

What is claimed is:

1. Use of a composition in the manufacture of a medicament for treating a neurodegenerative or neuroinflammatory disease or disorder in a subject in need thereof, wherein the composition comprises:

(i) a CTLA-4-containing protein; and

(ii) an IL-2 protein,

wherein the CTLA-4-containing protein and the IL-2 protein are to be administered to the subject, wherein the medicament mitigates one or more symptoms associated with the neurodegenerative or neuroinflammatory disease or disorder in the treated subject.

2. The use of claim 1, wherein the CTLA-4-containing protein:

(i) comprises a human CTLA-4 extracellular domain;

(ii) is glycosylated;

(iii) comprises the amino acid sequence of SEQ ID NO:1; and/or

(iv) comprises a homodimer of two monomers, each comprising the amino acid sequence of SEQ ID NO:1.

3. The use of claim 1, wherein the CTLA-4-containing protein is a fusion protein,

wherein the fusion protein comprises a human CTLA-4 extracellular domain and a human immunoglobulin Fc domain, optionally wherein the human immunoglobulin Fc domain is a modified Fc domain that comprises an immunoglobulin hinge region, CH2 region and CH3.

4. The use of claim 3, wherein the human immunoglobulin Fc domain is a human IgG1 Fc domain.

5. The use of claim 1, wherein the CTLA4-containing protein is abatacept.

6. The use of claim 1, wherein the IL-2 protein is a human IL-2 protein, wherein

(i) the human IL-2 protein comprises a serine at the amino acid position corresponding to native mature human IL-2 amino acid residue 125;

(ii) the human IL-2 protein lacks a N-terminal alanine amino acid;

(iii) the human IL-2 protein comprises the amino acid sequence of SEQ ID NO:3; and/or

(iv) the human IL-2 protein is not glycosylated.

7. The use of claim 1, wherein the IL-2 protein is aldesleukin.
8. The use of claim 1, wherein the CTLA-4-containing protein is abatacept, and wherein the IL-2 protein is aldesleukin.
9. The use of claim 8, wherein the abatacept and/or aldesleukin is to be administered by injection, by infusion, subcutaneously or intravenously.
10. The use of claim 8, wherein
 - (i) the abatacept is to be administered (a) once every week, optionally wherein the abatacept is to be administered once every week for three consecutive weeks, or (b) once every two weeks, optionally wherein the abatacept is to be administered once every two weeks for 15 weeks or for 6 months; and/or
 - (ii) the aldesleukin is to be administered once daily for two to five consecutive days, optionally wherein the aldesleukin is to be administered once daily for three consecutive days or once daily for five consecutive days.
11. The use of claim 8, wherein:
 - (a) (i) the abatacept is to be administered once every two weeks and (ii) the aldesleukin is to be administered once daily for three or five consecutive days beginning on the day the abatacept is administered; or
 - (b) (i) the abatacept is to be administered once every two weeks for fifteen weeks, (ii) aldesleukin administration begins on week three, and (iii) once aldesleukin administration begins, the aldesleukin is to be administered once daily for three or five consecutive days beginning on the day the abatacept is administered,optionally wherein the abatacept and the aldesleukin are to be administered subcutaneously.
12. The use of claim 8, wherein the abatacept is to be administered in an amount in the range of 50 mg to 125 mg, optionally wherein:
 - (i) the abatacept is to be administered in a 50 mg amount, further optionally wherein the abatacept is to be subcutaneously administered in a 0.4 mL volume;
 - (ii) the abatacept is to be administered in an 87.5 mg amount, further optionally wherein the abatacept is to be subcutaneously administered in a 0.7 mL volume; or

