Claims

We Claim:

1. A crystalline form of (10*R*)-7-amino-12-fluoro-2,10,16-trimethyl-15-oxo-10,15,16,17-tetrahydro-2*H*-8,4-(metheno)pyrazolo[4,3-*h*][2,5,11]benzoxadiazacyclotetradecine-3-carbonitrile (lorlatinib) free base, having a powder X-ray diffraction (PXRD) pattern comprising two or more peaks at 2θ values selected of: 9.6, 10.1 and 16.2 °2θ ± 0.2 °2θ.

2. The crystalline form of claim 1, having a PXRD pattern further comprising a peak at the 2θ value of: 17.3 °2θ ± 0.2 °2θ.

3. The crystalline form of claim 2, having a PXRD pattern further comprising a peak at the 2θ value of: 14.3 °2θ ± 0.2 °2θ.

4. The crystalline form of claims 1, having a Raman spectrum comprising wavenumber (cm^{-1}) values of: 2229 and 2240 cm^{-1} ± 2 cm^{-1}.

5. The crystalline form of claims 1, having a ^{13}C solid state NMR spectrum comprising resonance (ppm) values of: 39.1 and 142.1 ppm ± 0.2 ppm.

6. The crystalline form of claims 1, having a ^{19}F solid state NMR spectrum comprising resonance (ppm) values of: -108.2 and -115.2 ppm ± 0.2 ppm.

7. A crystalline form of lorlatinib free base, having a Raman spectrum comprising wavenumber (cm^{-1}) values of: 2229 and 2240 cm^{-1} ± 2 cm^{-1}.

8. The crystalline form of claim 7, having a Raman spectrum further comprising the wavenumber (cm^{-1}) value of: 1619 cm^{-1} ± 2 cm^{-1}.

9. The crystalline form of claim 8, having a Raman spectrum further comprising the wavenumber (cm^{-1}) value of: 1553 cm^{-1} ± 2 cm^{-1}.

10. The crystalline form of claim 9, having a Raman spectrum further comprising the wavenumber (cm^{-1}) value of: 774 cm^{-1} ± 2 cm^{-1}.

11. The crystalline form of claims 7, having a ^{13}C solid state NMR spectrum comprising resonance (ppm) values of: 39.1 and 142.1 ppm ± 0.2 ppm.

12. The crystalline form of claims 7, having a ^{19}F solid state NMR spectrum comprising resonance (ppm) values of: -108.2 and -115.2 ppm ± 0.2 ppm.

13. A crystalline form of lorlatinib free base, having a ^{13}C solid state NMR spectrum comprising two or more resonance (ppm) values of: 39.1and 142.1 ppm ± 0.2 ppm.

14. The crystalline form of claim 13, having a ^{13}C solid state NMR spectrum further comprising the resonance (ppm) value of: 112.3 ppm ± 0.2 ppm.

15. The crystalline form of claim 14, having a ^{13}C solid state NMR spectrum further comprising the resonance (ppm) value of: 25.8 ppm ± 0.2 ppm.

16. The crystalline form of claim 15, having a ^{13}C solid state NMR spectrum further comprising the resonance (ppm) value of: 117.7 ppm ± 0.2 ppm.

17. A crystalline form of lorlatinib free base, having a ^{19}F solid state NMR spectrum comprising a resonance (ppm) value selected from the group consisting of: -108.2 and -115.2 ppm ± 0.2 ppm.

18. A pharmaceutical composition comprising the crystalline form of lorlatinib free base according to claims 1, and a pharmaceutically acceptable carrier or excipient.

19. Use of the crystalline form of lorlatinib free base according to claim 1 in the manufacture of a medicament for the treatment of abnormal cell growth, wherein the abnormal cell growth is cancer mediated by anaplastic lymphoma kinase (ALK) or c-ros oncogene 1 receptor tyrosine kinase (ROS1).

20. Use of the crystalline form of lorlatinib free base according to claim 19, wherein the cancer is non-small cell lung cancer (NSCLC).

21. The crystalline form of lorlatinib free base according to claim 1 for use in the treatment of a cancer mediated by anaplastic lymphoma kinase (ALK) or c-ros oncogene 1 receptor tyrosine kinase (ROS1).