CLAIMS

1. Use of an ~~An~~ AXL inhibitor (AXLi) ~~and an immune checkpoint modulator (ICM)~~ in the manufacture of a medicament for ~~use in the~~ treatment of an AXL–related disease, wherein the medicament is formulated to administer the AXLi to a subject in separate, sequential, or simultaneous combination with an immune checkpoint modulator (ICM); and

wherein the AXL-related disease is characterised by the presence of cells having modified STK11 activity or expression~~; and/or~~

~~wherein the AXL-related disease is characterised by the presence of cells having increased KRAS activity or expression,~~

~~and wherein the AXLi and ICM are for administration separately, sequentially or simultaneously~~.

2. Use of an ~~An~~ AXL inhibitor (AXLi) ~~and an immune checkpoint modulator (ICM)~~ in the manufacture of a medicament for ~~use in the~~ treatment of an AXL–related disease, wherein the medicament is formulated to administer the AXLi to a subject in separate, sequential, or simultaneous combination with an immune checkpoint modulator (ICM); and wherein:

i) the the medicament is formulated to be administered to ~~said treatment comprising: identifying~~ subjects that have previously been treated with an ICM and which did not respond to or benefit from treatment with the ICM~~; and, selecting thus identified subjects for treatment,~~

~~wherein the AXLi and ICM are for administration separately, sequentially or simultaneously.~~; or

ii)

~~3. An AXL inhibitor (AXLi) and an immune checkpoint modulator (ICM) for use in the treatment of an AXL–related disease, wherein~~ the AXL-related disease is characterised by a reduced presence of $CD8^+$ cells having TCF1 activity or expression~~,~~

~~and wherein the AXLi and ICM are for administration separately, sequentially or simultaneously~~.

~~4. The AXLi and ICM for use according to any preceding claim, wherein the use further comprises the administration of a chemotherapeutic agent and / or radiotherapy.~~

~~5~~3. The ~~AXLi and ICM for~~ use according to any preceding claim, wherein the AXL-related disease is further characterised by:

i) the presence of cells having increased KRAS activity or expression;

ii) the presence of cells having decreased p53 activity or expression; and / or

iii) the presence of cells having increased AXL activity or expression.

~~6~~4. The ~~AXLi and ICM for~~ use according to any preceding claim, wherein increased or decreased expression is assessed by:

i) determining copy number of the gene encoding STK11, KRAS, or p53 relative to a control sample; and / or

ii) determining the level of STK11, KRAS, or p53 protein or mRNA relative to a control sample.

~~7~~5. The ~~AXLi and ICM for~~ use according to any preceding claim, wherein:

i) modified STK11 activity or expression is assessed by determining the presence or absence of a STK11 mutation and / or a STK11IP mutation;~~.~~ and / or

ii)

~~8. The AXLi and ICM for use according to any preceding claim, wherein~~ STK11 activity and/or expression is decreased relative to a control sample.

~~9~~6. The ~~AXLi and ICM for~~ use according to claim ~~7 or claim 8~~5, wherein the STK11 mutation or STK11IP mutation, is:

i) a mutation in the nucleotide sequence encoding STK11 or STK11IP;

ii) a mutation in a regulatory sequence controlling expression of the nucleotide sequence encoding STK11 or STK11IP;

iii) a mutation in a nucleotide encoding a protein which interacts with the transcription product of the STK11 or STK11IP gene;

iv) a mutation in the translation product of the STK11 or STK11IP gene; ~~and / or~~

v) a mutation in the transcription product of the STK11 or STK11IP gene; and / or

vi) a STK11 inactivating mutation, and / or a STK11IP activating mutation.

~~10. The AXLi and ICM for use according to any one of claims 7-9, wherein STK11 mutation is an inactivating mutation, and / or the STK11IP mutation is an activating mutation.~~

~~11~~7. The ~~AXLi and ICM for~~ use according to any preceding claim, wherein increased or decreased activity, expression, or population is determined in a sample derived from a subject; and / or ~~.~~

~~12. The AXLi and ICM for use according to any preceding claim, wherein~~ increased or decreased activity, expression, or population is determined relative to a control.

~~13~~8. The ~~AXLi and ICM for~~ use according to any preceding claim, wherein the AXL-related disease is cancer, preferably a cancer selected from the group consisting of: lung cancer, non-small-cell lung cancer, breast cancer, melanoma, mesothelioma, acute myeloid leukemia (AML), myelodysplatic syndrome (MDS), pancreas cancer, kidney cancer, urothelial carcinoma, and glioblastoma.

