Claims:

1. A pharmaceutical composition, comprising a PEGylated human hyaluronidase and a pharmaceutical carrier, wherein: the pharmaceutical composition is formulated for intravenous administration; and the PEGylated human hyaluronidase contains three to six PEG moieties per polypeptide.

2. The pharmaceutical composition of claim 1, wherein:

the hyaluronidase is a neutral active soluble hyaluronidase polypeptide containing at least one N-linked sugar moiety, wherein the N-linked sugar moiety is covalently attached to an asparagine residue of the polypeptide;

the hyaluronidase comprises a sequence of amino acids included in SEQ ID NO:1 or a sequence that has at least 91% amino acid sequence identity with a sequence of amino acids included in SEQ ID NO:1; and

the hyaluronidase is soluble and truncated at the C-terminus at an amino acid residue that is between amino acid residues 467 to 483, inclusive, of SEQ ID NO:1 or corresponding residues in a polypeptide that has 91% sequence identity.

3. The pharmaceutical composition of claim 2, wherein the hyaluronidase is encoded by a nucleic acid molecule that encodes amino acids 1-482 of SEQ ID NO:1 or amino acids 36-482 of SEQ ID NO:1.

4. The pharmaceutical composition of claim 3, wherein the nucleic acid molecule has a sequence of nucleotides set forth in SEQ ID NO:48.

5. The pharmaceutical composition of claim 1, wherein the hyaluronidase includes a sequence of amino acids set forth in SEQ ID NO:1 that is truncated at an amino acid residue selected from among 467, 477, 478, 479, 480, 481, 482 and 483.

6. The pharmaceutical composition of claim 3, wherein the hyaluronidase is secreted in CHO cells.

7. The pharmaceutical composition of any of claims 1-6, wherein the PEG moieties are branched.

8. The pharmaceutical composition of any of claims 1-6, wherein the PEG moieties result from reaction with a PEG reagent selected from among mPEG-SBA (5kDa), mPEG-SBA (20kDa), mPEG-SBA (30kDa), mPEG-SMB (20kDa) mPEG-SMB (30kDa), mPEG-butyrldehyde (30kDa), mPEG-SPA (20kDa), mPEG-SPA (30kDa), mPEG2-NHS (10kDa branched), mPEG2-NHS (20kDa branched), mPEG-NHS (40kDa branched), mPEG2-NHS (60kDa branched), PEG-NHS-biotin (5kDa biotinylated), PEG-p-nitrophenyl-carbonate (30kDa) and PEG-propionaldehyde (30kDa).

9. The pharmaceutical composition of any of claims 1-8, further comprising an active agent that is a therapeutic or cosmetic agent.

10. The pharmaceutical composition of claim 9, wherein the active agent is selected from a corticosteroid, a chemotherapeutic agent, an antibody, a botulinum toxin and an anti-microbial.

11. The pharmaceutical composition of claim 9 or claim 10, wherein the agent is selected from among alclometasones, algestones, beclomethasones, betamethasones, budesonides, clobetasols, clobetasones, clocortolones, cloprednols, corticosterones, cortisones and hydrocortisones, cortivazols, deflazacorts, desonides, desoximetasones, dexamethasones, diflorasones, diflucortolones, difluprednates, enoxolones, fluazacorts, flucloronides, flumethasones, flunisolides, fluocinolones, fluocinonides, fluocortins, fluocortolones, fluorometholones, fluperolones, fluprednidenes, fluprednisolones, flurandrenolides, fluticasones, formocortals, halcinonides, halobetasols, halometasones, halopredones, hydrocortamates, hydrocortisones, loteprednol etabonate, mazipredones, medrysones, meprednisones, methylprednisolones, mometasone furoate, paramethasones, prednicarbates, prednisolones (e.g. prednisolone 25-diethylamino-acetate, prednisolone sodium phosphate), prednisones, prednivals, prednylidenes, rimexolones, tixocortols and triamcinolones.

12. The pharmaceutical composition of claim 11, wherein the agent is selected from among hydrocortisone acetate, dexamethasone 21-phosphate, prednisolone 25-diethylamino-acetate, prednisolone sodium phosphate, triamcinolone acetonide, triamcinolone benetonide, and triamcinolone hexacetonide.

