**[00135]** The development of fibrosis is known to require inflammation, proliferation and recruitment of fibroblast that results in cells of myofibroblastic phenotype (Horowitz J. et al., *Semin Respir Crit Care Med.*, 27(6):600-612, 2006). MK2 has been shown to control gene expression at transcriptional and post-transcriptional levels (Neininger A. et al., *J Biol Chem.* 2002;277(5):3065-8, Thomas T. et al., *J Neurochem.*, 105(5): 2039-52, 2008; Johansen C. et al., *J Immunol.*, 176(3):1431-8, 2006; Rousseau S. et al., *EMBO J.* 21(23):6505-14, 2002) as well as cytoskeletal architecture (Lopes, L. et al., *Biochem Biophys Res Commun.*, 382(3):535-9, 2009). In addition, it was shown that activated MK2 increases translation and stability of inflammatory cytokine mRNAs and causes actin reorganization; and that inhibition of MK2 is associated with reduced inflammation (Ward, B. et al., *J Surg Res.*, 169(1):e27-36, 2011) and myofibroblast differentiation (Lopes, L. et al., *Biochem Biophys Res Commun.*, 382(3):535-9, 2009).

**[00136]** Together, these data suggest that inhibition of MK2 may provide therapeutic benefits to patients with fibrotic disorders or conditions, for example, idiopathic pulmonary fibrosis (IPF), acute lung injury (ALI), and transplant rejection. In this respect, the described invention offers an approach to intervene in the process of inflammation and fibrosis using cell-penetrating, peptide base inhibitors of MK2.

## SUMMARY ~~OF THE INVENTION~~

**[00137]** According to one ~~aspect~~embodiment, the ~~described invention~~ present disclosure provides a method for treating a disease, condition, or pathologic process characterized by aberrant fibroblast proliferation and extracellular matrix deposition in a tissue of a subject, the method comprising: administering to the subject a pharmaceutical composition comprising a therapeutic amount of a polypeptide of the amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) or a functional equivalent thereof, and a pharmaceutically acceptable carrier thereof, wherein the therapeutic amount is effective to reduce the fibroblast proliferation and extracellular matrix deposition in the tissue of the subject.

**[00138]** According to one embodiment of the method, the disease or the condition is acute lung injury (ALI) or acute respiratory distress syndrome (ARDS). According to another embodiment, the disease or the condition is radiation-induced fibrosis. According to another embodiment, the disease or the condition is transplant rejection. According to another embodiment, the tissue is a lung tissue. According to another embodiment, the disease or the

another embodiment, the first polypeptide is a polypeptide of amino acid sequence HRRIKAWLKKI (SEQ ID NO: 18). According to another embodiment, the carrier is selected from the group consisting of a controlled release carrier, a delayed release carrier, a sustained release carrier, and a long-term release carrier. According to another embodiment, the pharmaceutical composition is in a form of a dry powder. According to another embodiment, the dry powder comprises microparticles with Mass Median Aerodynamic Diameter (MMAD) of 1 to 5 microns. According to another embodiment, the therapeutic amount of the pharmaceutical composition is administered via an inhalation device. According to another embodiment, the inhalation device is a nebulizer. According to another embodiment, the inhalation device is a metered-dose inhaler (MDI). According to another embodiment, the inhalation device is a dry powder inhaler (DPI). According to another embodiment, the inhalation device is a dry powder nebulizer.

**[00139]** According to another ~~aspect~~embodiment, the ~~described invention~~ present disclosure provides a pharmaceutical composition for use in the treatment of a disease, condition, or pathologic process characterized by aberrant fibroblast proliferation and extracellular matrix deposition in a tissue of a subject, wherein the pharmaceutical composition comprises a therapeutic amount of a polypeptide of the amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) or a functional equivalent thereof, and a pharmaceutically acceptable carrier thereof, and wherein the therapeutic amount is effective to reduce the fibroblast proliferation and extracellular matrix deposition in the tissue of the subject.

**[00140]** According to one embodiment, the disease or the condition is acute lung injury (ALI) or acute respiratory distress syndrome (ARDS). According to another embodiment, the disease or the condition is radiation-induced fibrosis. According to another embodiment, the disease or the condition is transplant rejection. According to another embodiment, the tissue is a lung tissue. According to another embodiment, the disease or the condition is an interstitial lung disease. According to another embodiment, the disease or the condition is pulmonary fibrosis. According to another embodiment, the pulmonary fibrosis is idiopathic pulmonary fibrosis. According to another embodiment, the pulmonary fibrosis results from administration of bleomycin. According to another embodiment, the pulmonary fibrosis results from an allergic reaction, inhalation of environmental particulates, smoking, a bacterial infection, a viral infection, mechanical damage to a lung of the subject, lung transplantation rejection, an

dry powder comprises microparticles with Mass Median Aerodynamic Diameter (MMAD) of 1 to 5 microns. According to another embodiment, the therapeutic amount of the pharmaceutical composition is administered via an inhalation device. According to another embodiment, the inhalation device is a nebulizer. According to another embodiment, the inhalation device is a metered-dose inhaler (MDI). According to another embodiment, the inhalation device is a dry powder inhaler (DPI).