~~14~~9. The ~~AXLi and ICM for~~ use according to claim ~~13~~8, wherein the cancer is lung cancer, preferably non-small-cell lung cancer.

~~15. The AXLi and ICM for use according to any preceding claim, further comprising administering to the subject a therapeutically effective amount of an AXL inhibitor (AXLi), an immune checkpoint modulator (ICM), and / or a chemotherapeutic agent and / or radiotherapy.~~

~~16~~10. The ~~AXLi and ICM for~~ use according to any preceding claim, wherein the AXL inhibitor is:

i) selected from the group consisting of:

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-(7-(pyrrolidin-1-yl)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7-(S)-pyrrolidin-1-yl)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7-(R)-pyrrolidin-1-yl)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-pyrido[2',3':6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-(3-fluoro-4-(4-(pyrrolidin-1-yl)piperidin-1-yl)phenyl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N5-(7-(pyrrolidin-1-yl)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-1-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N5-(7-(S)-pyrrolidin-1-yl-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(t-butoxycarbonylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-(7-(acetamido)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-(7-((2R)-2-(methoxycarbonyl)pyrrolidin-1-yl)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-(7-(4,4-difluoropiperidin-1-yl)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-(7-((methoxycarbonylmethyl)(methyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-(7-((2R)-2-(carboxy)pyrrolidin-1-yl)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-(7-(4-(ethoxycarbonyl)piperidin-1-yl)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-(7-(4-(carboxy)piperidin-1-yl)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-(7-((carboxymethyl)(methyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-(7-(4-(ethoxycarbonylmethyl)piperazin-1-yl)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-(7-(4-(carboxymethyl)piperazin-1-yl)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-(7-(pyrrolidin-1-yl)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-1-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-amino-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7s)-7-(di(cyclopropylmethyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-((2-methylpropyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-((propyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(dipropylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(diethylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(cyclohexylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(cyclopentylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-((1-cyclopentylethyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(2-propylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-((3,3-dimethylbut-2-yl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-((cyclohexylmethyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(di(cyclohexylmethyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-((5-chlorothien-2-yl)methyl)amino-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-((2-carboxyphenyl)methyl)amino-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-((3-bromophenyl)methyl)amino-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(dimethylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(cyclobutylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(3-pentylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-((2,2-dimethylpropyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(di(cyclopentylmethyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-((cyclopentylmethyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(di(bicyclo[2.2.1]hept-2-en-5-ylmethyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-((bicyclo[2.2.1]hept-2-en-5-ylmethyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(3-methylbutylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(di(3-methylbutyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(2-ethylbutylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(but-2-enylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(butyl(but-2-enyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-pyrido[2',3':6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N5-((7S)-7-(t-butoxycarbonylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-pyrido[2',3':6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-amino-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-pyrido[2',3':6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(dimethylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-pyrido[2',3':6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(diethylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-pyrido[2',3':6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(dipropylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-pyrido[2',3':6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(di(cyclopropylmethyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-pyrido[2',3':6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(di(3-methylbutyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-pyrido[2',3':6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(cyclobutylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-pyrido[2',3':6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(cyclohexylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-pyrido[2',3':6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-((methylethyl)amino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5H-pyrido[2',3':6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(cyclopentylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine; and

1-(6,7-dihydro-5H-pyrido[2',3':6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-((7S)-7-(2-butylamino)-6,7,8,9-tetrahydro-5H-benzo[7]annulene-2-yl)-1H-1,2,4-triazole-3,5-diamine;

or pharmaceutically acceptable salts thereof;

ii)

~~17. The AXLi and ICM for use according to any preceding claim, wherein the AXL inhibitor is:~~

~~i) Bemcentinib (BGB324 / R428); or~~

~~ii)~~ selected from the group consisting of: dubermatinib (CAS No.1341200-45-0; UNII 14D65TV20J); gilteritinib (CAS No. 1254053-43-4; UNII 66D92MGC8M); cabozantinib (CAS No. 849217-68-1; UNII 1C39JW444G); SGI7079 (CAS No. 1239875-86-5); merestinib (CAS No. 1206799-15-6; UNII 5OGS5K699E); amuvatinib (CAS No. 850879-09-3; UNII SO9S6QZB4R); bosutinib (CAS No. 380843-75-4; UNII 5018V4AEZ0); glesatinib (CAS No. 936694-12-1; UNII 7Q29OXD98N); foretinib (CAS No. 849217-64-7; UNII 81FH7VK1C4); and, TP0903 (CAS No. 1341200-45-0); or

iii) an anti-AXL antibody.

