

We Claim:

1. A method of treating post-capillary pulmonary hypertension (PcPH), comprising administering to a patient in need thereof an effective amount of a polypeptide comprising an amino acid sequence that is at least 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to an amino acid sequence that begins at any one of amino acids 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 of SEQ ID NO: 1 and ends at any one of amino acids 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, or 135 of SEQ ID NO: 1.
2. A method of treating, preventing, or reducing the progression rate and/or severity of one or more complications of post-capillary pulmonary hypertension, comprising administering to a patient in need thereof an effective amount of a polypeptide comprising an amino acid sequence that is at least 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to an amino acid sequence that begins at any one of amino acids 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 of SEQ ID NO: 1 and ends at any one of amino acids 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, or 135 of SEQ ID NO: 1.
3. The method of claim 2, wherein the one or more complications of post-capillary pulmonary hypertension is selected from the group consisting of: smooth muscle and/or endothelial cell proliferation in the pulmonary artery, angiogenesis in the pulmonary artery, dyspnea, chest pain, pulmonary vascular remodeling, right ventricular hypertrophy, left ventricular hypertrophy, left atrium dilation, left ventricular fibrosis, right ventricular fibrosis, and pulmonary fibrosis.
4. The method of any one of claims 1-3, wherein the PcPH is isolated post-capillary pulmonary hypertension (IpcPH).
5. The method of any one of claims 1-3, wherein the PcPH is combined post- and pre-capillary PH (CpcPH).
6. The method of any one of claims 1-5, wherein the patient has Group 2 pulmonary hypertension as recognized by the World Health Organization (WHO).

7. The method of any one of claims 1-6, wherein the patient has pulmonary hypertension due to heart failure with preserved left ventricular ejection fraction (LVEF).
8. The method of any one of claims 1-6, wherein the patient has pulmonary hypertension due to heart failure with reduced left ventricular ejection fraction (LVEF).
- 5 9. The method of any one of claims 1-6, wherein the patient has valvular heart disease.
10. The method of any one of claims 1-6, wherein the patient has congenital/acquired cardiovascular conditions leading to post-capillary PH.
11. The method of any one of claims 1-5, wherein the patient has Group 5 pulmonary hypertension as recognized by the WHO.
- 10 12. The method of any one of claims 1-5 and 11, wherein the patient has pulmonary hypertension with unclear and/or multifactorial mechanisms.
13. The method of claim 9, wherein the valvular heart disease is aortic regurgitation.
14. The method of claim 9, wherein the valvular heart disease is aortic stenosis.
15. The method of claim 9, wherein the valvular heart disease is mitral valve regurgitation.
- 15 16. The method of claim 9, wherein the valvular heart disease is mitral valve stenosis.
17. The method of any one of claims 1-17, wherein the patient has a mean pulmonary arterial pressure (mPAP) selected from the group consisting of:
- a. an mPAP of at least 20 mmHg;
 - b. an mPAP of at least 25 mmHg;
 - 20 c. an mPAP of at least 30 mmHg;
 - d. an mPAP of at least 35 mmHg;
 - e. an mPAP of at least 40 mmHg;
 - f. an mPAP of at least 45 mmHg; and
 - g. an mPAP of at least 50 mmHg.
- 25 18. The method of any one of claims 1-17, wherein the method reduces mPAP in the patient.