[00140a] According to an aspect, the present disclosure provides the use of a pharmaceutical composition formulated for intratracheal, parenteral, intravenous, or intraperitoneal delivery, in the manufacture of a medicament for treating a disease, condition, or pathologic process selected from the group consisting of acute lung injury (ALI) or acute respiratory distress syndrome (ARDS), radiation-induced fibrosis, and transplant rejection characterized by aberrant fibroblast proliferation and extracellular matrix deposition in a tissue of a subject, wherein the pharmaceutical composition comprises a therapeutic amount of a functional equivalent of an MK2 or MK3 inhibitor polypeptide of the amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1), wherein the functional equivalent is made from a fusion between a first polypeptide that is a cell penetrating peptide (CPP) selected from the group consisting of a polypeptide of amino acid sequence WLRRIKAWLRRIKA (SEQ ID NO: 12), WLRRIKA (SEQ ID NO: 13), YGRKKRRQRRR (SEQ ID NO: 14), WLRRIKAWLRRI (SEQ ID NO: 15), FAKLAARLYR (SEQ ID NO: 16), KAFAKLAARLYR (SEQ ID NO: 17) and HRRIKAWLKKI (SEQ ID NO: 18), and a second polypeptide that is a therapeutic domain (TD) selected from the group consisting of a polypeptide of amino acid sequence KALARQLAVA (SEQ ID NO: 8), KALARQLGVA (SEQ ID NO: 9), and KALARQLGVAA (SEQ ID NO: 10), and a pharmaceutically acceptable carrier thereof, wherein the carrier is selected from the group consisting of a controlled release carrier, a delayed release carrier, a sustained release carrier, and a long-term release carrier and wherein the therapeutic amount is effective to reduce the aberrant fibroblast proliferation and extracellular matrix deposition in the tissue of the subject.

**[00141]** According to another ~~aspect~~embodiment, the ~~described invention~~ present disclosure provides use of a pharmaceutical composition in the manufacture of a medicament for treating a disease, condition, or pathologic process characterized by aberrant fibroblast proliferation and extracellular matrix deposition in a tissue of a subject, wherein the pharmaceutical composition comprises a therapeutic amount of a polypeptide of the amino acid

sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) or a functional equivalent thereof, and a pharmaceutically acceptable carrier thereof, and wherein the therapeutic amount is effective to reduce the fibroblast proliferation and extracellular matrix deposition in the tissue of the subject.

**[00142]** According to another embodiment, the disease or the condition is acute lung injury (ALI) or acute respiratory distress syndrome (ARDS). According to another embodiment, the disease or the condition is radiation-induced fibrosis. According to another embodiment, ~~The use according to claim 58, wherein~~ the disease or the condition is transplant rejection. According to another embodiment, the tissue is a lung tissue. According to another embodiment, the disease or the condition is an interstitial lung disease. According to another embodiment, the disease or the condition is pulmonary fibrosis. According to another embodiment, the pulmonary fibrosis is idiopathic pulmonary fibrosis. According to another embodiment, the pulmonary fibrosis is caused by administration of bleomycin. According to another embodiment, the pulmonary fibrosis results from an allergic reaction, inhalation of environmental particulates, smoking, a bacterial infection, a viral infection, mechanical damage to a lung of the subject, lung transplantation rejection, an autoimmune disorder, a genetic disorder, or a combination thereof. According to another embodiment, the disease or the condition is further characterized by an inflammation in the tissue. According to another embodiment, the inflammation is an acute or a chronic inflammation. According to another embodiment, the inflammation is mediated by at least one cytokine selected from the group consisting of Tumor Necrosis Factor-alpha (TNF-α), Interleukin-6 (IL-6), and Interleukin-1β (IL-1β). According to another embodiment, the aberrant

**CLAIMS**

We claim:

