presence of hACE2. In addition, human AXL or TIM-1 was expressed in some cells. Ad5 virus vectors (MOI=~50) delivered the human genes. N=8-16 (single experiment)

Figure 12

Ability of SARS-CoV-2 to infect HAE cultures in the presence of camostat, bemcentinib or E64. Shown are duplicate cultures from HAEs from 3 different donors.

Figure 13

Representative data from three of the lung tumor lines from John Minna that support SARS-COV-2 infection which is sensitive to both E64 and bemcentinib.

Figure 14

Ability of PS receptor inhibitors to decrease SARS-Cov-2 infection of Huh7 cells.

Figure 15

Polyclonal sera against hACE2 does not inhibit SARS-CoV-2 spike-dependent infection. Antisera concentrations noted above were added ~1 h prior to infection and maintained in the culture for the 24 h infection period.

Figure 16

(A) Vero E6 cell studies where it was observed that bemcentinib was highly effective at inhibiting SARS-CoV-2 spike dependent entry, but tilvestamab had no effect. VSV/SARS-CoV-2 spike pseudovirions were used this experiment.

(B) Tilvestamab has no effect on SARS-CoV-2 infection of CalU3 cells.

Figure 17

MHV present in livers of infected C57BL/6 mice at day 3 of infection. Virus was administered intraperitoneally. Virus was assessed by titering clarified liver homogenates on a murine CEACAM+ cell line (A) or by qRT-PCR (B-C). No statistical significance is achieved when treatments are grouped into n=5.

Figure 18

Virus load at day X of infection with 50,000 iu of MHV. Same data as shown in Fig. ~~18~~17C. However, untreated and vehicle only groups of mice given 50,000 iu of MHV are now pooled. When compared in a Student's t test, the bemcentinib group now has a significantly reduced virus load.

Figure 19

Expression changes in interferon related genes at day 3 in spleens of C57BL/6 mice infected with 500 iu of MHV in the presence of vehicle control (LH bar in each pair) or bemcentinib (RH bar in each pair).

Figure 20

CLAIMS

1. Use of an inhibitor of AXL activity or expression~~An~~ (AXLi) in the manufacture of a medicament for ~~use in a method for~~ treating a virus infection in a subject, preventing or reducing transmission of a virus infection in a subject, or increasing viral clearance from a subject, wherein the medicament is formulated to administer ~~the method comprising administering~~ to the subject an effective amount of ~~an inhibitor of AXL activity or expression (~~the AXLi~~)~~.

~~2. An AXLi for use in a method for preventing or reducing transmission of a virus infection, the method comprising administering to the subject an effective amount of an inhibitor of AXL activity or expression (AXLi).~~

~~3. An AXLi for use in a method for increasing viral clearance from a subject, the method comprising administering to the subject an effective amount of an inhibitor of AXL activity or expression (AXLi).~~

~~4~~2. The ~~AXLi for~~ use according to ~~any one of~~ claim~~s~~ 1 ~~to 3~~, wherein the virus infection is:

(i) a coronavirus infection;~~.~~

(ii)

~~5. The AXLi for use according to any one of claims 1 to 4, wherein the virus infection is~~ an alphaletovirus infection;~~.~~

(iii)

~~6 The AXLi for use according to any one of claims 1 to 4 wherein the virus infection is~~ an orthocoronavirus infection;~~.~~

(iv)

~~7. The AXLi for use according to any one of claims 1 to 4, or 6, wherein the virus infection is~~ an alphacoronavirus infection;~~.~~

(v)

~~8. The AXLi for use according to any one of claims 1 to 4, or 6, wherein the virus infection is~~ a betacoronavirus infection;~~.~~

(vi)

~~9. The AXLi for use according to any one of claims 1 to 4, or 6, wherein the virus infection is~~ a gammacoronavirus infection;~~.~~

(vii)

~~10. The AXLi for use according to any one of claims 1 to 4, or 6, wherein the virus infection is~~ a deltacoronavirus infection;~~.~~

(viii)

~~11. The AXLi for use according to any one of claims 1 to 4, 6, or 8, wherein the virus infection is~~ a betacoronavirus, lineage B, infection~~;~~.

(ix)

~~12. The AXLi for use according to any one of claims 1 to 4, 6, 8, or 11, wherein the virus infection is~~ a SARS-CoV infection~~;~~.