19. The method of any one of claims 1-18, wherein the method reduces the mPAP in the patient by at least 10% (*e.g.*, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or at least 50%).
20. The method of any one of claims 1-18, wherein the method reduces the mPAP by at least 3 mmHg (*e.g.*, at least 3, 5, 7, 10, 12, 15, 20, or 25 mm Hg) in the patient.
- 5 21. The method of any one of claims 1-20, wherein the patient has a pulmonary arterial wedge pressure (PAWP) of greater than 15 mmHg.
22. The method of claim 21, wherein the method decreases the PAWP in the patient.
23. The method of claim 22, wherein the method reduces the PAWP in the patient by at least 10% (*e.g.*, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or at least 50%).
- 10 24. The method of any one of claims 1-20, wherein the patient has a left ventricular end diastolic pressure (LVEDP) of greater than 15 mmHg.
25. The method of claim 24, wherein the method decreases the LVEDP in the patient.
26. The method of claim 24, wherein the method reduces the LVEDP in the patient by at least 10% (*e.g.*, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or at least 50%).
- 15 27. The method of any one of claims 1-4 and 6-26, wherein the patient has a diastolic pressure gradient (DPG) of less than 7 mmHg.
28. The method of any one of claims 1-3 and 5-26, wherein the patient has a DPG of at least 7 mmHg.
29. The method of claim 28, wherein the method decreases the DPG in the patient.
- 20 30. The method of claim 29, wherein the method reduces the DPG in the patient by at least 10% (*e.g.*, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or at least 50%).
31. The method of any one of claims 1-4 and 6-30, wherein the patient has a transpulmonary pressure gradient (TPG) of less than or equal to 12 mm Hg.
32. The method of any one of claims 1-3 and 5-30, wherein the patient has a TPG of greater
25 than 12 mm Hg.
33. The method of claim 32, wherein the method decreases the TPG in the patient.

34. The method of claim 33, wherein the method reduces the TPG in the patient by at least 10% (*e.g.*, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or at least 50%).
35. The method of any one of claims 1-3 and 5-34, wherein the patient has a pulmonary vascular resistance (PVR) greater than or equal to 3 Wood Units.
- 5 36. The method of claim 35, wherein the method decreases the PVR in the patient.
37. The method of claim 36, wherein the method reduces the PVR in the patient by at least 10% (*e.g.*, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or at least 50%).
38. The method of any one of claims 1-4 and 6-37, wherein the method prevents the progression of IpcPH to CpcPH.
- 10 39. The method of any one of claims 1-4 and 6-37, wherein the method reduces the development of a pre-capillary component of PH.
40. The method of any one of claims 1-6 and 8-39, wherein the patient has preserved left ventricular ejection fraction.
41. The method of claim 40, wherein the preserved left ventricular ejection fraction is
15 greater than 45%.
42. The method of claim 41, wherein the preserved left ventricular fraction is measured using echocardiography.
43. The method of any one of claims 1-42, wherein the patient has diastolic dysfunction of the left ventricle.
- 20 44. The method of any one of claims 1-42, wherein the patient has systolic dysfunction of the left ventricle.
45. The method of any one of claims 1-44, wherein the method decreases right ventricular hypertrophy in the patient.
46. The method of claim 45, wherein the method decreases right ventricular hypertrophy
25 in the patient by at least 10% (*e.g.*, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or at least 50%).
47. The method of any one of claims 1-46, wherein the method decreases left ventricular hypertrophy in the patient.

48. The method of claim 47, wherein the method decreases left ventricular hypertrophy in the patient by at least 10% (*e.g.*, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or at least 50%).
49. The method of any one of claims 1-48, wherein the method decreases smooth muscle hypertrophy in the patient.
- 5 50. The method of claim 49, wherein the method decreases smooth muscle hypertrophy in the patient by at least 10% (*e.g.*, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or at least 50%).
51. The method of any one of claims 1-50, wherein the method decreases pulmonary arteriole muscularity in the patient.
52. The method of claim 51, wherein the method decreases pulmonary arteriole muscularity
10 in the patient by at least 10% (*e.g.*, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or at least 50%).
53. The method of any one of claims 1-52, wherein the patient has a right ventricular systolic pressure (RVSP) of greater than 35 mmHg.
54. The method of claim 53, wherein the method decreases the RVSP in the patient.
- 15 55. The method of claim 54, wherein the method reduces the RVSP in the patient by at least 10% (*e.g.*, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or at least 50%).
56. The method of any one of claims 1-55, wherein the patient has left ventricular fibrosis.
57. The method of claim 56, wherein the method decreases the left ventricular fibrosis in the patient.
- 20 58. The method of claim 57, wherein the method reduces the left ventricular fibrosis in the patient by at least 10% (*e.g.*, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or at least 50%).
59. The method of any one of claims 1-58, wherein the patient has right ventricular fibrosis.
60. The method of claim 59, wherein the method decreases the right ventricular fibrosis in the patient.
- 25 61. The method of claim 60, wherein the method reduces the right ventricular fibrosis in the patient by at least 10% (*e.g.*, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or at least 50%).
62. The method of any one of claims 1-61, wherein the patient has pulmonary fibrosis.