1. Use of a pharmaceutical composition formulated for intratracheal, parenteral, intravenous, or intraperitoneal delivery, in the manufacture of a medicament for treating a disease, condition, or pathologic process selected from the group consisting of acute lung injury (ALI) or acute respiratory distress syndrome (ARDS), radiation-induced fibrosis, and transplant rejection characterized by aberrant fibroblast proliferation and extracellular matrix deposition in a tissue of a subject,

wherein the pharmaceutical composition comprises a therapeutic amount of a functional equivalent of an MK2 or MK3 inhibitor polypeptide of the amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1), wherein the functional equivalent is made from a fusion between a first polypeptide that is a cell penetrating peptide (CPP) selected from the group consisting of a polypeptide of amino acid sequence WLRRIKAWLRRIKA (SEQ ID NO: 12), WLRRIKA (SEQ ID NO: 13), YGRKKRRQRRR (SEQ ID NO: 14), WLRRIKAWLRRI (SEQ ID NO: 15), FAKLAARLYR (SEQ ID NO: 16), KAFAKLAARLYR (SEQ ID NO: 17) and HRRIKAWLKKI (SEQ ID NO: 18), and a second polypeptide that is a therapeutic domain (TD) selected from the group consisting of a polypeptide of amino acid sequence KALARQLAVA (SEQ ID NO: 8), KALARQLGVA (SEQ ID NO: 9), and KALARQLGVAA (SEQ ID NO: 10), and a pharmaceutically acceptable carrier thereof, wherein the carrier is selected from the group consisting of a controlled release carrier, a delayed release carrier, a sustained release carrier, and a long-term release carrier and

wherein the therapeutic amount is effective to reduce the aberrant fibroblast proliferation and extracellular matrix deposition in the tissue of the subject.

2. The use according to claim 1, wherein the tissue is a lung tissue.

3. The use according to claim 1 or 2, wherein the disease or the condition is an interstitial lung disease.

4. The use according to any one of the preceding claims, wherein the disease or the condition is pulmonary fibrosis.

5. The use according to claim 4, wherein the pulmonary fibrosis is idiopathic pulmonary fibrosis.

6. The use according to claim 4, wherein the pulmonary fibrosis is caused by administration of bleomycin.

7. The use according to claim 4, wherein the pulmonary fibrosis results from an allergic reaction, inhalation of environmental particulates, smoking, a bacterial infection, a viral infection,

mechanical damage to a lung of the subject, lung transplantation rejection, an autoimmune disorder, a genetic disorder, or a combination thereof.

8. The use according to any one of the preceding claims, wherein the disease or the condition is further characterized by an inflammation in the tissue.

9. The use according to claim 8, wherein the inflammation is an acute or a chronic inflammation.

10. The use according to claim 8, wherein the inflammation is mediated by at least one cytokine selected from the group consisting of Tumor Necrosis Factor-alpha (TNF-α), Interleukin-6 (IL-6), and Interleukin-1β (IL-1β).

11. The use according to any one of the preceding claims, wherein the aberrant fibroblast proliferation and extracellular matrix deposition in the tissue is characterized by an aberrant activity of Mitogen-Activated Protein Kinase-Activated Protein Kinase 2 (MK2) in the tissue compared to the activity of Mitogen-Activated Protein Kinase-Activated Protein Kinase 2 (MK2) in the tissue of a normal healthy control subject.

12. The use according to claim 4, wherein the pulmonary fibrosis is characterized by at least one pathology selected from the group consisting of an aberrant deposition of an extracellular matrix protein in a pulmonary interstitium, an aberrant promotion of fibroblast proliferation in the lung, an aberrant induction of myofibroblast differentiation in the lung, and an aberrant promotion of attachment of myofibroblasts to an extracellular matrix compared to a normal healthy control subject.

13. The use according to any one of the preceding claims, wherein the pharmaceutical composition is to be administered intratracheally.

14. The use according to any one of the preceding claims, wherein the pharmaceutical composition further comprises at least one additional therapeutic agent.

15. The use according to claim 14, wherein the additional therapeutic agent is selected from the group consisting of a purified bovine Type V collagen, an IL-13 receptor antagonist, a protein tyrosine kinase inhibitor, an endothelial receptor antagonist, a dual endothelin receptor antagonist, a prostacyclin analog, an anti-CTGF monoclonal antibody, an endothelin receptor

antagonist (A-selective), AB0024, a lysyl oxidase-like 2 (LOXL2) monoclonal antibody, a c-Jun N-terminal kinase (JNK) inhibitor, pirfenidone, IFN-γ1b, a pan-neutralizing IgG4 human antibody against all three TGF-β isoforms, a TGF-β activation inhibitor, a recombinant human Pentraxin-2 protein (rhPTX-2), a bispecific IL-4/IL-13 antibody, a humanized monoclonal antibody targeting integrin avβ6, N-acetylcysteine, sildenafil, a Tumor Necrosis Factor (TNF) antagonist (etanercept), and a combination thereof.

16. The use according to claim 14, wherein the additional therapeutic agent is a glucocorticoid selected from the group consisting of prednisone, budesonide, mometasone furoate, fluticasone propionate, fluticasone furoate, and a combination thereof.

17. The use according to claim 14, wherein the additional therapeutic agent is a bronchodilator selected from the group consisting of a leukotriene modifier, an anticholingertic bronchodilator, a short-acting β2-agonist, and long-acting β2-agonist, and a combination thereof.