- (iii) the abatacept is to be administered in a 125 mg amount, further optionally wherein the abatacept is to be subcutaneously administered in a 1.0 mL volume.
13. The use of claim 8, wherein the aldesleukin is to be administered:
- (i) in an amount in the range of 500,000 units to 3,000,000 units;
 - (ii) in an amount in the range of 500,000 units to 2,000,000 units; or
 - (iii) in an amount of 1,000,000 units,
- optionally wherein the aldesleukin is to be administered subcutaneously.
14. The use of claim 8, wherein the medicament is to be administered via a dosing cycle that begins on day 1 and the dosing cycle comprises administration of a formulation comprising abatacept and aldesleukin.
15. The use of claim 14, wherein the dosing cycle:
- (i) comprises administration of the formulation to the subject 1-10 times;
 - (ii) comprises a single administration of the formulation to the subject on day 1 of the dosing cycle;
 - (iii) comprises administration of the formulation to the subject daily for two consecutive days, beginning on day 1 of the dosing cycle;
 - (iv) comprises administration of the formulation to the subject daily for three consecutive days, beginning on day 1 of the dosing cycle;
 - (v) comprises administration of the formulation to the subject daily for four consecutive days, beginning on day 1 of the dosing cycle;
 - (vi) comprises administration of the formulation to the subject daily for five consecutive days, beginning on day 1 of the dosing cycle;
 - (vii) is to be repeated 1-12 times or 6 times, optionally wherein each repeated dosing cycle begins 10-28 days after day 1 of the previous dosing cycle, further optionally wherein each repeated dosing cycle begins 14 days after day 1 of the previous dosing cycle;
 - (viii) comprises administration of a formulation comprising 5 mg to 125 mg abatacept and 3×10^4 to 3×10^7 units aldesleukin;

- (ix) comprises administration of a formulation comprising 8.75 mg to 87.5 mg abatacept and 3×10^4 to 3×10^7 units aldesleukin;
- (x) comprises administration of a formulation comprising about 29.17 mg abatacept and about 1×10^5 units aldesleukin;
- (xi) comprises administration of a formulation comprising about 29.17 mg abatacept and about 1×10^6 units aldesleukin;
- (xii) comprises administration of a formulation comprising about 29.17 mg abatacept and about 1×10^7 units aldesleukin;
- (xiii) comprises administration of a formulation comprising 5 mg to 50 mg abatacept and 3×10^4 to 3×10^7 units aldesleukin;
- (xiv) comprises administration of a formulation comprising about 16.67 mg abatacept and about 1×10^5 units aldesleukin;
- (xv) comprises administration of a formulation comprising about 16.67 mg abatacept and about 1×10^6 units aldesleukin;
- (xvi) comprises administration of a formulation comprising about 16.67 mg abatacept and about 1×10^7 units aldesleukin;
- (xvii) comprises administration of a formulation comprising 12.5 mg to 125 mg abatacept and 3×10^4 to 3×10^7 units aldesleukin;
- (xviii) comprises administration of a formulation comprising about 41.67 mg abatacept and about 1×10^5 units aldesleukin;
- (xix) comprises administration of a formulation comprising about 41.67 mg abatacept and about 1×10^6 units aldesleukin;
- (xx) comprises administration of a formulation comprising about 41.67 mg abatacept and about 1×10^7 units aldesleukin; or
- (xxi) comprises administration of the formulation to the subject daily for three consecutive days, beginning on day 1 of the dosing cycle, wherein the formulation comprises about 29.17 mg abatacept and about 1×10^6 units aldesleukin.