(x) a betacoronavirus, lineage C, infection; or

(xi) a MERS-CoV infection.

~~13~~3. The ~~AXLi for~~ use according to ~~any one of~~ claim~~s~~ 1 ~~to 4, 6, 8, or 11~~, wherein the virus infection is a SARS-CoV-2 infection.

~~14~~4. The ~~AXLi for~~ use according to claim ~~13~~3, wherein the SARS-CoV-2 infection is caused by:

(i) a variant comprising a mutation at position E484, optionally wherein the mutation is a E484K substitution~~;~~.

(ii)

~~15. The AXLi for use according to either one of claims 13 or 14, wherein the SARS-CoV-2 infection is caused by~~ a variant comprising a mutation at position N501, optionally wherein the mutation is a N501Y substitution~~;~~.

(iii)

~~16 The AXLi for use according to any one of claims 13 to 15, wherein the SARS-CoV-2 infection is caused by~~ a variant comprising a mutation at position K417, optionally wherein the mutation is a K417N or a K417T substitution~~;~~.

(iv)

~~17. The AXLi for use according to any one of claims 13 to 16, wherein the SARS-CoV-2 infection is caused by~~ a variant comprising a mutation at one or more of the positions L18, L242-244, D80, D215, D614, and A701, optionally wherein the variant comprises a mutation at each of the positions~~;~~.

(v)

~~18. The AXLi for use according to any one of claims 13 to 16, wherein the SARS-CoV-2 infection is caused by~~ a variant comprising one or more of the mutations L18F, ΔL242-244, D80A, D215G, D614G, and A701V, optionally wherein the variant comprises all of the mutations~~;~~.

(vi)

~~19. The AXLi for use according to any one of claims 13 to 18, wherein the SARS-CoV-2 infection is caused by~~ the B.1.351 variant~~;~~.

(vii)

~~20. The AXLi for use according to claim 13, wherein the SARS-CoV-2 infection is caused by~~ the B.1.1.7 variant~~;~~.

(viii)

~~21. The AXLi for use according to claim 13, wherein the SARS-CoV-2 infection is caused by~~ the P.1 variant~~;~~ or

(ix)

~~22. The AXLi for use according to claim 13, wherein the SARS-CoV-2 infection is caused by~~ the B.1.526 variant.

~~23. The AXLi for use according to any one of claims 1 to 4, 6, or 8, wherein the virus infection is a betacoronavirus, lineage C, infection.~~

~~24. The AXLi for use according to any one of claims 1 to 4, 6, 8, or 23, wherein the virus infection is a MERS-CoV infection.~~

~~25~~5. The ~~AXLi for~~ use according to any one of claims 1 to 24, wherein the ~~AXLi is~~medicament is formulated to be administered in combination with a second antiviral agent, an anti-inflammatory agent, and / or an immunosuppressive agent.

~~26~~6. The ~~AXLi for~~ use according to claim ~~25~~5, wherein the second antiviral agent is:

(i) selected from the group consisting of: a protease inhibitor, a helicase inhibitor, and a cell entry inhibitor~~;~~

(ii)

~~27. The AXLi for use according to either one of claims 25 or 26, wherein the second antiviral agent is~~ selected from the group consisting of: ribavirin, an interferon, or a combination of both~~;~~ and / or

(iii)

~~28. The AXLi for use according to claim 25, wherein the second antiviral agent is~~ remdesivir.

~~29. The AXLi for use according to any one of claims 1 to 28, wherein the AXLi is administered in combination with an anti-inflammatory agent.~~

~~30~~7. The ~~AXLi for~~ use according to claim ~~29~~5, wherein the anti-inflammatory agent is:

(i) a corticosteroid~~;~~

(ii)

~~31. The AXLi for use according to claim 29, wherein the anti-inflammatory agent is~~ a glucocorticoid steroid~~;~~ and / or

(iii)

~~32. The AXLi for use according to claim 29, wherein the anti-inflammatory agent is~~ dexamethasone.

~~33. The AXLi for use according to any one of claims 1 to 32, wherein the AXLi is administered in combination with an immunosuppressive agent.~~

~~34~~8. The ~~AXLi for~~ use according to claim ~~33~~5, wherein the immunosuppressive agent is an IL-6 anatgonist or ~~.~~

~~35. The AXLi for use according to claim 33, wherein the immunosuppressive agent~~ is Tocilizumab.

