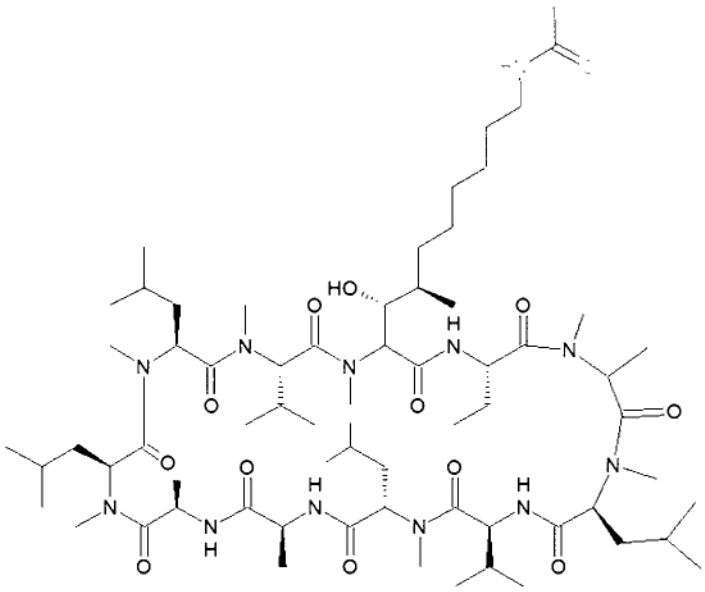


(CRV431).

[0023] In some embodiments, the pharmaceutical composition is for intravenous administration, oral administration, or parenteral administration. In some embodiments, the pharmaceutical composition is in the form of powder, pill, tablet, microtablet, pellet, micropellet, capsule, capsule containing microtablets, liquid, aerosols, or nanoparticles.

[0024] Disclosed herein include a kit, comprising

a pharmaceutical composition disclosed herein; and

a label, wherein the label indicating one or more of:

(a) the kit is for preventing or treating fibrosis,

(b) the kit is for reducing or inhibiting fibrosis formation,,

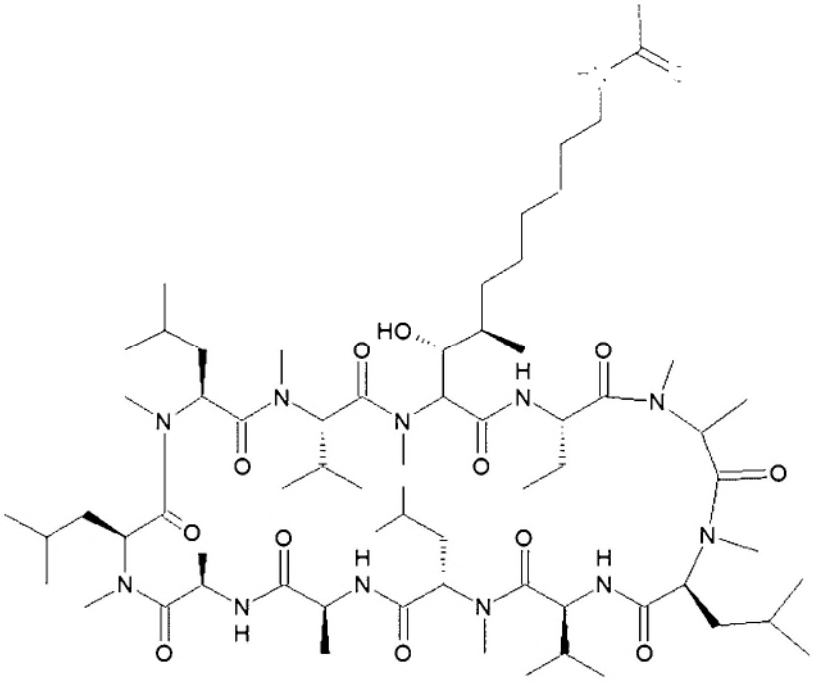
(c) the kit is for reversing fibrosis,

(d) the kit is for reducing the amount of fibrosis, and

(e) the kit is for delaying the onset of fibrosis.