16. The use of claim 14, wherein a total of:

- (i) 50 mg abatacept and 3×10^5 units aldesleukin are to be administered to the subject per dosing cycle, wherein the dosing cycle comprises 1-10 administrations of an abatacept/aldesleukin formulation as shown at Table 1A;
- (ii) 50 mg abatacept and 3×10^6 units aldesleukin are to be administered to the subject per dosing cycle, wherein the dosing cycle comprises 1-10 administrations of an abatacept/aldesleukin formulation as shown at Table 1B;
- (iii) 50 mg abatacept and 3×10^7 units aldesleukin are to be administered to the subject per dosing cycle, wherein the dosing cycle comprises 1-10 administrations of an abatacept/aldesleukin formulation as shown at Table 1C;
- (iv) 87.5 mg abatacept and 3×10^5 units aldesleukin are to be administered to the subject per dosing cycle, wherein the dosing cycle comprises 1-10 administrations of an abatacept/aldesleukin formulation as shown at Table 2A;
- (v) 87.5 mg abatacept and 3×10^6 units aldesleukin are to be administered to the subject per dosing cycle, wherein the dosing cycle comprises 1-10 administrations of an abatacept/aldesleukin formulation as shown at Table 2B;
- (vi) 87.5 mg abatacept and 3×10^7 units aldesleukin are to be administered to the subject per dosing cycle, wherein the dosing cycle comprises 1-10 administrations of an abatacept/aldesleukin formulation as shown at Table 2C;
- (vii) 125 mg abatacept and 3×10^5 units aldesleukin are to be administered to the subject per dosing cycle, wherein wherein the dosing cycle comprises 1-10 administrations of an abatacept/aldesleukin formulation as shown at Table 3A;
- (viii) 125 mg abatacept and 3×10^6 units aldesleukin are to be administered to the subject per dosing cycle, wherein the dosing cycle comprises 1-10 administrations of an abatacept/aldesleukin formulation as shown at Table 3B; or
- (ix) 125 mg abatacept and 3×10^7 units aldesleukin are to be administered to the subject per dosing cycle, wherein the dosing cycle comprises 1-10 administrations of an abatacept/aldesleukin formulation as shown at Table 3C.

17. The use of claim 14, wherein the dosing cycle is to be repeated 6 times, with each repeated dosing cycle beginning 14 days after day 1 of the previous dosing cycle.

18. The use of claim 14, further comprising administration of an abatacept formulation to the subject 14 days prior to day 1 of the first dosing cycle, wherein the abatacept formulation comprises:

- (i) abatacept;
- (ii) 50 mg to 125 mg abatacept; or
- (iii) 87.5 mg abatacept, and

optionally wherein the abatacept formulation is to be administered:

- (a) by injection or infusion;
- (b) subcutaneously; or
- (c) intravenously.

19. The use of any one of claims 1-18, wherein the neurodegenerative disease or disorder is amyotrophic lateral sclerosis, Alzheimer's disease, Parkinson's disease, multiple sclerosis, frontotemporal dementia or Huntington's disease.

20. The use of any one of claims 1-19, wherein the neuroinflammatory disease or disorder is associated with stroke, acute disseminated encephalomyelitis, acute optic neuritis, acute inflammatory demyelinating polyradiculoneuropathy, chronic inflammatory demyelinating polyradiculoneuropathy, Guillain-Barre syndrome, transverse myelitis, neuromyelitis optica, epilepsy, traumatic brain injury, spinal cord injury, encephalitis, central nervous system vasculitis, neurosarcoidosis, autoimmune or post-infectious encephalitis or chronic meningitis.

21. The use of claim 1, wherein the medicament is to be administered with an additional therapeutic intervention comprising:

- (i) a cognitive rehabilitation program, wherein the cognitive rehabilitation program is a computer-implemented cognitive rehabilitation program; and/or
- (ii) a neurostimulation technique, wherein the neurostimulation technique is:
 - (a) an invasive brain stimulation (IBS) technique, wherein the IBS technique is selected from the group consisting of deep brain stimulation (DBS) and invasive vagus nerve stimulation (VNS), and/or
 - (b) a non-invasive brain stimulation (NIBS) technique, wherein the NIBS technique is selected from the group consisting of transcranial magnetic

stimulation (TMS), transcranial direct current stimulation (tDCS), transcranial alternating current stimulation (tACS), electroconvulsive treatment (ECT), magnetic seizure therapy (MST), cranial electrostimulation (CES), and non-invasive VNS.