63. The method of claim 62, wherein the method decreases the pulmonary fibrosis in the patient.
64. The method of claim 63, wherein the method reduces the pulmonary fibrosis in the patient by at least 10% (*e.g.*, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or at least 50%).
- 5 65. The method of any one of claims 1-64, wherein the patient has a comorbidity selected from the group consisting of systemic hypertension, diabetes mellitus, obesity, coronary artery disease (CAD), heart failure, and anemia.
66. The method of any one of claims 1-65, comprising further administering to the patient an additional active agent and/or supportive therapy.
- 10 67. The method of claim 66, wherein the additional active agent and/or supportive therapy is selected from the group consisting of: beta-blockers, angiotensin-converting enzyme inhibitors (ACE inhibitors), angiotensin receptor blockers (ARBs), neprilysin inhibitors, angiotensin receptor-neprilysin inhibitors (ARNI), mineralocorticoid receptor antagonists (MRA), hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blockers, diuretic
15 agents, lipid-lowering medications, endothelin blockers, PDE5 inhibitors, prostacyclins, cardiac resynchronization therapy, valve replacement, valve repair, implantable cardioverter-defibrillator (ICD), or a left ventricular assist device (LVAD).
68. The method of claim 66, wherein the additional active agent and/or supportive therapy is selected from the group consisting of: prostacyclin and derivatives thereof (*e.g.*,
20 epoprostenol, treprostinil, and iloprost); prostacyclin receptor agonists (*e.g.*, selexipag); endothelin receptor antagonists (*e.g.*, thelin, ambrisentan, macitentan, and bosentan); calcium channel blockers (*e.g.*, amlodipine, diltiazem, and nifedipine); anticoagulants (*e.g.*, warfarin); diuretics; oxygen therapy; atrial septostomy; pulmonary thromboendarterectomy; phosphodiesterase type 5 inhibitors (*e.g.*, sildenafil and tadalafil); activators of soluble
25 guanylate cyclase (*e.g.*, cinaciguat and riociguat); ASK-1 inhibitors (*e.g.*, CHA; SCH79797; GS-4997; MSC2032964A; 3H-naphtho[1,2,3-de]quinoline-2,7-diones, NQDI-1; 2-thioxo-thiazolidines, 5-bromo-3-(4-oxo-2-thioxo-thiazolidine-5-ylidene)-1,3-dihydro-indol-2-one); NF- κ B antagonists (*e.g.*, dh404, CDDO-epoxide; 2,2-difluoropropionamide; C28 imidazole (CDDO-Im); 2-cyano-3,12-dioxoolean-1,9-dien-28-oic acid (CDDO); 3-Acetyloleanolic Acid;
30 3-Trifluoroacetyloleanolic Acid; 28-Methyl-3-acetyloleanane; 28-Methyl-3-trifluoroacetyloleanane; 28-Methoxyoleanolic Acid; SZC014; SCZ015; SZC017; PEGylated