~~36~~9. The ~~method~~ use of any one of claims 1 to ~~35~~8, wherein the medicament is formulated such that the AXLi and/or second antiviral agent is comprised in a pharmaceutical composition, optionally further comprising a pharmaceutically acceptable excipient, and optionally ~~.~~

~~37. The AXLi for use according to any one of claim 1 to 36,~~ wherein the medicament is formulated to be ~~AXLi and/or the second antiviral agent is~~ administered by inhalation.

~~38~~10. The ~~AXLi for~~ use according to any previous claim, wherein the subject:

(i) is human;~~.~~

(ii)

~~39. The AXLi for use according to any previous claim, wherein the subject~~ has, is suspected of having, or is at high risk of having a viral infection;~~.~~

(iii)

~~40. The method of any preceding claim wherein the subject~~ is a healthcare professional;~~.~~

(iv)

~~41. The AXLi for use according to any one of claims 1 to 40, wherein the subject~~ is at risk of severe symptoms if they were to catch the viral infection;~~.~~

(v)

~~42. The AXLi for use according to any one of claims 1 to 41, wherein the subject~~ has one or more comorbidity selected from: respiratory system disease, cardiovascular disease, diabetes, hypertension, cancer, or a suppressed immune system;~~.~~

(vi)

~~43. The AXLi for use according to claim 42, wherein the subject~~ has two or more ~~comorbidities.~~

~~44. The AXLi for use according to claim 43, wherein the subject has~~ or three or more comorbidities;~~.~~

(vii)

~~45. The AXLi for use according to any one of claims 1 to 44, wherein the subject~~ is at least 60 years old~~,~~.

~~46. The AXLi for use according to any one of claims 1 to 45, wherein the subject~~ is at least 70 years old~~,~~.

~~47. The AXLi for use according to any one of claims 1 to 46, wherein the subject~~ or is at least 80 years old~~;~~.

(viii)

~~48. The AXLi for use according to any one of claims 1 to 47, wherein the subject~~ is male~~;~~ and / or

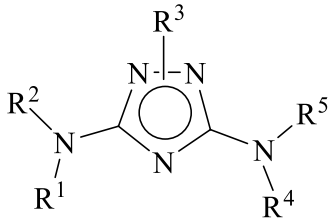
(ix) is selected for treatment on the basis of having one or more of the features of (ii) to (viii).

~~49~~11. The ~~AXLi for~~ use according to any one of claims 1 to ~~48~~9, wherein the subject's CRP level is at least 30 µg/mL~~.~~ or

~~50. The AXLi for use according to any one of claims 1 to 48, wherein the subject's CRP level~~ is at least 50 µg/mL.

~~51. The AXLi for use according to any one of claims 1 to 50, wherein the subject is selected for treatment on the basis of having one or more of the features of claims 39 to 50.~~

~~52~~12. The ~~AXLi for~~ use according to any one of claims 1 to ~~51~~11, wherein the AXLi is a compound of formula (I):



(I)

wherein:

R^1, R^4 and R^5 are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, aryl, aralkyl, $-C(O)R^8$, $-C(O)N(R^6)R^7$, and $-C(=NR^6)N(R^6)R^7$;

R^2 and R^3 are each independently a polycyclic heteroaryl containing more than 14 ring atoms optionally substituted by one or more substituents selected from the group consisting of oxo, thioxo, cyano, nitro, halo, haloalkyl, alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heterocyclyl, $-R^9-OR^8$, $-R^9-O-R^{10}-OR^8$, $-R^9-O-R^{10}-O-R^{10}-OR^8$, $-R^9-O-R^{10}-CN$, $-R^9-O-R^{10}-C(O)OR^8$, $-R^9-O-R^{10}-C(O)N(R^6)R^7$, $-R^9-O-R^{10}-S(O)_pR^8$ (where p is 0, 1 or 2), $-R^9-O-R^{10}-N(R^6)R^7$, $-R^9-O-R^{10}-C(NR^{11})N(R^{11})H$, $-R^9-OC(O)-R^8$, $-R^9-N(R^6)R^7$, $-R^9-C(O)R^8$, $-R^9-C(O)OR^8$, $-R^9-C(O)N(R^6)R^7$, $-R^9-N(R^6)C(O)OR^8$, $-R^9-N(R^6)C(O)R^8$, $-R^9-N(R^6)S(O)_tR^8$ (where t is 1 or 2), $-R^9-S(O)_tOR^8$ (where t is 1 or 2), $-R^9-S(O)_pR^8$ (where p is 0, 1 or 2), and $-R^9-S(O)_tN(R^6)R^7$ (where t is 1 or 2);