13. The pharmaceutical composition of claim 11, wherein the agent is selected from among anti-cancer antibodies, insulins, interferons, pegylated interferons and chemotherapeutic agents

14. Use of a pharmaceutical composition of any of claims 1-13 in the manufacture of a medicament for intravenous administration.

15. A combination, comprising: a pharmaceutical composition of any of claims 1-13; and a second composition comprising an active agent that is a therapeutic or cosmetic agent.

16. The combination of claim 15, wherein the active agent is selected from among a corticosteroid, a chemotherapeutic agent, an antibody, a botulinum toxin and an anti-microbial.

17. The combination of claim 16, wherein the active agent is a corticosteroid.

18. The combination of claim 17, wherein the agent is selected from among alclometasones, algestones, beclomethasones, betamethasones, budesonides, clobetasols, clobetasones, clocortolones, cloprednols, corticosterones, cortisones and hydrocortisones, cortivazols, deflazacorts, desonides, desoximetasones, dexamethasones, diflorasones, diflucortolones, difluprednates, enoxolones, fluazacorts, flucloronides, flumethasones, flunisolides, fluocinolones, fluocinonides, fluocortins, fluocortolones, fluorometholones, fluperolones, fluprednidenes, fluprednisolones, flurandrenolides, fluticasones, formocortals, halcinonides, halobetasols, halometasones, halopredones, hydrocortamates, hydrocortisones, loteprednol etabonate, mazipredones, medrysones, meprednisones, methylprednisolones, mometasone furoate, paramethasones, prednicarbates, prednisolones, prednisones, prednivals, prednylidenes, rimexolones, tixocortols and triamcinolones.

19. The combination of claim 18, wherein the agent is selected from among hydrocortisone acetate, dexamethasone 21-phosphate, prednisolone 25-diethylamino-acetate, prednisolone sodium phosphate, triamcinolone acetonide, triamcinolone benetonide, and triamcinolone hexacetonide.

20. The combination of claim 15, wherein the agent is selected from among anti-cancer antibodies, insulins, interferons, pegylated interferons and chemotherapeutic agents.

21. The combination of claim 15, wherein the agent is an immunoglobulin.

22. The combination of claim 15, wherein the agent is selected from among interferon-alphas and interferon betas.

23. The combination of claim 20, wherein the agent is an insulin.

24. The combination of claim 20, wherein the agent is selected from among Docetaxels, Doxorubicins; Doxorubicin liposomals; and bevacizumabs.

25. A combination, comprising:

a) a pharmaceutical composition of any of claims 1-8; and

b) a blood modifier drug.

26. The combination of claim 25, wherein the blood modifier is selected from among antihemophilic factors, anti-inhibitor coagulant complexes, antithrombin III, coagulation Factor V, coagulation Factor VIII, coagulation Factor IX, plasma protein fractions, von Willebrand factors; antiplatelet agents, abciximabs, anagrelides, cilostazols, clopidogrel bisulfates, dipyridamoles, epoprostenols, eptifibatides, tirofibans; colony stimulating factors (CSFs), Granulocyte CSFs, Granulocyte Macrophage CSFs; erythropoiesis stimulators, erythropoietins, darbepoetin alfas, epoetin alfas; hemostatics and albumins, aprotinins, combinations of antihemophilic factors and plasma, Desmopressin Acetates, and albumins; immune globulins, as well as hepatitis B immune globulins; thrombin inhibitors, lepirudin, and drotrecogin alfas; anticoagulants, dalteparins, enoxaparins, heparins, and warfarins.

27. The pharmaceutical composition of any of claims 1-13 further comprising a blood modifier drug.

28. The pharmaceutical composition of claim 27, wherein the blood modifier is selected from among antihemophilic factors, anti-inhibitor coagulant complexes, antithrombin III, coagulation Factor V, coagulation Factor VIII, coagulation Factor IX,

plasma protein fractions, von Willebrand factors; antiplatelet agents, abciximabs, anagrelides, cilostazols, clopidogrel bisulfates, dipyridamoles, epoprostenols, eptifibatides, tirofibans; colony stimulating factors (CSFs), Granulocyte CSFs, Granulocyte Macrophage CSFs; erythropoiesis stimulators, erythropoietins, darbepoetin alfas, epoetin alfas; hemostatics and albumins, aprotinins, combinations of antihemophilic factors and plasma, Desmopressin Acetates, and albumins; immune globulins, as well as hepatitis B immune globulins; thrombin inhibitors, lepirudin, and drotrecogin alfas; anticoagulants, dalteparins, enoxaparins, heparins, and warfarins.