18. The use according to claim 14, wherein the additional therapeutic agent is an analgesic agent.

19. The use according to claim 14, wherein the additional therapeutic agent is an anti-infective agent.

20. The use according to claim 1, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence FAKLAARLYRKALARQLGVAA (SEQ ID NO: 3).

21. The use according to claim 1, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence KAFAKLAARLYRKALARQLGVAA (SEQ ID NO: 4).

22. The use according to claim 1, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence YARAAARQARAKALARQLAVA (SEQ ID NO: 5).

23. The use according to claim 1, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence YARAAARQARAKALARQLGVA (SEQ ID NO: 6).

24. The use according to claim 1, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence HRRIKAWLKKIKALARQLGVAA (SEQ ID NO: 7).

25. The use according to claim 1, wherein the therapeutic domain (TD) of the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) made from the fusion of the first polypeptide that is the cell penetrating peptide (CPP) operatively linked to the second polypeptide that is the therapeutic domain (TD), is a polypeptide whose sequence has a substantial identity to amino acid sequence KALARQLGVAA (SEQ ID NO: 2).

26. The use according to claim 25, wherein the second polypeptide is a polypeptide of amino acid sequence KALARQLAVA (SEQ ID NO: 8).

27. The use according to claim 25, wherein the second polypeptide is a polypeptide of amino acid sequence KALARQLGVA (SEQ ID NO: 9).

28. The use according to claim 25, wherein the second polypeptide is a polypeptide of amino acid sequence KALARQLGVAA (SEQ ID NO: 10).

29. The use according to claim 1, wherein the fusion protein comprises the first polypeptide operatively linked to the second polypeptide, and the second polypeptide is of amino acid sequence KALARQLGVAA (SEQ ID NO: 2).

30. The use according to claim 29, wherein the first polypeptide is a polypeptide of amino acid sequence WLRRIKAWLRRIKA (SEQ ID NO: 12).

31. The use according to claim 29, wherein the first polypeptide is a polypeptide of amino acid sequence WLRRIKA (SEQ ID NO: 13).

32. The use according to claim 29, wherein the first polypeptide is a polypeptide of amino acid sequence YGRKKRRQRRR (SEQ ID NO: 14).

33. The use according to claim 29, wherein the first polypeptide is a polypeptide of amino acid sequence WLRRIKAWLRRI (SEQ ID NO: 15).

34. The use according to claim 29, wherein the first polypeptide is a polypeptide of amino acid sequence FAKLAARLYR (SEQ ID NO: 16).

35. The use according to claim 29, wherein the first polypeptide is a polypeptide of amino acid sequence KAFAKLAARLYR (SEQ ID NO: 17).

36. The use according to claim 29, wherein the first polypeptide is a polypeptide of amino acid sequence HRRIKAWLKKI (SEQ ID NO: 18).

37. The use according to any one of the preceding claims, wherein the pharmaceutical composition is in a form of a dry powder.

38. The use according to claim 37, wherein the dry powder comprises microparticles with Mass Median Aerodynamic Diameter (MMAD) of 1 to 5 microns.

39. The use according to claim 37, wherein the therapeutic amount of the pharmaceutical composition is administered via an inhalation device.

40. The use according to claim 39, wherein the inhalation device is a nebulizer.

41. The use according to claim 39, wherein the inhalation device is a metered-dose inhaler (MDI).

42. The use according to claim 39, wherein the inhalation device is a dry powder inhaler (DPI).

43. The use according to claim 39, wherein the inhalation device is a dry powder nebulizer.

## CLAIMS

We claim:

1. A pharmaceutical composition for use in the treatment of a disease, condition, or pathologic process characterized by aberrant fibroblast proliferation and extracellular matrix deposition in a tissue of a subject,

wherein the pharmaceutical composition comprises a therapeutic amount of a polypeptide of the amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) or a functional equivalent thereof, and a pharmaceutically acceptable carrier thereof, and

wherein the therapeutic amount is effective to reduce the fibroblast proliferation and extracellular matrix deposition in the tissue of the subject.

2. The pharmaceutical composition according to claim 1, wherein the disease or the condition is acute lung injury (ALI) or acute respiratory distress syndrome (ARDS).

3. The pharmaceutical composition according to claim 1, wherein the disease or the condition is radiation-induced fibrosis.

4. The pharmaceutical composition according to claim 1, wherein the disease or the condition is transplant rejection.

5. The pharmaceutical composition according to claim 1, wherein the tissue is a lung tissue.

6. The pharmaceutical composition according to claim 1, wherein the disease or the condition is an interstitial lung disease.

7. The pharmaceutical composition according to claim 1, wherein the disease or the condition is pulmonary fibrosis.

8. The pharmaceutical composition according to claim 7, wherein the pulmonary fibrosis is idiopathic pulmonary fibrosis.

9. The pharmaceutical composition according to claim 7, wherein the pulmonary fibrosis results from administration of bleomycin.

