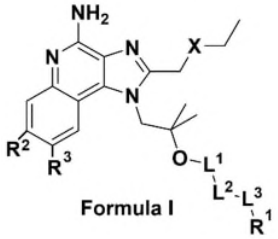
CLAIMS

1. A compound according to formula I



Formula I

or a pharmaceutically acceptable salt thereof,

wherein X is an oxygen atom, C1-C5-alkyl (preferably CH_2) or NH;

wherein R^2 and R^3 are each independently selected from the group consisting of hydrogen, C1-C5-alkyl, C4-C7-cycloalkyl, C4-C7-heterocycloalkyl, aryl and heteroaryl; preferably both R^2 and R^3 are each hydrogen;

and wherein L^1, L^2, L^3 and R^1 are as defined below under (a) or (b) or (c):

(a) L^1 is C2-C6 alkyl;
L^2 is a 5- or 6-membered heterocycle or OH; L^3 is absent or selected from the group consisting of hydrogen, C1-C2 alkyl and $CH_2C(CH_3)_2$; and
R^1 is absent or selected from the group consisting of hydrogen, NH_2, OH and SCH_3;

(b) L^1 is C2-C6 alkyl;
L^2 is selected from the group consisting of C(O), $NHC(O)CH_2$ and $NHC(O)C(CH_3)_2$;
L^3 is selected from the group consisting of a 6-membered heterocycle, OH, C(O)O, S, SO_2 and SO_3H; and
R^1 is absent or methyl or hydrogen;

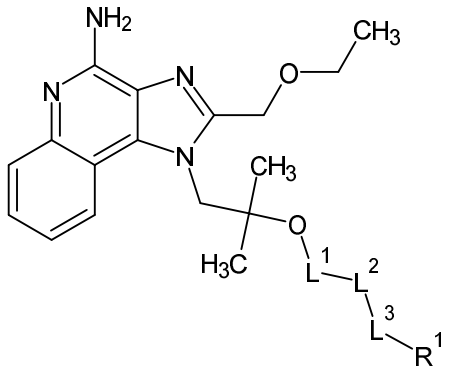
(c) L^1 is $C(O)CH_2$;
L^2 is a 6-membered heterocycle or NH_2;
L^3 is not present; and
R^1 is methyl or hydrogen or absent;

and wherein if L^3 is not present then L^2 is directly bound via a covalent bond to R^1.

2. The compound according to claim 1, wherein R^2 and R^3 are hydrogen.

3. Compound according to claim 1 or 2, wherein X is an oxygen atom.

4. Compound according to claim 3, wherein the compound has a structure according to formula II



Formula II

wherein L^1, L^2, L^3 and R^1 are as defined below under (d), (e) or (f)

(d) L^1 is C2-C6 alkyl;
L^2 is a 5- or 6-membered heterocycle (preferably triazole or piperazine), or OH;
L^3 is absent or selected from the group consisting of hydrogen, C1-C2 alkyl and $CH_2C(CH_3)_2$; and
R^1 is absent or selected from the group consisting of hydrogen, NH_2, OH and SCH_3;

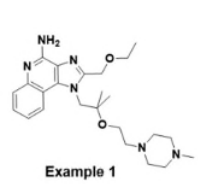
(e) L^1 is C2-C3 alkyl;
L^2 is selected from the group consisting of C(O), $NHC(O)CH_2$ and $NHC(O)C(CH_3)_2$;
L^3 is selected from the group consisting of a 6-membered heterocycle (preferably piperazine), OH, C(O)O, S, SO_2 and SO_3H; and
R^1 is absent or methyl or hydrogen;

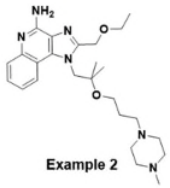
(f) L^1 is $C(O)CH_2$;
L^2 is a 6-membered heterocycle (preferably piperazine) or NH_2;
L^3 is not present; and
R^1 is methyl or hydrogen or absent;

5. Compound according to claim 4, wherein
L^1 is C2-C6 alkyl;

L^2 is a 5- or 6-membered heterocycle or OH; L^3 is absent or selected from the group consisting of hydrogen, C1-C2 alkyl and $CH_2C(CH_3)_2$; and
R^1 is absent or selected from the group consisting of NH_2, OH and SCH_3;

