CLAIMS

WHAT IS CLAIMED IS:

1. Use of a combination comprising a therapeutically effective amount of: (a) (R)-2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile or a pharmaceutically acceptable salt thereof, and (b) 2-{3-[4-(1H-indazol-5-ylamino)-2-quinazolinyl]phenoxy}-N-(propan-2-yl) acetamide or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of systemic sclerosis (scleroderma) in a human patient.

2. Use of a combination comprising a therapeutically effective amount of: (a) (R)-2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile or a pharmaceutically acceptable salt thereof, and (b) 2-{3-[4-(1H-indazol-5-ylamino)-2-quinazolinyl]phenoxy}-N-(propan-2-yl) acetamide or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of chronic lung allograft dysfunction (CLAD) in a human patient.

3. Use of a combination comprising a therapeutically effective amount of: (a) (R)-2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile or a pharmaceutically acceptable salt thereof, and (b) 2-{3-[4-(1H-indazol-5-ylamino)-2-quinazolinyl]phenoxy}-N-(propan-2-yl) acetamide or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of restrictive allograft syndrome (RAS) in a human patient.

4. Use of a combination comprising a therapeutically effective amount of: (a) (R)-2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile or a pharmaceutically acceptable salt thereof, and (b) 2-{3-[4-(1H-indazol-5-ylamino)-2-quinazolinyl]phenoxy}-N-(propan-2-yl) acetamide or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of bronchiolitis obliterans syndrome (BOS) in a human patient.

5. Use of a combination comprising a therapeutically effective amount of: (a) (R)-2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-

methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile or a pharmaceutically acceptable salt thereof, and (b) 2-{3-[4-(1H-indazol-5-ylamino)-2-quinazolinyl]phenoxy}-N-(propan-2-yl) acetamide or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of graft-versus-host disease (GVHD) in a human patient.

6. The use of claim 5, wherein GVHD is chronic GVHD (cGVHD).

7. The use of any one of claims 1-6, wherein the 2-{3-[4-(1H-indazol-5-ylamino)-2-quinazolinyl]phenoxy}-N-(propan-2-yl) acetamide or a pharmaceutically acceptable salt thereof is to be administered at a daily dosage equivalent to up to about 400 mg of the free base.

8. The use of claim 7, wherein the 2-{3-[4-(1H-indazol-5-ylamino)-2-quinazolinyl]phenoxy}-N-(propan-2-yl) acetamide or a pharmaceutically acceptable salt thereof is to be administered at a daily dosage equivalent to about 50-400 mg of the free base.

9. The use of claim 7 or 8, wherein the 2-{3-[4-(1H-indazol-5-ylamino)-2-quinazolinyl]phenoxy}-N-(propan-2-yl) acetamide or a pharmaceutically acceptable salt thereof is to be administered at a dose equivalent to about 50 mg of the free base, 100 mg of the free base, 150 mg of the free base, or 200 mg of the free base.

10. The use of claim 9, wherein the dose is to be administered once or twice daily.

11. The use of any one of claims 1-10, wherein the 2-{3-[4-(1H-indazol-5-ylamino)-2-quinazolinyl]phenoxy}-N-(propan-2-yl) acetamide or a pharmaceutically acceptable salt thereof is to be administered orally.

12. The use of any one of claims 1-11, wherein the (R)-2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile or pharmaceutically acceptable salt thereof is to be administered at a daily dosage of up to about 800 mg, or at a daily dosage of about 50-800 mg.

13. The use of claim 12, wherein the (R)-2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile or a pharmaceutically acceptable salt thereof is to be administered at a dose of about 100 mg, 200 mg, or 400 mg.

14. The use of claim 13, wherein the dose of the (R)-2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile or a pharmaceutically acceptable salt thereof is to be administered once a day or twice a day.

15. The use of any one of claims 1-14, wherein the medicament comprises:

(a) (E) isomer (R)-2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile, or a pharmaceutically acceptable salt thereof;

(b) the (Z) isomer (R)-2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile, or a pharmaceutically acceptable salt thereof; or

(c) a mixture of (E) and (Z) isomers of (R)-2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile, or a pharmaceutically acceptable salt thereof.

16. The use of any one of claims 1-15, wherein the (R)-2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile or pharmaceutically acceptable salt thereof is to be administered orally.

17. The use of any one of claims 1-16, wherein the (R)-2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile or a pharmaceutically acceptable salt thereof, and 2-{3-[4-(1H-indazol-5-ylamino)-2-quinazolinyl]phenoxy}-N-(propan-2-yl) acetamide or a pharmaceutically acceptable salt thereof, are to be administered separately, sequentially, or simultaneously.