[0025] In some embodiments, the kit further comprises instructions for identifying a subject at risk of development fibrosis, instructions for identifying a subject suffering from fibrosis, or both

[0025a] In one aspect, disclosed herein is a use of a composition comprising CRV431, or a pharmaceutically acceptable salt, solvate, stereoisomer thereof, in the manufacture of a medicament for treating non-liver fibrosis, for reducing non-liver fibrosis, reversing non-liver fibrosis, for preventing non-liver fibrosis, for preventing or reducing non-liver fibrosis formation, for reducing the amount of non-liver fibrosis, and/or for delaying the onset of non-liver fibrosis, in a subject in need thereof,



(CRV431),

wherein the non-liver fibrosis comprises fibrosis in lung, kidney, heart, skin, eye, gastrointestinal tract, peritoneum, bone marrow, muscle, blood vessel, vasculature, or any combination thereof, and/or wherein the subject in need thereof is a subject suffering from a fibrotic disorder selected from the group consisting of idiopathic pulmonary fibrosis (IPF), cardiac fibrosis, dermal fibrosis, renal fibrosis, or a combination thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

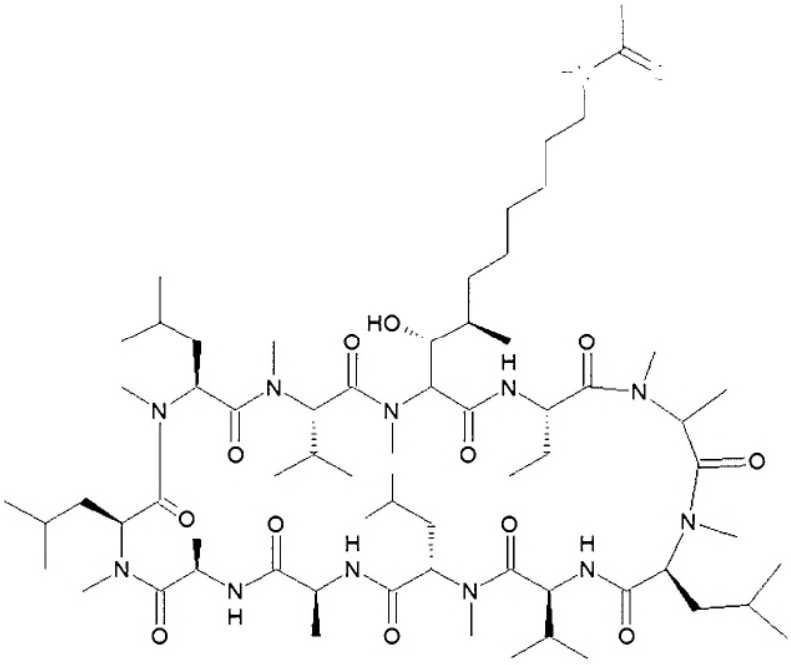
[0026] FIGS. 1A-B are histograms showing dose-dependent decreases in the abundance of procollagen and fibronectin caused by CRV431 treatment in human LX-2 hepatic stellate cell culture.

[0027] FIGS. 2A-B are histograms showing dose-dependent decreases in the abundance of procollagen and fibronectin caused by CRV431 treatment in human IPF lung fibroblast culture.

[0028] FIGS. 3A-B are histograms showing dose-dependent decreases in the

WHAT IS CLAIMED IS:

1. Use of a composition comprising CRV431, or a pharmaceutically acceptable salt, solvate, stereoisomer thereof, in the manufacture of a medicament for treating non-liver fibrosis, for reducing non-liver fibrosis, reversing non-liver fibrosis, for preventing non-liver fibrosis, for preventing or reducing non-liver fibrosis formation, for reducing the amount of non-liver fibrosis, and/or for delaying the onset of non-liver fibrosis in a subject in need thereof,



(CRV431),

wherein the non-liver fibrosis comprises fibrosis in lung, kidney, heart, skin, eye, gastrointestinal tract, peritoneum, bone marrow, muscle, blood vessel, vasculature, or any combination thereof, and/or wherein the subject in need thereof is a subject suffering from a fibrotic disorder selected from the group consisting of idiopathic pulmonary fibrosis (IPF), cardiac fibrosis, dermal fibrosis, renal fibrosis, or a combination thereof.

2. The use of claim 1, wherein the amount of non-liver fibrosis in the subject is reduced, and optionally wherein the amount of non-liver fibrosis in the subject is reduced by 5%, 10%, 20%, or more, and/or wherein the formation of non-liver fibrosis in the subject is reduced, and optionally wherein the formation of non-liver fibrosis in the subject is reduced by 5%, 10%, 20%, or more.