11. The use according to any preceding claim, wherein the AXL inhibitor is bemcentinib (BGB324 / R428).

~~18~~12. The ~~AXLi and ICM for~~ use according to any preceding claim, wherein the immune checkpoint modulator includes one or more immune checkpoint inhibitors (ICI),

optionally wherein the immune checkpoint modulator:

i) is selected from the group consisting of: anti-CTLA-4 antibodies, anti-PD-1 antibodies, anti-PD-L1 antibodies, anti-4-1BB antibodies, anti-OX-40 antibodies, anti-GITR antibodies, anti-CD27 antibodies, anti-CD28 antibodies, anti-CD40 antibodies, anti-LAG3 antibodies, anti-ICOS antibodies, anti-TWEAKR antibodies, anti-HVEM antibodies, anti-TIM-1 antibodies, anti-TIM-3 antibodies, anti-VISTA antibodies, and anti-TIGIT antibodies~~.~~;

ii)

~~19. The AXLi and ICM for use according to any preceding claim, wherein the immune checkpoint modulator~~ is selected from the group consisting of: anti-CTLA-4 antibodies, anti-PD-1 antibodies, and anti-PD-L1 antibodies~~;~~ or

iii)

~~20. The AXLi and ICM for use according to any preceding claim, wherein the immune checkpoint modulator~~ includes, or is: pembrolizumab; ipilimumab; ipilimumab and nivolumab; ipilimumab and pembrolizumab; tremelilumab and durvalumab.

13. The use according to any predecing claim, wherein the immune checkpoint modulator includes, or is an anti-PD-1 antibody; wherein the anti-PD-1 antibody is preferably pembrolizumab.

~~21~~14. The ~~AXLi and ICM for~~ use according to any ~~one of claims 4 to 20~~preceding claim, wherein the medicament is formulated to be administered in combination with administration of a chemotherapeutic agent and / or radiotherapy;

optionally wherein the chemotherapeutic agent is:

i) a chemotherapeutic agent which induces immunogenic cell death of cancer cells,~~.~~

~~22. The AXLi and ICM for use according to any one of claims 4 to 21, wherein the chemotherapeutic agent is a chemotherapeutic agent which~~ induces an immune response in the subject, ~~optionally wherein the chemotherapeutic agent is a chemotherapeutic agent which~~and / or induces a type I interferon response in the subject;~~.~~

ii)

~~23. The AXLi and ICM for use according to any one of claims 4 to 22, wherein the chemotherapeutic agent is~~ an anthracycline~~,~~;

iii) ~~optionally wherein the~~ an anthracycline ~~is~~ selected from doxorubicin, daunorubicin, epirubicin, idarubicin, mitoxantrone, or valrubicin; ~~preferably~~

iv) doxorubicin;~~.~~

v) carboplatin;

vi) pemetrexed disodium;

vii) pemetrexed disodium and platinum chemotherapy; or

viii) pemetrexed disodium and carboplatin.

~~24~~15. A method of selecting a subject for treatment with a combination of an AXL inhibitor (AXLi) and an immune checkpoint modulator (ICM), the method comprising:

i) identifying subjects having an AXL-related disease characterised by the presence of cells having modified STK11 activity or expression; and, selecting thus identified subjects for treatment;~~.~~

ii)

~~25. A method of selecting a subject for treatment with a combination of an AXL inhibitor (AXLi) and an immune checkpoint modulator (ICM), the method comprising:~~ identifying subjects having an AXL-related disease characterised by the presence of cells having increased KRAS activity or expression; and, selecting thus identified subjects for treatment;~~.~~

iii)

~~26. A method of selecting a subject for treatment with a combination of an AXL inhibitor (AXLi) and an immune checkpoint modulator (ICM), the method~~

~~comprising:~~ identifying subjects that have previously been treated with an immune checkpoint modulator (ICM) and which did not respond to or benefit from treatment with the ICM; and, selecting thus identified subjects for treatment;~~,~~ Or

iv)

~~27. A method of selecting a subject for treatment with a combination of an AXL inhibitor (AXLi) and an immune checkpoint modulator (ICM), the method comprising:~~ identifying subjects having an AXL-related disease characterised by a reduced presence of $CD8^+$ cells having TCF1 activity or expression; and, selecting thus identified subjects for treatment.