22. A kit, comprising, in separate containers, (i) one or more doses of a formulation comprising 50 to 125 mg abatacept, and (ii) one or more doses of a formulation comprising 500,000 to 3,000,000 units aldesleukin, optionally wherein

- (a) the kit comprises one or more doses of a formulation comprising 50 mg abatacept;
- (b) the kit comprises one or more doses of a formulation comprising 87.5 mg abatacept;
- (c) the kit comprises one or more doses of a formulation comprising 125 mg abatacept;
- (d) the kit comprises one or more doses of a formulation of 500,000 to 2,000,000 units aldesleukin;
- (e) the kit comprises one or more doses of a formulation of 500,000 to 3,000,000 units aldesleukin;
- (f) the kit comprises one or more doses of a formulation of 1,000,000 units aldesleukin;
- (g) the one or more doses of abatacept are present in lyophilized form;
- (h) the one or more doses of abatacept are present as a lyophilized powder or lyophilized cake;
- (i) the one or more doses of aldesleukin are present in lyophilized form; and/or
- (j) the one or more doses of aldesleukin are present as a lyophilized powder or lyophilized cake.

23. A pharmaceutical composition comprising one or more abatacept/aldesleukin doses, comprising:

- (i) 5 mg to 125 mg abatacept and 3×10^4 to 3×10^7 units aldesleukin;
- (ii) 8.75 mg to 87.5 mg abatacept and 3×10^4 to 3×10^7 units aldesleukin;
- (iii) about 29.17 mg abatacept and about 1×10^5 units aldesleukin;
- (iv) about 29.17 mg abatacept and about 1×10^6 units aldesleukin;
- (v) about 29.17 mg abatacept and about 1×10^7 units aldesleukin;
- (vi) 5 mg to 50 mg abatacept and 3×10^4 to 3×10^7 units aldesleukin;

- (vii) about 16.67 mg abatacept and about 1×10^5 units aldesleukin;
- (viii) about 16.67 mg abatacept and about 1×10^6 units aldesleukin;
- (ix) about 16.67 mg abatacept and about 1×10^7 units aldesleukin;
- (x) 12.5 mg to 125 mg abatacept and 3×10^4 to 3×10^7 units aldesleukin;
- (xi) about 41.67 mg abatacept and about 1×10^5 units aldesleukin;
- (xii) about 41.67 mg abatacept and about 1×10^6 units aldesleukin;
- (xiii) about 41.67 mg abatacept and about 1×10^7 units aldesleukin; or
- (xiv) doses as shown at Table 4.

24. The pharmaceutical composition of claim 23, wherein the pharmaceutical composition:
- (i) is present in lyophilized form, optionally wherein the pharmaceutical composition is present as a lyophilized powder or lyophilized cake; or
 - (ii) is a solution, optionally wherein the pharmaceutical composition is present as an aqueous solution,

wherein the solution comprises the one or more abatacept/aldesleukin doses at a concentration of:

- (a) 1 abatacept/aldesleukin dose/0.4 ml;
- (b) 1 abatacept/aldesleukin dose/0.7 ml;
- (c) 1 abatacept/aldesleukin dose/1.0 ml;
- (d) 1 abatacept/aldesleukin dose/1.5 ml; or
- (e) 1 abatacept/aldesleukin dose/2.0 ml,

wherein the pharmaceutical composition is suitable for subcutaneous or intravenous administration.

25. Use of a composition in the manufacture of a medicament for treating a disease or disorder in a subject in need thereof, wherein the composition comprises:

- (i) a CTLA-4-containing protein; and
- (ii) an IL-2 protein;

wherein the CTLA-4-containing protein and the IL-2 protein are to be administered to the subject, wherein the disease or disorder is graft-versus-host disease or an autoimmune disease or disorder, and

wherein the medicament mitigates one or more symptoms associated with the autoimmune disease or disorder in the treated subject.

26. The use of claim 25, wherein the autoimmune disease or disorder is associated with systemic sclerosis (scleroderma), polymyositis, ulcerative colitis, inflammatory bowel disease, Crohn's disease, celiac disease, multiple sclerosis (MS), rheumatoid arthritis (RA), Type I diabetes, psoriasis, dermatomyositis, systemic lupus erythematosus, cutaneous lupus, myasthenia gravis, autoimmune nephropathy, autoimmune hemolytic anemia, autoimmune cytopenia autoimmune hepatitis, autoimmune uveitis, alopecia, thyroiditis or pemphigus.