- derivatives of oleanolic acid; 3-O-(beta-D-glucopyranosyl) oleanolic acid; 3-O-[beta-D-glucopyranosyl-(1-->3)-beta-D-glucopyranosyl] oleanolic acid; 3-O-[beta-D-glucopyranosyl-(1-->2)-beta-D-glucopyranosyl] oleanolic acid; 3-O-[beta-D-glucopyranosyl-(1-->3)-beta-D-glucopyranosyl] oleanolic acid 28-O-beta-D-glucopyranosyl ester; 3-O-[beta-D-glucopyranosyl-(1-->2)-beta-D-glucopyranosyl] oleanolic acid 28-O-beta-D-glucopyranosyl ester; 3-O-[alpha-L-rhamnopyranosyl-(1-->3)-beta-D-glucuronopyranosyl] oleanolic acid; 3-O-[alpha-L-rhamnopyranosyl-(1-->3)-beta-D-glucuronopyranosyl] oleanolic acid 28-O-beta-D-glucopyranosyl ester; 28-O-beta-D-glucopyranosyl-oleanolic acid; 3-O-beta-D-glucopyranosyl (1-->3)-beta-D-glucopyranosiduronic acid (CS1); oleanolic acid 3-O-beta-D-glucopyranosyl (1-->3)-beta-D-glucopyranosiduronic acid (CS2); methyl 3,11-dioxolean-12-en-28-olate (DIOXOL); ZCVI4-2; Benzyl 3-dehydr-oxy-1,2,5-oxadiazolo[3',4':2,3]oleanolate); eplerenone, spironolactone, ivabradine, implantable cardioverter-defibrillator (ICD), a left ventricular assist device (LVAD), or lung and/or heart transplantation.
69. The method of any one of claims 1-68, wherein the patient has elevated brain natriuretic peptide (BNP) levels as compared to a healthy patient.
70. The method of claim 69, wherein the patient has a BNP level of at least 100 pg/mL (*e.g.*, 100, 150, 200, 300, 400, 500, 1000, 3000, 5000, 10,000, 15,000, or 20,000 pg/mL).
71. The method of claim 69 or claim 70, wherein the method decreases BNP levels in the patient by at least 10% (*e.g.*, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, or at least 80%).
72. The method of any one of claims 1-70, wherein the method decreases BNP levels to normal levels (*i.e.*, <100 pg/ml).
73. The method of any one of claims 1-72, wherein the method decreases NT-proBNP levels in the patient.
74. The method of any one of claims 1-73, wherein the method decreases NT-proBNP levels in the patient by at least 10% (*e.g.*, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, or at least 80%).
75. The method of any one of claims 1-74, wherein the method decreases NT-proBNP levels in the patient by at least 30%.

76. The method of any one of claims 1-75, wherein the method decreases NT-proBNP levels to normal levels.
77. The method of claim 76, wherein the normal level of NT-proBNP is <100 pg/ml.
78. The method of any one of claims 1-77, wherein the method increases exercise capacity
5 of the patient.
79. The method of any one of claims 1-78, wherein the patient has a 6-minute walk distance from 150 to 400 meters.
80. The method of any one of claims 1-78, wherein the patient has a 6-minute walk distance from 150 to 550 meters.
- 10 81. The method of any one of claims 1-80, wherein the method increases the patient's 6-minute walk distance.
82. The method of any one of claims 1-81, wherein the method increases the patient's 6-minute walk distance by at least 10 meters (*e.g.*, at least 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, 250, 300, or more than 400 meters).
- 15 83. The method of any one of claims 1-82, wherein the method reduces the patient's Borg dyspnea index (BDI).
84. The method of any one of claims 1-83, wherein the method reduces the patient's BDI by at least 0.5 index points (*e.g.*, at least 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 6.5, 7, 7.5, 8, 8.5, 9, 9.5, or 10 index points).
- 20 85. The method of any one of claims 1-84, wherein the patient has decreased renal function.
86. The method of any one of claims 1-85, wherein the method further improves renal function.
87. The method of any one of claims 1-86, wherein the patient has Functional Class II or Class III pulmonary hypertension in accordance with the World Health Organization's
25 functional classification system for pulmonary hypertension.
88. The method of any one of claims 1-86, wherein the patient has Functional Class I, Class II, Class III, or Class IV pulmonary hypertension as recognized by the World Health Organization.