~~28. A method of increasing a population of desired T cells in a subject comprising treating the subject with an AXL inhibitor (AXLi).~~

~~29. The method of claim 28, wherein the desired T cell population is a CD8+ T cell population.~~

~~30~~16. Use of an AXL inhibitor (AXLi) in the manufacture of a medicament for~~A method of~~ treating an AXL-related disease in a subject, wherein the medicament is formulated to ~~with a combination of an AXL inhibitor (AXLi) and an immune checkpoint modulator (ICM), the method comprising~~:

(i) administer~~ing~~ the AXLi to the subject in ~~a~~ combination ~~of the AXLi and the~~ with an immune checkpoint modulator (ICM) ~~to the subject~~;

(ii) administer~~ing~~ the AXLi to the subject, wherein ~~the~~ an immune checkpoint modulator (ICM) has been, is, or will be, administered to the subject; ~~or~~

~~(iii) administering the ICM to the subject, wherein the AXLi has been, is, or will be, administered to the subject;~~

wherein the AXL-related disease is characterised by: the presence of cells having decreased STK11 activity or expression; and / or the presence of cells having a STK11 mutation and / or a STK11IP mutation.~~;~~

17. Use of an immune checkpoint modulator (ICM) in the manufacture of a medicament for treating an AXL-related disease in a subject, wherein the medicament is formulated to:

(i) administer the ICM to the subject in combination with an AXL inhibitor (AXLi);

(ii) administer the ICM to the subject, wherein an AXL inhibitor (AXLi) has been, is, or will be, administered to the subject;

wherein the AXL-related disease is characterised by: the presence of cells having decreased STK11 activity or expression; and / or the presence of cells having a STK11 mutation and / or a STK11IP mutation.

18. The use ~~optionally~~ according to claim 16 or 17, wherein the subject has been selected for treatment using a method as defined in ~~any one of~~ claim~~s 1 -23~~15.

~~31. A method of treating an AXL-related disease in a subject with a combination of an AXL inhibitor (AXLi) and an immune checkpoint modulator (ICM), the method comprising:~~

~~(i) administering a combination of the AXLi and the ICM to the subject;~~

~~(ii) administering the AXLi to the subject, wherein the ICM has been, is, or will be, administered to the subject; or~~

~~(iii) administering the ICM to the subject, wherein the AXLi has been, is, or will be, administered to the subject;~~

~~wherein the AXL-related disease is characterised by: the presence of cells having increased KRAS activity or expression; and / or the presence of cells having a KRAS mutation;~~

~~optionally wherein the subject has been selected for treatment using a method as defined in any one of claims 1 -23.~~

~~32. The method of claim 30 or 31, wherein the subject is treated with a combination of an AXL inhibitor (AXLi), an immune checkpoint modulator (ICM), and a chemotherapeutic agent and / or radiotherapy.~~

~~33~~19. A method of prognosing susceptibility of a subject to treatment with a combination of an AXL inhibitor (AXLi) and an immune checkpoint modulator (ICM), the method comprising:

determining: i) the presence or absence of a STK11 mutation and / or STK11IP mutation; and / or ii) the level of STK11 activity or expression in the subject or a sample derived from the subject;

wherein the presence of a STK11 mutation and / or presence of a STK11IP mutation, and / or a modified level of STK11 activity or expression is indicative of susceptibility to treatment with a combination of an AXL inhibitor (AXLi) and an immune checkpoint modulator (ICM), preferably wherein the modified level of STK11 activity or expression is a decreased level of STK11 activity or expression.

~~34~~20. A method of prognosing susceptibility of a subject to treatment with a combination of an AXL inhibitor (AXLi) and an immune checkpoint modulator (ICM), the method comprising:

determining: i) the presence or absence of a KRAS mutation; and / or ii) the level of STK11 activity or expression in the subject or a sample derived from the subject;

wherein the presence of a KRAS mutation, and / or an increased level of STK11 activity or expression is indicative of susceptibility to treatment with a combination of an AXL inhibitor (AXLi) and an immune checkpoint modulator (ICM).

~~35. A method of treating an AXL-related disease in a subject in need of such treatment, the method comprising administering to the subject a combination of an AXL inhibitor (AXLi) and an immune checkpoint modulator (ICM), wherein the AXLi and ICM may be administered to the subject simultaneously, separately or sequentially.~~

~~36. An AXL inhibitor (AXLi) and an immune checkpoint modulator (ICM) for use in the treatment of an AXL-related disease in a subject, wherein the AXLi and ICM may be administered to the subject simultaneously, separately or sequentially.~~