29. The pharmaceutical composition of claim 9, wherein the agent is an anti-cancer agent or an anti-infective agent.

30. Use of the pharmaceutical composition of any of claims 1-8 and 27-29 or the combination of claim 25 or claim 26 for formulation of a medicament for treatment of a tumor.

31. A pharmaceutical composition of any of claims 1-8 and 27-29 formulated for use in treating a tumor.

32. A pharmaceutical composition of any of claims 1-8 and 27-29 formulated as a medicament for use in treating a tumor, wherein the tumor is an invasive tumor.

33. The pharmaceutical composition of any of claims 1-8 and 27-29 formulated as a medicament for use in treating a disorder of the mammalian eye by inducing liquefaction of vitreous; for use in treating disorders involving an excess of glycosaminoglycans by removal of glycosaminoglycans; or for use in treating a mammal who has had a stroke or other CNS injury by ameliorating the consequences of the stroke or other CNS injury.

34. The pharmaceutical composition of claim 9, wherein the agent is an antibody.

35. The pharmaceutical composition of claim 9, wherein the agent is a monoclonal antibody.

Claims:

1. A pharmaceutical composition, comprising a PEGylated soluble human hyaluronidase glycoprotein in a pharmaceutical carrier, wherein:

the pharmaceutical composition is formulated for use in intravenous administration;

the hyaluronidase contains three to six PEG moieties per polypeptide;

the hyaluronidase is neutral active;

the hyaluronidase is soluble; and

the hyaluronidase is a glycoprotein containing at least one N-linked sugar moiety, wherein the N-linked sugar moiety is covalently attached to an asparagine residue of the polypeptide.

2. The pharmaceutical composition of claim 1, wherein the hyaluronidase comprises a sequence of amino acids that exhibits at least 95% sequence identity to SEQ ID NO:1 or SEQ ID NO:3, with the proviso that the polypeptide does not consist of the sequence of amino acids set forth in SEQ ID NO:1.

3. The pharmaceutical composition of claim 1 or claim 2, wherein the hyaluronidase comprises a sequence of amino acids that minimally comprises the sequence of amino acids set forth as amino acid residues 36-464 of SEQ ID NO:1, with the proviso that the polypeptide does not consist of the sequence of amino acids set forth in SEQ ID NO:1.

4. The pharmaceutical composition of any of claims 1-3, wherein the hyaluronidase consists of the sequence of amino acids set forth as amino acids 1-483 of SEQ ID NO:1, or a sequence of amino acids that exhibits at least 95% sequence identity to amino acids 36-483 of SEQ ID NO:1.

5. The pharmaceutical composition of any of claims 1-4, wherein the hyaluronidase comprises a C-terminal amino acid residue that is selected from among amino acid residue 477, 478, 479, 480, 481 and 482 in the sequence of amino acid residues set forth in SEQ ID NO:1.

6. The pharmaceutical composition of any of claims 1-5, wherein the hyaluronidase is encoded by a nucleic acid molecule having a sequence of nucleotides set forth as nucleotides 106-1446 of SEQ ID NO:6, or a portion thereof that encodes a catalytically active polypeptide.

7. The pharmaceutical composition of claim 6, wherein the hyaluronidase comprises recombinant human PH20 (rHUPH20) that is expressed and secreted from CHO cells.

8. The pharmaceutical composition of any of claims 1-7, wherein said PEG moieties are branched.

9. The pharmaceutical composition of any of claims 1-8, wherein said PEG moieties result from reaction with a PEG reagent selected from among mPEG-SBA (5kDa), mPEG-SBA (2OkDa), mPEG-SBA 3OkDa), mPEG-SMB (2OkDa) mPEG-SMB (3OkDa), mPEG-butyrldehyde (3OkDa), mPEG-SPA (2OkDa), mPEG-SPA (3OkDa), mPEG2-NHS (1OkDa branched), mPEG2- NHS (2OkDa branched), mPEG-NHS (4OkDa branched), mPEG2-NHS (6OkDa branched), PEG-NHS-biotin (5kDa biotinylated), PEG-p-nitrophenyl-carbonate (3OkDa) and PEG-propionaldehyde (3OkDa).