or R^2 is a polycyclic heteroaryl containing more than 14 ring atoms as described above and R^3 is selected from the group consisting of aryl and heteroaryl, where the aryl and the heteroaryl are each independently optionally substituted by one or more substitutents selected from the group consisting of alkyl, alkenyl, alkynyl, halo, haloalkyl, haloalkenyl, haloalkynyl, oxo, thioxo, cyano, nitro, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted aralkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted cycloalkylalkynyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heterocyclylalkynyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, optionally substituted heteroarylalkenyl, optionally substituted heteroarylalkynyl, $-R^{13}-OR^{12}$, $-R^{13}-OC(O)-R^{12}$, $-R^{13}-O-R^{14}-N(R^{12})_2$, $-R^{13}-N(R^{12})-R^{14}-N(R^{12})_2$, $-R^{13}-N(R^{12})-R^{14}-N(R^{12})_2$, $-R^{13}-N(R^{12})_2$, $-R^{13}-C(O)R^{12}$, $-R^{13}-C(O)OR^{12}$, $-R^{13}-C(O)N(R^{12})_2$, $-R^{13}-C(O)N(R^{12})-R^{14}-N(R^{12})R^{13}$, $-R^{13}-C(O)N(R^{12})-R^{14}-OR^{12}$, $-R^{13}-N(R^{12})C(O)OR^{12}$, $-R^{13}-N(R^{12})C(O)R^{12}$, $-R^{13}-N(R^{12})S(O)_tR^{12}$ (where t is 1 or 2), $-R^{13}-S(O)_tOR^{12}$ (where t is 1 or 2), $-R^{13}-S(O)_pR^{12}$ (where p is 0, 1 or 2), and $-R^{13}-S(O)_tN(R^{12})_2$ (where t is 1 or 2);

or R^3 is a polycyclic heteroaryl containing more than 14 ring atoms as described above, and R^2 is selected from the group consisting of aryl and heteroaryl, where the aryl and the heteroaryl are each independently optionally substituted by one or more substitutents selected from the group consisting of alkyl, alkenyl, alkynyl, halo, haloalkyl, haloalkenyl, haloalkynyl, oxo, thioxo, cyano, nitro, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted aralkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted cycloalkylalkynyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heterocyclylalkynyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, optionally substituted heteroarylalkenyl, optionally substituted heteroarylalkynyl, $-R^{13}-OR^{12}$, $-R^{13}-OC(O)-R^{12}$, $-R^{13}-O-R^{14}-N(R^{12})_2$, $-R^{13}-N(R^{12})-R^{14}-N(R^{12})_2$, $-R^{13}-N(R^{12})-R^{14}-N(R^{12})_2$, $-R^{13}-N(R^{12})_2$, $-R^{13}-C(O)R^{12}$, $-R^{13}-C(O)OR^{12}$, $-R^{13}-C(O)N(R^{12})_2$, $-R^{13}-C(O)N(R^{12})-R^{14}-N(R^{12})R^{13}$, $-R^{13}-C(O)N(R^{12})-R^{14}-OR^{12}$, $-R^{13}-N(R^{12})C(O)OR^{12}$, $-R^{13}-N(R^{12})C(O)R^{12}$, $-R^{13}-N(R^{12})S(O)_tR^{12}$ (where t is 1 or 2), $-R^{13}-S(O)_tOR^{12}$ (where t is 1 or 2), $-R^{13}-S(O)_pR^{12}$ (where p is 0, 1 or 2), and $-R^{13}-S(O)_tN(R^{12})_2$ (where t is 1 or 2);