10. The pharmaceutical composition according to claim 7, wherein the pulmonary fibrosis results from an allergic reaction, inhalation of environmental particulates, smoking, a bacterial infection, a viral infection, mechanical damage to a lung of the subject, lung transplantation rejection, an autoimmune disorder, a genetic disorder, or a combination thereof.

11. The pharmaceutical composition according to claim 1, wherein the disease or the condition is further characterized by an inflammation in the tissue.

12. The pharmaceutical composition according to claim 11, wherein the inflammation is an acute or a chronic inflammation.

13. The pharmaceutical composition according to claim 11, wherein the inflammation is mediated by at least one cytokine selected from the group consisting of Tumor Necrosis Factor-alpha (TNF-α), Interleukin-6 (IL-6), and Interleukin-1β (IL-1β).

14. The pharmaceutical composition according to claim 1, wherein the aberrant fibroblast proliferation and extracellular matrix deposition in the tissue is characterized by an aberrant activity of Mitogen-Activated Protein Kinase-Activated Protein Kinase 2 (MK2) in the tissue compared to the activity of Mitogen-Activated Protein Kinase-Activated Protein Kinase 2 (MK2) in the tissue of a normal healthy control subject.

15. The pharmaceutical composition according to claim 7, wherein the pulmonary fibrosis is characterized by at least one pathology selected from the group consisting of an aberrant deposition of an extracellular matrix protein in a pulmonary interstitium, an aberrant promotion of fibroblast proliferation in the lung, an aberrant induction of myofibroblast differentiation in the lung, and an aberrant promotion of attachment of myofibroblasts to an extracellular matrix compared to a normal healthy control subject.

16. The pharmaceutical composition according to claim 1, wherein the pharmaceutical composition is to be administered intratracheally, parenterally, intravenously, or intraperitoneally.

17. The pharmaceutical composition according to claim 1, wherein the pharmaceutical composition is to be administered intratracheally.

18. The pharmaceutical composition according to claim 1, wherein the pharmaceutical composition is to be administered at one time as a single dose.

19. The pharmaceutical composition according to claim 1, wherein the pharmaceutical composition is to be administered as a plurality of doses over a period of time.

20. The pharmaceutical composition according to claim 19, wherein the period of time is a day, a week, a month, a month, a year, or multiples thereof.

21. The pharmaceutical composition according to claim 1, wherein the pharmaceutical composition is to be administered at least once monthly, at least once weekly, or at least one daily.

22. The pharmaceutical composition according to claim 1, wherein the pharmaceutical composition further comprises at least one additional therapeutic agent.

23. The pharmaceutical composition according to claim 22, wherein the additional therapeutic agent is selected from the group consisting of a purified bovine Type V collagen, an IL-13 receptor antagonist, a protein tyrosine kinase inhibitor, an endothelial receptor antagonist, a dual endothelin receptor antagonist, a prostacyclin analog, an anti-CTGF monoclonal antibody, an endothelin receptor antagonist (A-selective), AB0024, a lysyl oxidase-like 2 (LOXL2) monoclonal antibody, a c-Jun N-terminal kinase (JNK) inhibitor, pirfenidone, IFN-γ1b, a pan-neutralizing IgG4 human antibody against all three TGF-β isoforms, a TGF-β activation inhibitor, a recombinant human Pentraxin-2 protein (rhPTX-2), a bispecific IL-4/IL-13 antibody, a humanized monoclonal antibody targeting integrin αvβ6, N-acetylcysteine, sildenafil, a Tumor Necrosis Factor (TNF) antagonist (etanercept), and a combination thereof.

24. The pharmaceutical composition according to claim 22, wherein the additional therapeutic agent is a glucocorticoid selected from the group consisting of prednisone, budesonide, mometasone furoate, fluticasone propionate, fluticasone furoate, and a combination thereof.

25. The pharmaceutical composition according to claim 22, wherein the additional therapeutic agent is a bronchodilator selected from the group consisting of a leukotriene

modifer, an anticholingertic bronchodilator, a short-acting β2-agonist, and long-acting β2-agonist, and a combination thereof.

26. The pharmaceutical composition according to claim 22, wherein the additional therapeutic agent is an analgesic agent.

27. The pharmaceutical composition according to claim 22, wherein the additional therapeutic agent is an anti-infective agent.

28. The pharmaceutical composition according to claim 1, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) has at least 85 percent sequence identity to amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1).

29. The pharmaceutical composition according to claim 1, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence FAKLAARLYRKALARQLGVAA (SEQ ID NO: 3).

30. The pharmaceutical composition according to claim 1, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence KAFAKLAARLYRKALARQLGVAA (SEQ ID NO: 4).