3. The use of claim 1, wherein the subject in need thereof is a subject at a risk of developing fibrosis.

4. The use of claim 3, wherein the subject in need thereof is a subject having no fibrosis progression.

5. The use of claim 3 or 4, wherein the risk of developing fibrosis in the subject is reduced by at least 5%, 10%, 20% or more as compared to untreated subjects.

6. The use of any one of claims 1-5, wherein the onset of non-liver fibrosis is delayed in the subject by at least a month, a year, or more, and/or wherein the fibrosis formation is reduced in the subject by at least a month, a year, or more as compared to untreated subjects.

7. The use of claim 1, wherein the subject in need thereof is a subject suffering from non-liver fibrosis.

8. The use of any one of claims 1-7, wherein non-liver fibrosis formation is inhibited in the subject.

9. The use of any one of claims 1-8, wherein the composition comprises a therapeutically or prophylactically effective amount of CRV431, or a pharmaceutically acceptable salt, solvate, stereoisomer thereof.

10. The use of any one of claims 1-9, wherein the non-liver fibrosis is induced by a therapeutic agent, an injury, or a combination thereof, wherein the non-liver fibrosis is associated with the accumulation of extracellular matrix constituents that occurs following trauma, inflammation, tissue repair, immunological reactions, cellular hyperplasia, neoplasia, or a combination thereof, wherein the non-liver fibrosis or fibrosis is associated with major organ diseases, fibroproliferative disorders, scarring associated with trauma, or a combination thereof, and/or wherein the fibrosis is associated with interstitial lung disease, liver cirrhosis, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, kidney disease, heart or vascular disease, diseases of the eye, systemic and local scleroderma, keloids, hypertrophic scars, atherosclerosis, restenosis, Dupuytren's contracture, surgical complications, chemotherapeutics drug-induced fibrosis, radiation-induced fibrosis, accidental injury and burns, retroperitoneal fibrosis, peritoneal fibrosis/peritoneal scarring, or a combination thereof, and optionally wherein the fibrosis associated with interstitial lung disease is sarcoidosis, silicosis, drug reactions, infections, collagen vascular diseases, rheumatoid arthritis, systemic sclerosis, scleroderma, pulmonary fibrosis, idiopathic pulmonary fibrosis, usual interstitial pneumonitis, interstitial lung disease, cryptogenic fibrosing alveolitis, bronchiolitis obliterans, bronchiectasis, or a combination thereof.

11. The use of any one of claims 1-10, wherein the subject is a mammal, and optionally wherein the subject is a human.

12. The use of any one of claims 1-11, wherein the composition comprises one or more pharmaceutically acceptable excipients, and/or wherein the composition comprises one or more additional therapeutic agents.

13. The use of any one of claims 1-12, wherein the composition is formulated to be administered to the subject and further comprises one or more additional therapeutic agents.

14. The use of claim 12 or 13, wherein the one or more additional therapeutic agents comprise an additional antifibrotic agent, and/or wherein the one or more additional therapeutic agents comprises Type II interferon receptor agonists, pirfenidone and pirfenidone analogs, nintedanib and nintedanib analogs, anti-angiogenic agents, anti-inflammatory agents, IL-1 antagonists, angiotensin-converting-enzyme (ACE) inhibitors, angiotensin receptor blockers and aldosterone antagonists, mitomycin C (MMC), 5-fluorouracil (5-FU), adenylyl cyclase activators, β-adenoreceptor agonists, flavonoids, mast cell stabilizers, phosphodiesterase inhibitors, procyanidins, or a combination thereof.

15. The use of any one of claims 12-14, wherein at least one of the one or more additional therapeutic agents is formulated to be co-administered to the subject with the composition.

16. The use of any one of claims 12-14, wherein at least one of the one or more additional therapeutic agents is formulated to be administered to the subject before the administration of the composition, after the administration of the composition, or both.

17. The use of any one of claims 1-16, wherein the composition is formulated to be administered to the subject by intravenous administration, oral administration, or parenteral administration, and/or wherein the composition is in the form of powder, pill, tablet, microtablet, pellet, micropellet, capsule, capsule containing microtablets, liquid, aerosols, or nanoparticles.

18. The use of any one of claims 1-17, wherein the composition for use is formulated to be administered to the subject at an effective daily dose of 10 mg to 250 mg.