89. The method of any one of claims 1-88, wherein the method prevents or delays pulmonary hypertension Functional Class progression (*e.g.*, prevents or delays progression from Functional Class I to Class II, Class II to Class III, or Class III to Class IV pulmonary hypertension as recognized by the World Health Organization).
- 5 90. The method of any one of claims 1-88, wherein the method promotes or increases pulmonary hypertension Functional Class regression (*e.g.*, promotes or increases regression from Class IV to Class III, Class III to Class II, or Class II to Class I pulmonary hypertension as recognized by the World Health Organization).
91. The method of any one of claims 1-82, wherein the patient has Functional Class II or
10 Class III pulmonary hypertension in accordance with the New York Heart Association's functional classification system for pulmonary hypertension.
92. The method of any one of claims 1-82, wherein the patient has Functional Class I, Class II, Class III, or Class IV pulmonary hypertension as recognized by the New York Heart Association.
- 15 93. The method of any one of claims 1-82, 91, and 92, wherein the method prevents or delays pulmonary hypertension Functional Class progression (*e.g.*, prevents or delays progression from Functional Class I to Class II, Class II to Class III, or Class III to Class IV pulmonary hypertension as recognized by the New York Heart Association).
94. The method of any one of claims 1-82, 91, and 92, wherein the method promotes or
20 increases pulmonary hypertension Functional Class regression (*e.g.*, promotes or increases regression from Class IV to Class III, Class III to Class II, or Class II to Class I pulmonary hypertension as recognized by the New York Heart Association).
95. The method of any one of claims 1-94, wherein the method delays clinical worsening of PcPH.
- 25 96. The method of claim 95, wherein the method delays clinical worsening of PcPH in accordance with the World Health Organization's functional classification system for pulmonary hypertension.
97. The method of claim 95, wherein the method delays clinical worsening of PcPH in
30 accordance with the New York Heart Association's functional classification system for pulmonary hypertension.

98. The method of any one of claims 1-97, wherein the method reduces the risk of hospitalization for one or more complications associated with PcPH.
99. The method of any one of claims 1-98, wherein the patient has a hemoglobin level from >8 and <15 g/dl.
- 5 100. The method of any one of claims 1-99, wherein the patient has been treated with one or more vasodilators.
101. The method of any one of claims 1-100, wherein the patient has been treated with one or more agents selected from the group consisting of: phosphodiesterase type 5 inhibitors, soluble guanylate cyclase stimulators, prostacyclin receptor agonist, and endothelin receptor
10 antagonists.
102. The method of claim 101, wherein the one or more agents is selected from the group consisting of: bosentan, sildenafil, beraprost, macitentan, selexipag, epoprostenol, treprostinil, iloprost, ambrisentan, and tadalafil.
103. The method of any one of claims 1-102, wherein the method further comprises
15 administration of one or more vasodilators.
104. The method of any one of claims 1-103, wherein the method further comprises administration of one or more agents selected from the group consisting of: phosphodiesterase type 5 inhibitors, soluble guanylate cyclase stimulators, prostacyclin receptor agonist, and endothelin receptor antagonists.
- 20 105. The method of claim 104, wherein the one or more agents is selected from the group consisting of: bosentan, sildenafil, beraprost, macitentan, selexipag, epoprostenol, treprostinil, iloprost, ambrisentan, and tadalafil.
106. The method of any one of claims 1-105, wherein the ActRII polypeptide comprises an amino acid sequence that is at least 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%,
25 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the sequence of amino acids corresponding to residues 30-110 of SEQ ID NO: 1.
107. The method of any one of claims 1-105, wherein the ActRII polypeptide comprises an amino acid sequence that is at least 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence
30 SEQ ID NO: 2.