31. The pharmaceutical composition according to claim 1, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence YARAAARQARAKALARQLAVA (SEQ ID NO: 5).

32. The pharmaceutical composition according to claim 1, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence YARAAARQARAKALARQLGVA (SEQ ID NO: 6).

33. The pharmaceutical composition according to claim 1, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence HRRIKAWLKKIKALARQLGVAA (SEQ ID NO: 7).

34. The pharmaceutical composition according to claim 1, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is a fusion protein comprising a first polypeptide operatively linked to a second polypeptide, wherein the first polypeptide is of amino acid sequence YARAAARQARA (SEQ ID NO:

11), and the second polypeptide comprises a therapeutic domain whose sequence has a substantial identity to amino acid sequence KALARQLGVAA (SEQ ID NO: 2).

35. The pharmaceutical composition according to claim 34, wherein the second polypeptide has at least 70 percent sequence identity to amino acid sequence KALARQLGVAA (SEQ ID NO: 2).

36. The pharmaceutical composition according to claim 34, wherein the second polypeptide has at least 80 percent sequence identity to amino acid sequence KALARQLGVAA (SEQ ID NO: 2).

37. The pharmaceutical composition according to claim 34, wherein the second polypeptide has at least 90 percent sequence identity to amino acid sequence KALARQLGVAA (SEQ ID NO: 2).

38. The pharmaceutical composition according to claim 34, wherein the second polypeptide has at least 95 percent sequence identity to amino acid sequence KALARQLGVAA (SEQ ID NO: 2).

39. The pharmaceutical composition according to claim 34, wherein the second polypeptide is a polypeptide of amino acid sequence KALARQLAVA (SEQ ID NO: 8).

40. The pharmaceutical composition according to claim 34, wherein the second polypeptide is a polypeptide of amino acid sequence KALARQLGVA (SEQ ID NO: 9).

41. The pharmaceutical composition according to claim 34, wherein the second polypeptide is a polypeptide of amino acid sequence KALARQLGVAA (SEQ ID NO: 10).

42. The pharmaceutical composition according to claim 1, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is a fusion protein comprising a first polypeptide operatively linked to a second polypeptide, wherein the first polypeptide comprises a cell penetrating peptide functionally equivalent to YARAAARQARA (SEQ ID NO: 11), and the second polypeptide is of amino acid sequence KALARQLGVAA (SEQ ID NO: 2).

43. The pharmaceutical composition according to claim 42, wherein the first polypeptide is a polypeptide of amino acid sequence WLRRIKAWLRRIKA (SEQ ID NO: 12).

44. The pharmaceutical composition according to claim 42, wherein the first polypeptide is a polypeptide of amino acid sequence WLRRIKA (SEQ ID NO: 13).

45. The pharmaceutical composition according to claim 42, wherein the first polypeptide is a polypeptide of amino acid sequence YGRKKRRQRRR (SEQ ID NO: 14).

46. The pharmaceutical composition according to claim 42, wherein the first polypeptide is a polypeptide of amino acid sequence WLRRIKAWLRRI (SEQ ID NO: 15).

47. The pharmaceutical composition according to claim 42, wherein the first polypeptide is a polypeptide of amino acid sequence FAKLAARLYR (SEQ ID NO: 16).

48. The pharmaceutical composition according to claim 42, wherein the first polypeptide is a polypeptide of amino acid sequence KAFAKLAARLYR (SEQ ID NO: 17).

49. The pharmaceutical composition according to claim 42, wherein the first polypeptide is a polypeptide of amino acid sequence HRRIKAWLKKI (SEQ ID NO: 18).

50. The pharmaceutical composition according to claim 1, wherein the carrier is selected from the group consisting of a controlled release carrier, a delayed release carrier, a sustained release carrier, and a long-term release carrier.

51. The pharmaceutical composition according to claim 1, wherein the pharmaceutical composition is in a form of a dry powder.

52. The pharmaceutical composition according to claim 51, wherein the dry powder comprises microparticles with Mass Median Aerodynamic Diameter (MMAD) of 1 to 5 microns.

53. The pharmaceutical composition according to claim 1, wherein the therapeutic amount of the pharmaceutical composition is administered via an inhalation device.

54. The pharmaceutical composition according to claim 53, wherein the inhalation device is a nebulizer.

55. The pharmaceutical composition according to claim 53, wherein the inhalation device is a metered-dose inhaler (MDI).

56. The pharmaceutical composition according to claim 53, wherein the inhalation device is a dry powder inhaler (DPI).

57. The pharmaceutical composition according to claim 53, wherein the inhalation device is a dry powder nebulizer.

58. Use of a pharmaceutical composition in the manufacture of a medicament for treating a disease, condition, or pathologic process characterized by aberrant fibroblast proliferation and extracellular matrix deposition in a tissue of a subject,

wherein the pharmaceutical composition comprises a therapeutic amount of a polypeptide of the amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) or a functional equivalent thereof, and a pharmaceutically acceptable carrier thereof, and

wherein the therapeutic amount is effective to reduce the fibroblast proliferation and extracellular matrix deposition in the tissue of the subject.