each R^6 and R^7 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted aralkenyl, optionally substituted aralkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted cycloalkylalkynyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heterocyclylalkynyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, optionally substituted heteroarylalkenyl, optionally substituted heteroarylalkynyl, $-R^{10}-OR^8$, $-R^{10}-CN$, $-R^{10}-NO_2$, $-R^{10}-N(R^8)_2$, $-R^{10}-C(O)OR^8$ and $-R^{10}-C(O)N(R^8)_2$, or any R^6 and R^7, together with the common nitrogen to which they are both attached, form an optionally substituted *N*-heteroaryl or an optionally substituted *N*-heterocyclyl;

each R^8 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, optionally substituted aryl, optionally substituted

aralkyl, optionally substituted aralkenyl, optionally substituted aralkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted cycloalkylalkenyl, optionally substituted cycloalkylalkynyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkenyl, optionally substituted heterocyclylalkynyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, optionally substituted heteroarylalkenyl, and optionally substituted heteroarylalkynyl;

each R^9 is independently selected from the group consisting of a direct bond, an optionally substituted straight or branched alkylene chain, an optionally substituted straight or branched alkenylene chain and an optionally substituted straight or branched alkynylene chain;

each R^{10} is independently selected from the group consisting of an optionally substituted straight or branched alkylene chain, an optionally substituted straight or branched alkenylene chain and an optionally substituted straight or branched alkynylene chain;

each R^{11} is independently selected from the group consisting of hydrogen, alkyl, cyano, nitro and $-OR^8$;

each R^{12} is independently selected from the group consisting of hydrogen, alkyl, alkenyl, haloalkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heteroaryl , optionally substituted heteroarylalkyl, $-R^{10}-OR^8$, $-R^{10}-CN$, $-R^{10}-NO_2$, $-R^{10}-N(R^8)_2$, $-R^{10}-C(O)OR^8$ and $-R^{10}-C(O)N(R^8)_2$, or two $R^{12's}$, together with the common nitrogen to which they are both attached, form an optionally substituted *N*-heterocyclyl or an optionally substituted *N*-heteroaryl;

each R^{13} is independently selected from the group consisting of a direct bond, an optionally substituted straight or branched alkylene chain and an optionally substituted straight or branched alkenylene chain; and

each R^{14} is independently selected from the group consisting of an optionally substituted straight or branched alkylene chain and an optionally substituted straight or branched alkenylene chain;

as an isolated stereoisomer or mixture thereof or as a tautomer or mixture thereof, or a pharmaceutically acceptable salt or N-oxide thereof.

~~64~~13. The ~~AXLi for~~ use according to any one of claims 1 to ~~62~~11, wherein the AXLi is selected from the group consisting of:

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

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

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

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

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

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

1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(*t*-butoxycarbonylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-(7-(acetamido)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-(7-((2*R*)-2-(methoxycarbonyl)pyrrolidin-1-yl)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-(7-(4,4-difluoropiperidin-1-yl)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-(7-((methoxycarbonylmethyl)(methyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-(7-((2*R*)-2-(carboxy)pyrrolidin-1-yl)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-(7-(4-(ethoxycarbonyl)piperidin-1-yl)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-(7-(4-(carboxy)piperidin-1-yl)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-(7-((carboxymethyl)(methyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-(7-(4-(ethoxycarbonylmethyl)piperazin-1-yl)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-(7-(4-(carboxymethyl)piperazin-1-yl)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-(7-(pyrrolidin-1-yl)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-1-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-amino-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*s*)-7-(di(cyclopropylmethyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-((2-methylpropyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-((propyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(dipropylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(diethylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(cyclohexylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(cyclopentylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-((1-cyclopentylethyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(2-propylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-((3,3-dimethylbut-2-yl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-((cyclohexylmethyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(di(cyclohexylmethyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-((5-chlorothien-2-yl)methyl)amino-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-((2-carboxyphenyl)methyl)amino-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-((3-bromophenyl)methyl)amino-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(dimethylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(cyclobutylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(3-pentylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-((2,2-dimethylpropyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(di(cyclopentylmethyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-((cyclopentylmethyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(di(bicyclo[2.2.1]hept-2-en-5-ylmethyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-((bicyclo[2.2.1]hept-2-en-5-ylmethyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;