108. The method of any one of claims 1-105, wherein the ActRII polypeptide comprises an amino acid sequence that is at least 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 3.
- 5 109. The method of any one of claims 106-108, wherein the ActRII polypeptide is a fusion protein further comprising an Fc domain of an immunoglobulin.
110. The method of claim 109, wherein the Fc domain of the immunoglobulin is an Fc domain of an IgG1 immunoglobulin.
111. The method of claim 109 or 110, wherein the Fc fusion protein further comprises a
10 linker domain positioned between the ActRII polypeptide domain and the Fc domain of the immunoglobulin.
112. The method of claim 111, 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: 22), GGGGS (SEQ ID NO: 22), GGG (SEQ ID NO: 16), GGGG (SEQ ID NO: 17), and SGGG
15 (SEQ ID NO: 21).
113. The method of any one of claims 1-112, wherein the ActRII polypeptide comprises an amino acid sequence that is at least 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 23.
- 20 114. The method of any one of claims 1-105, wherein the polypeptide comprises an amino acid sequence that is at least 90% identical to an amino acid sequence corresponding to residues 30-110 of SEQ ID NO: 1, wherein the polypeptide binds to activating and/or GDF11.
115. The method of any one of claims 1-105, wherein the polypeptide comprises an amino acid sequence that is at least 90% identical to an amino acid sequence corresponding to residues
25 21-135 of SEQ ID NO: 1, wherein the polypeptide binds to activating and/or GDF11.
116. The method of any one of claims 1-115, wherein the polypeptide is lyophilized.
117. The method of any one of claims 1-116, wherein the polypeptide is soluble.
118. The method of any one of claims 1-117, wherein the polypeptide is administered using subcutaneous injection.

119. The method of any one of claims 1-118, wherein the polypeptide is administered every 4 weeks.
120. The method of any one of claims 1-119, wherein the polypeptide is part of a homodimer protein complex.
- 5 121. The method of any one of claims 1-120, wherein the polypeptide is glycosylated.
122. The method of any one of claims 1-121, wherein the polypeptide has a glycosylation pattern obtainable by expression in a Chinese hamster ovary cell.
123. The method of any one of claims 1-122, wherein the ActRII polypeptide binds to one or more ligands selected from the group consisting of: activin A, activin B, and GDF11.
- 10 124. The method of claim 123, wherein the ActRII polypeptide further binds to one or more ligands selected from the group consisting of: BMP10, GDF8, and BMP6.
125. A kit comprising a lyophilized polypeptide and an injection device, wherein the polypeptide is an ActRII polypeptide comprising an amino acid sequence that is at least 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%,
15 99%, or 100% identical to an amino acid sequence that begins at any one of amino acids 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 of SEQ ID NO: 1 and ends at any one of amino acids 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, or 135 of SEQ ID NO: 1.
126. The kit of claim 125, wherein the polypeptide is a polypeptide comprising an amino
20 acid sequence that is at least 90% identical to an amino acid sequence corresponding to residues 30-110 of SEQ ID NO: 1.
127. The kit of claim 125 or 126, wherein the polypeptide is a polypeptide comprising an amino acid sequence that is at least 95% identical to the amino acid sequence corresponding to residues 30-110 of SEQ ID NO: 1.
- 25 128. The kit of any one of claims 125-127, wherein the polypeptide is a polypeptide comprising an amino acid sequence that is at least 99% identical to the amino acid sequence corresponding to residues 30-110 of SEQ ID NO: 1.
129. The kit of any one of claims 125-128, wherein the polypeptide is a polypeptide comprising the amino acid sequence corresponding to residues 30-110 of SEQ ID NO: 1.