59. The use according to claim 58, wherein the disease or the condition is acute lung injury (ALI) or acute respiratory distress syndrome (ARDS).

60. The use according to claim 58, wherein the disease or the condition is radiation-induced fibrosis.

61. The use according to claim 58, wherein the disease or the condition is transplant rejection.

62. The use according to claim 58, wherein the tissue is a lung tissue.

63. The use according to claim 58, wherein the disease or the condition is an interstitial lung disease.

64. The use according to claim 58, wherein the disease or the condition is pulmonary fibrosis.

65. The use according to claim 64, wherein the pulmonary fibrosis is idiopathic pulmonary fibrosis.

66. The use according to claim 64, wherein the pulmonary fibrosis is caused by administration of bleomycin.

67. The use according to claim 64, wherein the pulmonary fibrosis results from an allergic reaction, inhalation of environmental particulates, smoking, a bacterial infection, a

viral infection, mechanical damage to a lung of the subject, lung transplantation rejection, an autoimmune disorder, a genetic disorder, or a combination thereof.

68. The use according to claim 58, wherein the disease or the condition is further characterized by an inflammation in the tissue.

69. The use according to claim 68, wherein the inflammation is an acute or a chronic inflammation.

70. The use according to claim 68, wherein the inflammation is mediated by at least one cytokine selected from the group consisting of Tumor Necrosis Factor-alpha (TNF-α), Interleukin-6 (IL-6), and Interleukin-1β (IL-1β).

71. The use according to claim 58, wherein the aberrant fibroblast proliferation and extracellular matrix deposition in the tissue is characterized by an aberrant activity of Mitogen-Activated Protein Kinase-Activated Protein Kinase 2 (MK2) in the tissue compared to the activity of Mitogen-Activated Protein Kinase-Activated Protein Kinase 2 (MK2) in the tissue of a normal healthy control subject.

72. The use according to claim 64, wherein the pulmonary fibrosis is characterized by at least one pathology selected from the group consisting of an aberrant deposition of an extracellular matrix protein in a pulmonary interstitium, an aberrant promotion of fibroblast proliferation in the lung, an aberrant induction of myofibroblast differentiation in the lung, and an aberrant promotion of attachment of myofibroblasts to an extracellular matrix compared to a normal healthy control subject.

73. The use according to claim 58, wherein the pharmaceutical composition is to be administered intratracheally, parenterally, intravenously, or intraperitoneally.

74. The use according to claim 58, wherein the pharmaceutical composition is to be administered intratracheally.

75. The use according to claim 58, wherein the pharmaceutical composition is to be administered at one time as a single dose.

76. The use according to claim 58, wherein the pharmaceutical composition is to be administered as a plurality of doses over a period of time.

77. The use according to claim 76, wherein the period of time is a day, a week, a month, a month, a year, or multiples thereof.

78. The use according to claim 58, wherein the pharmaceutical composition is to be administered at least once monthly, at least once weekly, or at least one daily.

79. The use according to claim 58, wherein the pharmaceutical composition further comprises at least one additional therapeutic agent.

80. The use according to claim 79, wherein the additional therapeutic agent is selected from the group consisting of a purified bovine Type V collagen, an IL-13 receptor antagonist, a protein tyrosine kinase inhibitor, an endothelial receptor antagonist, a dual endothelin receptor antagonist, a prostacyclin analog, an anti-CTGF monoclonal antibody, an endothelin receptor antagonist (A-selective), AB0024, a lysyl oxidase-like 2 (LOXL2) monoclonal antibody, a c-Jun N-terminal kinase (JNK) inhibitor, pirfenidone, IFN-γ1b, a pan-neutralizing IgG4 human antibody against all three TGF-β isoforms, a TGF-β activation inhibitor, a recombinant human Pentraxin-2 protein (rhPTX-2), a bispecific IL-4/IL-13 antibody, a humanized monoclonal antibody targeting integrin αvβ6, N-acetylcysteine, sildenafil, a Tumor Necrosis Factor (TNF) antagonist (etanercept), and a combination thereof.

81. The use according to claim 79, wherein the additional therapeutic agent is a glucocorticoid selected from the group consisting of prednisone, budesonide, mometasone furoate, fluticasone propionate, fluticasone furoate, and a combination thereof.

82. The use according to claim 79, wherein the additional therapeutic agent is a bronchodilator selected from the group consisting of a leukotriene modifer, an anticholingertic bronchodilator, a short-acting β2-agonist, and long-acting β2-agonist, and a combination thereof.

