

WE CLAIM:

1. Use of a composition in the manufacture of a medicament for treating pulmonary hypertension associated with lung disease, the composition comprising a fusion protein comprising:

a) an ActRIIA polypeptide comprising an amino acid sequence that is at least 95% identical to an amino acid sequence corresponding to residues 30-110 of SEQ ID NO: 1;

b) an Fc domain of an IgG1 immunoglobulin; and

c) a linker domain,

wherein the linker domain is positioned between the ActRIIA polypeptide and the Fc domain of the IgG1 immunoglobulin, and wherein the administration of the composition reduces the right ventricular systolic pressure (RVSP) by at least 10%.

2. The use according to claim 1, wherein the ActRII polypeptide comprises an amino acid sequence of SEQ ID NO: 2.

3. The use according to claim 1 or 2, wherein the linker domain is selected from the group consisting of: TGGG (SEQ ID NO: 20), TGGGG (SEQ ID NO: 18), SGGGG (SEQ ID NO: 19), GGGGS (SEQ ID NO: 22), GGG (SEQ ID NO: 16), GGGG (SEQ ID NO: 17), and SGGG (SEQ ID NO: 21).

4. The use according to any one of claims 1-3, wherein the linker domain is TGGG (SEQ ID NO: 20).

5. The use according to any one of claims 1-4, wherein the Fc domain comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO: 32.

6. The use according to any one of claims 1-4, wherein the Fc domain comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 32.

7. The use according to any one of claims 1-6, wherein the Fc domain comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 32.
8. The use according to any one of claims 1-7, wherein the fusion protein comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO: 23.
9. The use according to any one of claims 1-7, wherein the fusion protein comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 23.
10. The use according to any one of claims 1-7, wherein the fusion protein comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 23.
11. The use according to any one of claims 1-7, wherein the fusion protein comprises an amino acid sequence of SEQ ID NO: 23.
12. The use according to any one of claims 1-7, wherein the fusion protein comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO: 41.
13. The use according to any one of claims 1-7, wherein the fusion protein comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 41.
14. The use according to any one of claims 1-7, wherein the fusion protein comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 41.
15. The use according to any one of claims 1-7, wherein the fusion protein comprises an amino acid sequence of SEQ ID NO: 41.
16. The use according to any one of claims 1-15, wherein the fusion protein is part of a homodimer protein complex.
17. The use according to any one of claims 1-16, wherein the fusion protein is glycosylated.
18. The use according to any one of claims 1-17, wherein the fusion protein binds to one or more ligands selected from the group consisting of: activin A, activin B, GDF11, BMP10, GDF8, and BMP6.

19. Use of a composition in the manufacture of a medicament for treating pulmonary hypertension associated with obstructive lung disease, the composition comprising a fusion protein comprising:

a) an ActRIIA polypeptide comprising an amino acid sequence that is at least 95% identical to an amino acid sequence corresponding to residues 30-110 of SEQ ID NO: 1;

b) an Fc domain of an IgG1 immunoglobulin; and

c) a linker domain,

wherein the linker domain is positioned between the ActRIIA polypeptide and the Fc domain of the IgG1 immunoglobulin.

20. The use according to claim 19, wherein the ActRII polypeptide comprises an amino acid sequence of SEQ ID NO: 2.

21. The use according to claim 19 or 20, wherein the linker domain is selected from the group consisting of: TGGG (SEQ ID NO: 20), TGGGG (SEQ ID NO: 18), SGGGG (SEQ ID NO: 19), GGGGS (SEQ ID NO: 22), GGG (SEQ ID NO: 16), GGGG (SEQ ID NO: 17), and SGGG (SEQ ID NO: 21).

22. The use according to any one of claims 19-21, wherein the linker domain is TGGG (SEQ ID NO: 20).

23. The use according to any one of claims 19-22, wherein the Fc domain comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO: 32.

24. The use according to any one of claims 19-23, wherein the Fc domain comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 32.

25. The use according to any one of claims 19-24, wherein the Fc domain comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 32.

26. The use according to any one of claims 19-25, wherein the fusion protein comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO: 23.

27. The use according to any one of claims 19-25, wherein the fusion protein comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 23.
28. The use according to any one of claims 19-25, wherein the fusion protein comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 23.
29. The use according to any one of claims 19-25, wherein the fusion protein comprises an amino acid sequence of SEQ ID NO: 23.
30. The use according to any one of claims 19-25, wherein the fusion protein comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO: 41.
31. The use according to any one of claims 19-25, wherein the fusion protein comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 41.
32. The use according to any one of claims 19-25, wherein the fusion protein comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 41.
33. The use according to any one of claims 19-25, wherein the fusion protein comprises an amino acid sequence of SEQ ID NO: 41.
34. The use according to any one of claims 19-33, wherein the fusion protein is part of a homodimer protein complex.
35. The use according to any one of claims 19-34, wherein the fusion protein is glycosylated.
37. The use according to any one of claims 19-35, wherein the obstructive lung disease is selected from the group consisting of chronic obstructive pulmonary disease (COPD), cystic fibrosis, asthma, emphysema, lymphangioleiomyomatosis, and chronic bronchitis.
38. The use according to any one of claims 1-37, wherein the administration of the composition prevents or reduces pulmonary hypertension Functional Class progression as recognized by the World Health Organization (WHO).