130. The kit of any one of claims 125-129, wherein the polypeptide is a polypeptide consisting of the amino acid sequence corresponding to residues 30-110 of SEQ ID NO: 1.
131. The kit of claim 125, wherein the polypeptide is a polypeptide comprising an amino acid sequence that is at least 90% identical to the amino acid sequence corresponding to residues 21-135 of SEQ ID NO: 1.
132. The kit of claim 125 or claim 131, wherein the polypeptide is a polypeptide comprising an amino acid sequence that is at least 95% identical to the amino acid sequence corresponding to residues 21-135 of SEQ ID NO: 1.
133. The kit of any one of claims 125, 131, or 132, wherein the polypeptide is a polypeptide comprising an amino acid sequence that is at least 99% identical to the amino acid sequence corresponding to residues 21-135 of SEQ ID NO: 1.
134. The kit of any one of claims 125 or 131-133, wherein the polypeptide is a polypeptide comprising the amino acid sequence corresponding to residues 21-135 of SEQ ID NO: 1.
135. The kit of any one of claims 125 or 131-134, wherein the polypeptide is a polypeptide consisting of the amino acid sequence corresponding to residues 21-135 of SEQ ID NO: 1.
136. The kit of claim 125, wherein the polypeptide is a polypeptide comprising an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO: 2.
137. The kit of claim 125 or claim 136, wherein the polypeptide is a polypeptide comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 2.
138. The kit of any one of claims 125, 136, or 137, wherein the polypeptide is a polypeptide comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 2.
139. The kit of any one of claims 125 or 136-138, wherein the polypeptide is a polypeptide comprising the amino acid sequence of SEQ ID NO: 2.
140. The kit of any one of claims 125 or 136-139, wherein the polypeptide is a polypeptide consisting of the amino acid sequence of SEQ ID NO: 2.

141. The kit of claim 125, wherein the polypeptide is a polypeptide comprising an amino acid sequence that is at least 90% identical to the amino acid sequence of SEQ ID NO: 3.
142. The kit of claim 125 or claim 141, wherein the polypeptide is a polypeptide comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 3.
143. The kit of any one of claims 125, 141, or 142, wherein the polypeptide is a polypeptide comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 3.
144. The kit of any one of claims 125 or 141-143, wherein the polypeptide is a polypeptide comprising the amino acid sequence of SEQ ID NO: 3.
145. The kit of any one of claims 125 or 141-144, wherein the polypeptide is a polypeptide consisting of the amino acid sequence of SEQ ID NO: 3.
146. The kit of any one of claims 125-145, wherein the polypeptide is a fusion protein further comprising an Fc domain of an immunoglobulin.
147. The kit of claim 146, wherein the Fc domain of the immunoglobulin is an Fc domain of an IgG1 immunoglobulin.
148. The kit of claim 146 or claim 147, wherein the fusion protein further comprises a linker domain positioned between the polypeptide domain and the Fc domain of the immunoglobulin.
149. The kit of claim 148, 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).
150. The kit of claim 148 or claim 149, wherein the linker domain comprises TGGG (SEQ ID NO: 20).
151. The kit of any one of claims 125-150, wherein the ActRII polypeptide comprises an amino acid sequence that is at least 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%,

92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 23.

152. The kit of any one of claims 125-151, wherein the ActRII polypeptide comprises the amino acid sequence of SEQ ID NO: 23.

5 153. The kit of any one of claims 125-152, wherein the ActRII polypeptide consists of the amino acid sequence of SEQ ID NO: 23.

154. The kit of any one of claims 125-153, wherein the polypeptide is part of a homodimer protein complex.

155. The kit of any one of claims 125-154, wherein the polypeptide is glycosylated.

10 156. The kit of any one of claims 125-155, wherein the polypeptide binds to one or more ligands selected from the group consisting of: activin A, activin B, and GDF11.

157. The kit of claim 156, wherein the polypeptide further binds to one or more ligands selected from the group consisting of: BMP10, GDF8, and BMP6.

15 158. The kit of any one of claims 125-155, wherein the polypeptide binds to activin and/or GDF11.

159. The kit of any one of claims 125-158, wherein the kit comprises one or more vials containing the lyophilized polypeptide.

160. The kit of any one of claims 125-159, wherein the injection device comprises a pre-filled syringe.

20 161. The kit of any one of claims 125-159, wherein the injection device comprises a pump apparatus.

162. The kit of claim 161, wherein the pump apparatus comprises an electromechanical pumping assembly.

163. The kit of claim 161, wherein the pump apparatus is a wearable pump apparatus.

25 164. The kit of claim 162, wherein the pre-filled syringe comprises a reconstitution solution.