83. The use according to claim 79, wherein the additional therapeutic agent is an analgesic agent.

84. The use according to claim 79, wherein the additional therapeutic agent is an anti-infective agent.

85. The use according to claim 58, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) has at least 85 percent sequence identity to amino acid sequence YARAAARQARAKALARQLGVAA (SEQ ID NO: 1).

86. The use according to claim 58, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence FAKLAARLYRKALARQLGVAA (SEQ ID NO: 3).

87. The use according to claim 58, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence KAFAKLAARLYRKALARQLGVAA (SEQ ID NO: 4).

88. The use according to claim 58, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence YARAAARQARAKALARQLAVA (SEQ ID NO: 5).

89. The use according to claim 58, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence YARAAARQARAKALARQLGVA (SEQ ID NO: 6).

90. The use according to claim 58, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is of amino acid sequence HRRIKAWLKKIKALARQLGVAA (SEQ ID NO: 7).

91. The use according to claim 58, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is a fusion protein comprising a first polypeptide operatively linked to a second polypeptide, wherein the first polypeptide is of amino acid sequence YARAAARQARA (SEQ ID NO: 11), and the second polypeptide comprises a therapeutic domain whose sequence has a substantial identity to amino acid sequence KALARQLGVAA (SEQ ID NO: 2).

92. The use according to claim 91, wherein the second polypeptide has at least 70 percent sequence identity to amino acid sequence KALARQLGVAA (SEQ ID NO: 2).

93. The use according to claim 91, wherein the second polypeptide has at least 80 percent sequence identity to amino acid sequence KALARQLGVAA (SEQ ID NO: 2).

94. The use according to claim 91, wherein the second polypeptide has at least 90 percent sequence identity to amino acid sequence KALARQLGVAA (SEQ ID NO: 2).

95. The use according to claim 91, wherein the second polypeptide has at least 95 percent sequence identity to amino acid sequence KALARQLGVAA (SEQ ID NO: 2).

96. The use according to claim 91, wherein the second polypeptide is a polypeptide of amino acid sequence KALARQLAVA (SEQ ID NO: 8).

97. The use according to claim 91, wherein the second polypeptide is a polypeptide of amino acid sequence KALARQLGVA (SEQ ID NO: 9).

98. The use according to claim 91, wherein the second polypeptide is a polypeptide of amino acid sequence KALARQLGVAA (SEQ ID NO: 10).

99. The use according to claim 58, wherein the functional equivalent of the polypeptide YARAAARQARAKALARQLGVAA (SEQ ID NO: 1) is a fusion protein comprising a first polypeptide operatively linked to a second polypeptide, wherein the first polypeptide comprises a cell penetrating peptide functionally equivalent to YARAAARQARA (SEQ ID NO: 11), and the second polypeptide is of amino acid sequence KALARQLGVAA (SEQ ID NO: 2).

100. The use according to claim 99, wherein the first polypeptide is a polypeptide of amino acid sequence WLRRIKAWLRRIKA (SEQ ID NO: 12).

101. The use according to claim 99, wherein the first polypeptide is a polypeptide of amino acid sequence WLRRIKA (SEQ ID NO: 13).

102. The use according to claim 99, wherein the first polypeptide is a polypeptide of amino acid sequence YGRKKRRQRRR (SEQ ID NO: 14).

103. The use according to claim 99, wherein the first polypeptide is a polypeptide of amino acid sequence WLRRIKAWLRRI (SEQ ID NO: 15).

104. The use according to claim 99, wherein the first polypeptide is a polypeptide of amino acid sequence FAKLAARLYR (SEQ ID NO: 16).

105. The use according to claim 99, wherein the first polypeptide is a polypeptide of amino acid sequence KAFAKLAARLYR (SEQ ID NO: 17).

106. The use according to claim 99, wherein the first polypeptide is a polypeptide of amino acid sequence HRRIKAWLKKI (SEQ ID NO: 18).

107. The use according to claim 58, wherein the carrier is selected from the group consisting of a controlled release carrier, a delayed release carrier, a sustained release carrier, and a long-term release carrier.

108. The use according to claim 58, wherein the pharmaceutical composition is in a form of a dry powder.

109. The use according to claim 108, wherein the dry powder comprises microparticles with Mass Median Aerodynamic Diameter (MMAD) of 1 to 5 microns.

110. The use according to claim 58, wherein the therapeutic amount of the pharmaceutical composition is administered via an inhalation device.

111. The use according to claim 110, wherein the inhalation device is a nebulizer.

112. The use according to claim 110, wherein the inhalation device is a metered-dose inhaler (MDI).

113. The use according to claim 110, wherein the inhalation device is a dry powder inhaler (DPI).

114. The use according to claim 110, wherein the inhalation device is a dry powder nebulizer.