6. Compound according to any of the preceding claims, wherein the compound has a structure selected from the group consisting of the structures listed below that are designated as Example 1 through Example 27:


Example 1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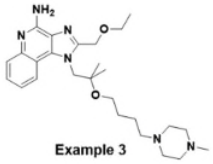
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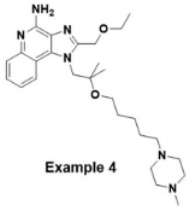
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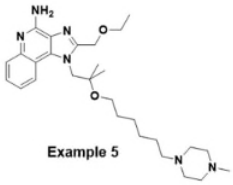
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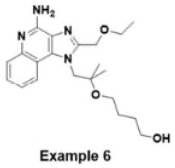
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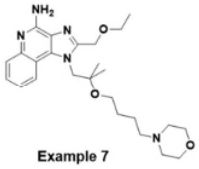
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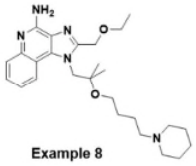
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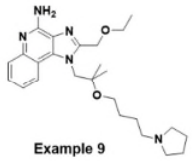
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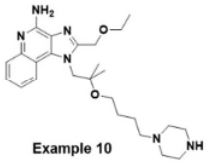
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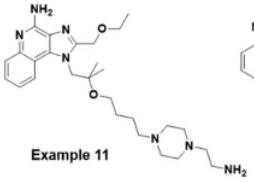
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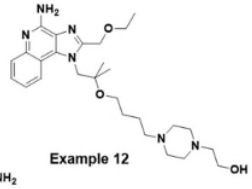
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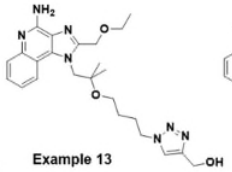
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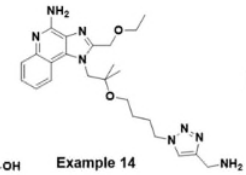
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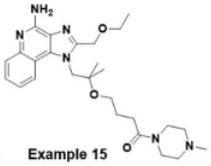
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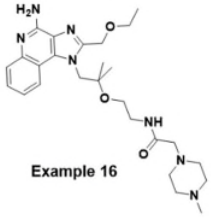
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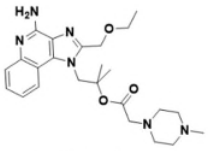
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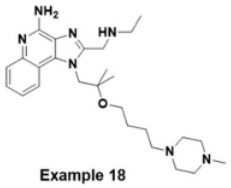
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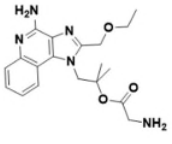
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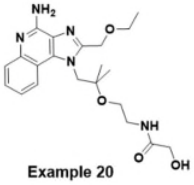
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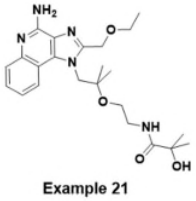
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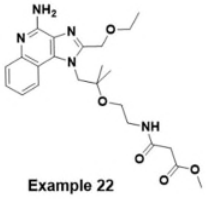
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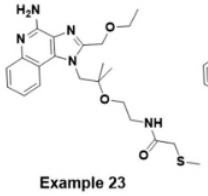
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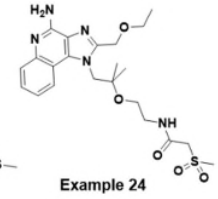
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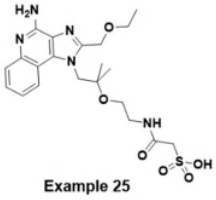
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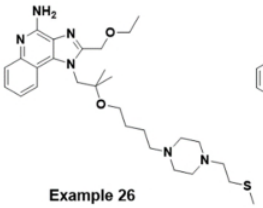
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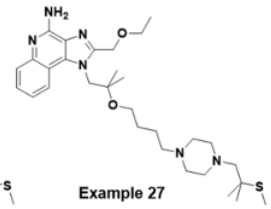
Example 27

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7. Compound according to claim 1, wherein

X is NH;

L^1 is C2-C6 alkyl;

L^2 is a 5- or 6-membered heterocycle;

L^3 is not present; and

R^1 is methyl or hydrogen; and

R^2 and R^3 are each hydrogen.