165. The kit of claim 162, wherein the reconstitution solution comprises a pharmaceutically acceptable carrier and/or excipient.
166. The kit of claim 165, wherein the pharmaceutically acceptable carrier is selected from saline solution, purified water, or sterile water for injection.
- 5 167. The kit of claim 165, wherein the pharmaceutically acceptable excipient is selected from a buffering agent [*e.g.*, citric acid (monohydrate) and/or trisodium citrate (dehydrate)], a surfactant (*e.g.*, polysorbate 80), a stabilizer (*e.g.*, sucrose), and a lyoprotectant (*e.g.*, sucrose).
168. The kit of any one of claims 125-167, wherein the injection device comprises a vial
10 adapter.
169. The kit of claim 168, wherein the vial adapter is capable of attaching to a vial.
170. The kit of claim 168 or claim 169, wherein the vial adapter is capable of attaching to a pre-filled syringe.
171. The kit of claim 170, wherein the pre-filled syringe and the vial are attached to
15 opposite ends of the vial adapter.
172. The kit of claim 171, wherein the reconstitution solution is transferred from the pre-filled syringe to the vial.
173. The kit of claim 125-172, wherein the lyophilized polypeptide is reconstituted into a sterile injectable solution.
- 20 174. The kit of claim 125-172, wherein the lyophilized polypeptide is reconstituted into a sterile injectable solution prior to use.
175. The kit claim of 173 or claim 174, wherein the sterile injectable solution is sterile water for injection.
176. The kit of any one of claims 173-175, wherein the sterile injectable solution is
25 administered parenterally.
177. The kit of claim 176, wherein the injection device is used to administer the sterile injectable solution parenterally.

178. The kit of any one of claims 173-177, wherein the sterile injectable solution is administered via subcutaneous injection.
179. The kit of any one of claims 173-177, wherein the sterile injectable solution is administered via intradermal injection.
- 5 180. The kit of any one of claims 173-177, wherein the sterile injectable solution is administered via intramuscular injection.
181. The kit of any one of claims 173-177, wherein the sterile injectable solution is administered via intravenous injection.
182. The kit of any one of claims 173-177, wherein the sterile injectable solution is self-
10 administered.
183. The kit of any one of claims 125-182, wherein the sterile injectable solution comprises a therapeutically effective dose.
184. The kit of claim 183, wherein the therapeutically effective dose comprises a weight based dose.
- 15 185. The kit of any one of claims 125-184, wherein the lyophilized polypeptide is administered every 4 weeks.
186. The kit of any one of claims 125-185, wherein the kit is used to treat post-capillary pulmonary hypertension (PcPH).
187. The kit of claim 186, wherein the PcPH is isolated post-capillary pulmonary
20 hypertension (IpcPH).
188. The kit of claim 186, wherein the PcPH is combined post- and pre-capillary PH (CpcPH).
189. The kit of any one of claims 186-188, wherein the patient has Group 2 pulmonary hypertension as recognized by the WHO.
- 25 190. The kit of any one of claims 186-189, wherein the patient has pulmonary hypertension due to heart failure with preserved left ventricular ejection fraction (LVEF).

191. The kit of any one of claims 186-189, wherein the patient has pulmonary hypertension due to heart failure with reduced left ventricular ejection fraction (LVEF).
192. The kit of any one of claims 186-189, wherein the patient has valvular heart disease.
193. The kit of any one of claims 186-189, wherein the patient has congenital/acquired
5 cardiovascular conditions leading to post-capillary PH.
194. The kit of any one of claims 186-188, wherein the patient has Group 5 pulmonary hypertension as recognized by the WHO.
195. The kit of any one of claims 186-188, wherein the patient has pulmonary hypertension with unclear and/or multifactorial mechanisms.
- 10 196. The kit of any one of claims 1-195, wherein the shelf life of the lyophilized polypeptide is at least 1, 1.5, 2, 2.5, or 3 years.
197. The kit of any one of claims 1-195, wherein the lyophilized polypeptide is reconstituted.
198. The kit of claim 197, wherein the reconstituted polypeptide has a shelf life of at least 2 hrs, 3 hrs, or 4 hrs.