CLAIMS

What is claimed is:

1. Use of an effective amount of an IL-22 dimer, in the manufacture of a medicament for:

(a) preventing or treating a virus-induced organ injury or failure in an individual;

(b) protecting an organ from virus-induced organ injury or failure in an individual;

(c) promoting regeneration of injured tissue or organ due to virus infection in an individual;

(d) treating or preventing endothelial dysfunction in an injured tissue or organ due to virus infection in an individual; or

(e) reducing inflammation due to virus infection in an individual.

2. The use of claim 1, wherein the virus-induced organ injury or failure is

(a) virus-induced lung injury or failure; or

(b) virus-induced sepsis, septic shock, or multiple organ dysfunction syndrome (MODS).

3. The use of claim 2, wherein the virus-induced lung injury or failure is pulmonary fibrosis, pneumonia, acute lung injury (ALI), acute respiratory distress syndrome (ARDS), Severe Acute Respiratory Syndrome coronavirus (SARS), Middle East Respiratory Syndrome coronavirus (MERS), Coronavirus disease 2019 (COVID-19), Influenza A virus subtype H1N1 (H1N1) swine flu, or Influenza A virus subtype H5N1 (H5N1) bird flu.

4. The use of any one of claims 1-3, wherein the virus-induced organ injury or failure is caused by a virus of any one of the *Orthomyxoviridae*, *Filoviridae*, *Flaviviridae*, *Coronaviridae*, and *Poxviridae* families.

5. The use of claim 4,

(a) wherein the virus is an *Orthomyxoviridae* virus selected from the group consisting of Influenza A virus, Influenza B virus, Influenza C virus, and any subtype or reassortant thereof;

(b) wherein the virus is a *Coronaviridae* virus selected from the group consisting of alpha coronaviruses 229E (HCoV-229E), New Haven coronavirus NL63 (HCoV-NL63), beta coronaviruses OC43 (HCoV-OC43), coronavirus HKU1 (HCoV-HKU1), Severe Acute Respiratory Syndrome coronavirus (SARS-CoV), Middle East Respiratory Syndrome coronavirus (MERS-CoV), and Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2);

(c) wherein the virus is a *Filoviridae* virus selected from Ebola virus (EBOV) and Marburg virus (MARV); or

(d) wherein the virus is a *Flaviviridae* virus selected from the group consisting of Zika

virus (ZIKV), West Nile virus (WNV), Dengue virus (DENV), and Yellow Fever virus (YFV).

6. The use of claim 5, wherein the virus is

(a) Influenza A virus subtype H1N1 (H1N1) or Influenza A virus subtype H5N1 (H5N1); or

(b) SARS-CoV-2 or variant thereof.

7. The use of any one of claims 1-6, wherein another therapeutic agent is to be further administered to the individual.

8. The use of claim 7, wherein the other therapeutic agent is selected from the group consisting of a corticosteroid, an anti-inflammatory signal transduction modulator, a β2-adrenoreceptor agonist bronchodilator, an anticholinergic, a mucolytic agent, an antiviral agent, an anti-fibrotic agent, hypertonic saline, an antibody, a vaccine, and mixtures thereof.

9. The use of claim 8,

(a) wherein the antiviral agent is selected from the group consisting of remdesivir, lopinavir/ritonavir, IFNα, lopinavir, ritonavir, penciclovir, galidesivir, disulfiram, darunavir, cobicistat, ASC09F, disulfiram, nafamostat, griffithsin, alisporivir, chloroquine, nitazoxanide, baloxavir marboxil, oseltamivir, zanamivir, peramivir, amantadine, rimantadine, favipiravir, laninamivir, ribavirin, umifenovir, and any combinations thereof; or

(b) the anti-fibrotic agent is selected from the group consisting of nintedanib, pirfenidone, and N-Acetylcysteine (NAC).

10. The use of claim 9, wherein:

(a) the other therapeutic agent is i) remdesivir or ii) lopinavir/ritonavir and IFNα, and the virus-induced organ injury or failure is induced by SARS-CoV-2; or

(b) the other therapeutic agent is selected from the group consisting of oseltamivir, zanamivir, peramivir, lopinavir/ritonavir, IFNα, and any combinations thereof, and the virus-induced organ injury or failure is induced by H1N1 or H5N1.

11. The use of any one of claims 1-10,

(a) wherein the virus-induced organ injury or failure comprises endothelial cell injury, dysfunction, or death; and/or

(b) wherein the injured tissue or organ comprises injured or dysfunctional endothelial cells.

12. The use of any one of claims 1-11, wherein endothelial dysfunction comprises endothelial glycocalyx degradation.

13. The use of any one of claims 1-12, wherein the use comprises preventing and/or reducing endothelial glycocalyx degradation, down-regulating Toll-like Receptor 4 (TLR4) signaling, and/or regenerating endothelial glycocalyx.

14. The use of any one of claims 11-13, wherein the endothelial cell is a pulmonary endothelial cell.

15. The use of any one of claims 1-14, wherein the IL-22 dimer comprises two monomeric subunits, and wherein each monomeric subunit comprises an IL-22 monomer and a dimerization domain.

16. The use of claim 15, wherein the IL-22 monomer is connected to the dimerization domain via a linker.

17. The use of claim 16, wherein the linker:

(a) comprises the sequence of any one of SEQ ID NOs: 1-20 and 32;

(b) is about 6 to about 30 amino acids in length; and/or

(c) comprises the sequence of SEQ ID NO: 1 or 10.

18. The use of any one of claims 15-17, wherein the dimerization domain comprises:

(a) at least two cysteines capable of forming intermolecular disulfide bonds; and/or

(b) at least a portion of an Fc fragment.

19. The use of claim 18, wherein the Fc fragment comprises:

(a) CH2 and CH3 domains; and/or

(b) the sequence of SEQ ID NO: 22 or 23.

20. The use of any one of claims 15-19, wherein the IL-22 monomer comprises the sequence of SEQ ID NO: 21.

21. The use of any one of claims 15-20,

(a) wherein the IL-22 monomer is N-terminal to the dimerization domain; or

(b) wherein the IL-22 monomer is C-terminal to the dimerization domain.

22. The use of any one of claims 15-21,

(a) wherein each monomeric subunit comprises the sequence of any of SEQ ID NOs: 24-27; and/or

(b) wherein each monomeric subunit comprises the sequence of SEQ ID NO: 24.

23. The use of any one of claims 1-22, wherein the effective amount of the IL-22 dimer is:

(a) about 2 μg/kg to about 200 μg /kg;

(b) about 5 μg/kg to about 80 μg/kg;

(c) about 10 μg/kg to about 45 μg/kg; or

(d) about 30 μg/kg to about 45 μg/kg.

24. The use of any one of claims 1-23, wherein:

(a) the IL-22 dimer is to be administered intravenously, intrapulmonarily, via inhalation, or via insufflation;

(b) the IL-22 dimer is to be administered at least once a week; and/or

(c) the IL-22 dimer is to be administered on day 1 and day 6 of a 10-day treatment cycle, or day 1 and day 8 of a 14-day treatment cycle.

25. The use of any one of claims 1-24, wherein:

(a) the individual is at least about 55 years old; and/or

(b) the use further comprising selecting an individual based on that the individual is at least about 55 years old.