8. Compound according to any of the preceding claims, wherein the compound

(i) activates TLR7 more strongly than TLR8; and/or

(ii) induces IL-6, IL1-b and TNF-α production; and/or

(iii) induces upregulation of CD40 and/or CD86 in peripheral blood mononuclear cells (PBMC).

9. Compound according to any of the preceding claims, wherein the compound induces TNFα secretion from peripheral blood mononuclear cells (PBMC) if the compound contacts said cells.

10. Compound according to any of the preceding claims, wherein the compound has for TLR7 an EC50 of less than 10µM and preferably less than 0.01 µM, preferably when tested in a test system described Example 6.2.1.

11. Pharmaceutical composition comprising a compound of any of claims 1 – 10.

12. Compound of any of claims 1 -10 for the use as a medicament.

13. Compound of any of claims 1 -10 for the use in the treatment of a disease wherein said compound is used in said treatment in combination with the further compounds Imiquimod and/or Resiquimod (R848).

14. A composition comprising the compound of any of claims 1-10 for use in the treatment of a condition selected from the group consisting of cancer, a viral infection, non-cancerous skin lesions, pre-cancerous skin lesions, cancerous skin lesions, bladder cancer, virally mediated skin disease, said composition optionally being formulated for enhanced penetration following topical administration, said composition preferably initiating a local specific inflammatory cytokine response while limiting undesirable erythema and other inflammatory reactions.

15. The composition of claim 11 or 14 comprising between 0.01% -1% (wt/vol) of the compound of any of claims 1-10.

16. The composition of claim 14 or 15 for use in the treatment of bladder cancer, wherein the composition is formulated for intracystic administration.

17. The composition of any of claims 11, 14, 15 or 16, further comprising additional components of one of the groups i through xiii outlined below:

i. Oleic acid (50%) and isopropyl myristate (50%) in a solution containing 50 ml phosphate buffered saline and 50 ml ethanol at a total concentration of 1% wt/vol, or

ii. Isopropyl myristate (50%) and sodium lauryl sulfate (50%) in a solution containing 50 ml phosphate buffered saline and 50 ml ethanol at a total concentration of 0.5% wt/vol, or iii. Oleic acid (50%) and sodium lauryl sulfate (50%) in a solution containing 50 ml phosphate buffered saline and 50 ml ethanol at a total concentration of 0.5% wt/vol, or iv. Oleic acid (33%), isopropyl myristate (33%) and sodium lauryl sulfate (33%) in a solution containing 50 ml phosphate buffered saline and 50 ml ethanol at a total concentration of 0.5% wt/vol, or

v. Isopropyl palmitate (50%) and sodium oleate (50%) in a solution containing 50 ml phosphate buffered saline and 50 ml ethanol at a total concentration of 2% wt/vol, or

vi. Sodium lauryl sulfate (25%) and linoleic acid (75%) in a solution containing 50 ml phosphate buffered saline and 50 ml ethanol at a total concentration of 1.0% wt/vol, or vii. Palmitic acid (50%) and isopropyl laurate (50%) in a solution containing 50 ml phosphate buffered saline and 50 ml ethanol at a total concentration of 2.0% wt/vol, or

viii. Oleic acid (50%) and linoleic acid (50%) in a solution containing 50 ml phosphate buffered saline and 50 ml ethanol at a total concentration of 1.5% wt/vol, or

ix. Linoleic acid (25%), oleic acid (25%) and isopropyl linoleate (50%) in a solution containing 50 ml phosphate buffered saline and 50 ml ethanol at a total concentration of 0.5% wt/vol, or

x. Sodium oleate (33%), oleic acid (33%) and methyl palmitate (33%) in a solution containing 50 ml phosphate buffered saline and 50 ml ethanol at a total concentration of 2.0% wt/vol, or

xi. A solution containing 50 ml phosphate buffered saline and 50 ml ethanol, or

xii. Oleic acid (10%) in a solution containing 50 ml phosphate buffered saline and 50 ml ethanol, or

xiii. Oleic acid (2%) and sodium lauryl sulfate (5%) in a solution containing 50 ml phosphate buffered saline and 50 ml ethanol.

18. A method of activating TLR 7 and/or 8 in a biological sample, comprising contacting said biological sample with a compound according to any of claims 1-10.

19. Compound of any of claims 1-10 for use as a vaccine adjuvant or for use in the treatment of cancer in combination with an anti-cancer immunotherapy agent (preferably ipilimumab, nivolumab, or pembrolizumab).