounds, vitamins, vaccines, and combinations thereof.
53. The one or more compounds for use according to claim 52, wherein the at least one other therapeutic agent comprises a sirtuin-activating agent, a PARP inhibitor, an antioxidant, a natural compound or a vitamin, or any combination thereof.
54. The one or more compounds for use according to claim 52 or 53, wherein the sirtuin-activating agent is selected from polyphenols (e.g., butein, fisetin, isoliquiritigenin, piceatannol, quercetin and resveratrol), methylene blue, SRT-1720 and lamin A.
55. The one or more compounds for use according to claim 52 or 53, wherein the PARP inhibitor is selected from niraparib, olaparib, rucaparib, talazoparib, veliparib, 4-amino-1,8-naphthalimide, BGB290, CEP9722 and E7016.
56. The one or more compounds for use according to claim 55, wherein the PARP inhibitor (e.g., olaparib) is administered in a dose significantly lower than its recommended dose as an anticancer agent.
57. The one or more compounds for use according to claim 52 or 53, wherein the antioxidant or/and the natural compound is/are selected from resveratrol, pterostilbene, ellagic acid, urolithin A, quercetin, coenzyme Q, glutathione, *N*-acetyl-L-cysteine, α -lipoic acid, melatonin, creatine, *S*-adenosyl methionine, pyruvic acid/pyruvate, and combinations thereof.
58. The one or more compounds for use according to claim 52 or 53, wherein the vitamin is a member of the vitamin B family selected from thiamine (B₁), riboflavin (B₂), niacin (B₃), pantothenic acid (B₅), pyridoxine (B₆), biotin (B₇), folic acid (B₉), cobalamin (B₁₂), and combinations thereof.
59. The one or more compounds for use according to claim 52, wherein the anti-inflammatory agent is selected from NSAIDs, inhibitors of pro-inflammatory cytokines and receptors therefor and their production, and combinations thereof.

60. The one or more compounds for use according to claim 52, wherein the antidiabetic agent is selected from AMPK agonists (e.g., metformin), PPAR- γ agonists, GLP-1 agonists, SGLT2 inhibitors, and combinations thereof.
61. The one or more compounds for use according to claim 52, wherein the antibiotic
5 comprises ethionamide and optionally SMART-420.
62. The one or more compounds for use according to claim 52, wherein the anticancer agent comprises radiation therapy, chemotherapy or cancer immunotherapy, or any combination or all thereof.
63. The one or more compounds for use according to claim 62, wherein the chemotherapy
10 comprises a PARP inhibitor (e.g., olaparib), a TGF- β inhibitor or a cytotoxic agent, or any combination or all thereof.
64. The one or more compounds for use according to claim 62, wherein the cancer immunotherapy comprises an anti-PD1 agent, an anti-PDL1 agent or an anti-CTLA4 agent, or any combination thereof.
- 15 65. One or more compounds of any one of claims 1 to 39 or a pharmaceutically acceptable salt, solvate, hydrate, clathrate, polymorph or stereoisomer thereof for use in elevating nicotinamide adenine dinucleotide (NAD⁺) level or/and providing cytoprotection in at least one cell type or tissue of a subject.
66. The one or more compounds for use according to claim 65, wherein the subject
20 suffers from a disorder or condition characterized by NAD⁺ depletion or/and cell injury, damage or death.
67. The one or more compounds for use according to claim 66, wherein the NAD⁺ depletion or/and the cell injury, damage or death are associated with or result from DNA damage.
- 25 68. The one or more compounds for use according to any one of claims 65 to 67, wherein the one or more compounds elevate NAD⁺ level in the mitochondria or/and the cytoplasm of a cell (e.g., total cellular NAD⁺ level).
69. The one or more compounds for use according to any one of claims 65 to 68, wherein the providing cytoprotection comprises reducing cell injury, damage or death.
- 30 70. The one or more compounds for use according to any one of claims 65 to 69, wherein the one or more compounds comprise a compound of Formula I and a compound of Formula

II, or a compound of Formula III and a compound of Formula IV.

71. One or more nicotinic riboside compounds in combination with a poly(ADP-ribose) polymerase (PARP) inhibitor for use in increasing nicotinamide adenine dinucleotide (NAD⁺) level or/and providing cytoprotection in at least one cell type or tissue of a subject.

5 72. The one or more compounds for use according to claim 71, wherein the subject suffers from a disorder or condition characterized by NAD⁺ depletion or/and cell injury, damage or death.

73. The one or more compounds for use according to claim 72, wherein the NAD⁺ depletion or/and the cell injury, damage or death are associated with or result from DNA
10 damage.

74. The one or more compounds for use according to any one of claims 71 to 73, wherein the increasing NAD⁺ level comprises increasing NAD⁺ level in the mitochondria or/and the cytoplasm of a cell (e.g., total cellular NAD⁺ level).

75. The one or more compounds for use according to any one of claims 71 to 74, wherein
15 the providing cytoprotection comprises reducing cell injury, damage or death.

76. The one or more compounds for use according to any one of claims 71 to 75, wherein the one or more nicotinic riboside compounds comprise one or more of nicotinamide riboside (NR), reduced NR (NRH), nicotinic acid riboside (NAR), reduced NAR (NARH) and pharmaceutically acceptable salts and stereoisomers thereof, or/and one or more derivatives
20 thereof (NR/NAR derivatives).

77. The one or more compounds for use according to claim 76, wherein the one or more NR/NAR derivatives comprise one or more compounds of any one of claims 1 to 39 or a pharmaceutically acceptable salt, solvate, hydrate, clathrate, polymorph or stereoisomer thereof.

25 78. The one or more compounds for use according to claim 77, wherein the one or more NR/NAR derivatives comprise a compound of Formula I and a compound of Formula II, or a compound of Formula III and a compound of Formula IV.

79. The one or more compounds for use according to any one of claims 71 to 78, wherein the PARP inhibitor is selected from niraparib, olaparib, rucaparib, talazoparib, veliparib, 4-amino-1,8-naphthalimide, BGB290, CEP9722, E7016 and pharmaceutically acceptable salts
30 thereof.

80. The one or more compounds for use according to any one of claims 71 to 79, wherein the PARP inhibitor is administered in a dose significantly lower than its recommended dose as an anticancer agent.

81. The one or more compounds for use according to claim 80, wherein the dose of the
5 PARP inhibitor is no more than about 10%, 5%, 1%, 0.5% or 0.1% of its recommended dose as an anticancer agent.

82. The one or more compounds for use according to any one of claims 71 to 81, wherein the PARP inhibitor is olaparib, and the dose (e.g., per day) of olaparib is no more than about 10 mg, 5 mg, 1 mg, 0.5 mg or 0.1 mg; or is from about 0.01 or 0.1 mg to about 10 mg, from
10 about 0.01 or 0.1 mg to about 1 mg, or from about 1 mg to about 10 mg; or is about 0.01-0.1 mg, 0.1-0.5 mg, 0.5-1 mg, 1-5 mg or 5-10 mg; or is about 10 µg, 50 µg, 0.1 mg, 0.5 mg, 1 mg, 5 mg or 10 mg.

83. The one or more compounds for use according to any one of claims 71 to 82, wherein the one or more nicotinic riboside compounds and the PARP inhibitor synergistically increase
15 NAD⁺ level or/and provide cytoprotection (e.g., reduce cytotoxicity).