1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(3-methylbutylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(di(3-methylbutyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(2-ethylbutylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(but-2-enylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(butyl(but-2-enyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-pyrido[2',3':6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^5-((7*S*)-7-(*t*-butoxycarbonylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-pyrido[2',3':6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-amino-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-pyrido[2',3':6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(dimethylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-pyrido[2',3':6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(diethylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-pyrido[2',3':6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(dipropylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-pyrido[2',3':6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(di(cyclopropylmethyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-pyrido[2',3':6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(di(3-methylbutyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-pyrido[2',3':6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(cyclobutylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-pyrido[2',3':6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(cyclohexylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-pyrido[2',3':6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-((methylethyl)amino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
1-(6,7-dihydro-5*H*-pyrido[2',3':6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(cyclopentylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine; and
1-(6,7-dihydro-5*H*-pyrido[2',3':6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7*S*)-7-(2-butylamino)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine;
or pharmaceutically acceptable salts thereof.

5314. The ~~AXLi for~~ use according to any one of claims 1 to ~~51~~11, wherein the AXLi is:

(i) 1-(6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*c*]pyridazin-3-yl)-N^3-((7-(*S*)-pyrrolidin-1-yl)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulene-2-yl)-1*H*-1,2,4-triazole-3,5-diamine, or a pharmaceutically acceptable salt thereof;~~.~~ Or

(ii)

~~54. The AXLi for use according to any one of claims 1 to 51, wherein the AXLi is~~ bemcentinib.

5515. The ~~AXLi for~~ use according to any one of claims 1 to ~~51~~11, wherein the AXLi is 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);
- Sitravatinib (CAS No. 1123837-84-2 ; UNII CWG62Q1VTB);
- XL092;
- Glesatinib (CAS No. 936694-12-1; UNII 7Q29OXD98N); and
- foretinib (CAS No. 849217-64-7; UNII 81FH7VK1C4).

5616. The ~~AXLi for~~ use according to any one of claims 1 to ~~51~~11, wherein the AXLi is an antibody.

5717. The ~~AXLi for~~ use according to claim ~~56~~16 wherein the antibody:

(i) is selected from the group consisting of:

- the 1613F12 antibody disclosed in WO/2013/064685;
- the 110D7 antibody disclosed in WO/2014/068139;
- the 1003A2 antibody disclosed in WO/2014/068139;
- the 1024G11 antibody disclosed in WO/2014/068139;
- the hu10G5 antibody disclosed in WO/2017/220695; and
- the YW327.6S2 antibody disclosed in WO/2011/159980~~.~~;

(ii)

~~58. The AXLi for use according to claim 57, wherein the antibody~~ comprises the 6 CDRs having the sequences of SEQ ID Nos. 1 to 6;~~.~~

(iii)

~~59. The AXLi for use according to claim 57, wherein the antibody~~ comprises the 6 CDRs having the sequences of SEQ ID Nos. 7 to 12;~~.~~

(iv)

~~60. The AXLi for use according to claim 57, wherein the antibody~~ comprises:

- a VH domain having the sequence of SEQ ID No. 13 and a VL domain having the sequence of SEQ ID NO.15;

- a VH domain having the sequence of SEQ ID No. 13 and a VL domain having the sequence of SEQ ID NO.16;
- a VH domain having the sequence of SEQ ID No. 14 and a VL domain having the sequence of SEQ ID NO.15; or
- a VH domain having the sequence of SEQ ID No. 14 and a VL domain having the sequence of SEQ ID NO.16;.

(v)

~~61. The AXLi for use according to claim 57, wherein the antibody~~ comprises all 6 of the CDRs comprised in:

- a VH domain having the sequence of SEQ ID No. 13 and a VL domain having the sequence of SEQ ID NO.15;
- a VH domain having the sequence of SEQ ID No. 13 and a VL domain having the sequence of SEQ ID NO.16;
- a VH domain having the sequence of SEQ ID No. 14 and a VL domain having the sequence of SEQ ID NO.15; or
- a VH domain having the sequence of SEQ ID No. 14 and a VL domain having the sequence of SEQ ID NO.16;.

~~62~~18. The ~~AXLi for~~ use according to claim ~~56~~16, wherein the antibody is Tilvestamab,

~~63~~19. A pharmaceutical compostion comprising an AXLi ~~according to~~as defined in any one of claims ~~52~~ 12 to ~~62~~ 18 and a second anti-viral agent.

~~64~~20. The pharmaceutical compostion of claim ~~5~~19, wherein the second anti-viral agent is as defined in any one of claims ~~25~~ 5 to ~~35~~8.