10. A pharmaceutical composition of any of claims 1-9 for use in increasing the delivery or diffusion of a pharmacologic agent to a subject.

11. The pharmaceutical composition of claim 10, wherein the Agent is selected from among a chemotherapeutic agent, an analgesic agent, an anti-inflammatory agent, an antimicrobial agent, an amoebicidal agent, a trichomonocidal agent, an anti-parkinson agent, an anti-malarial agent, an anticonvulsant agent, an anti-depressant agent, an antiarthritics agent, an anti-fungal agent, an antihypertensive agent, an antipyretic agent, an anti-parasitic agent, an antihistamine agent, an alpha-adrenargic agonist agent, an alpha blocker agent, an anesthetic agent, a bronchial dilator agent, a biocide agent, a bactericide agent, a bacteriostatic agent, a beta adrenergic blocker agent, a calcium channel blocker agent, a cardiovascular drug agent, a contraceptive agent, a decongestant agent, a diuretic agent, a depressant agent, a diagnostic agent, an electrolyte agent, a hypnotic agent, a hormone agent, a hyperglycemic agent, a muscle relaxant agent, a muscle contractant agent, an ophthalmic agent, a parasympathomimetic agent, a psychic energizer agent, a sedative agent, a sleep inducer, a sympathomimetic agent, a tranquilizer agent, a urinary agent, a vaginal agent, a viricide agent, a vitamin agent, a non-steroidal anti-inflammatory agent, an angiotensin converting enzyme inhibitor agent, a polypeptide, a protein, a nucleic acid, a drug, and an organic molecule.

12. The pharmaceutical composition of claim 10, wherein the agent is selected from among a detectable molecule or other diagnostic agent, or a pharmacologic or pharmaceutically effective agent.

13. The pharmaceutical composition of claim 10, wherein the agent is an anti-cancer agent or an anti- infective agent.

14. The pharmaceutical composition of claim 10, wherein the agent is a blood-modifying pharmacologic agent.

15. The pharmaceutical composition of claim 10, wherein the agent is a molecule or macromolecular complex of between 20 nm and 200 nm in diameter.

16. The pharmaceutical composition of claim 10, wherein the agent is selected from among an Adalimumab, Agalsidase Beta, Aldesleukin, Alefacept, Ampicillin, Anakinra, Antipoliomyelitic Vaccine, Anti-Thymocyte, Azithromycin, Becaplermin, Caspofungin, Cefazolin, Cefepime, Cefotetan, Ceftazidime, Ceftriaxone, Cetuximab, Cilastatin, Clavulanic Acid, Clindamycin, Darbepoetin Alfa, Deaclizumab, Diphtheria Toxoid, Efalizumab, Epinephrine, Erythropoietin Alpha, Etanercept, Filgrastim, Fluconazole, Follicle- Stimulating Hormones such as Follitropin Alpha and Follitropin Beta, Fosphenytoin, Fluconazole, Gadodiamide, Gadopentetate, Gatifloxacin, Glatiramer, GM- CSF, Goserelin, Granisetron, Haemophilus Influenza B, Haloperidol, Hepatitis A Vaccine, Hepatitis B Vaccine, Ibritumomab Tiuxetan, Immunoglobulin, Influenza Virus Vaccine, Infliximab, Insulin, Insulin Glargine, Interferon Alfa-2a, Interferon Alfa-2b, Interferon Alfacon-1, Interferon Alfa-n3, Interferon Beta, Interferon Beta- la, Interferon Gamma, Iodixanol, Iohexol, lopamidol, Ioversol, Ketorolac, Laronidase, Levofloxacin, Lidocaine, Linezolid, Lorazepam, Measles Vaccine, Measles-Mumps-Rubella Virus Vaccine, Medroxyprogesterone, Meropenem, Methylprednisolone, Midazolam, Morphine, Octreotide, Omalizumab, Ondansetron, Palivizumab, Pantoprazole, Pegaspargase, Pegfilgrastim, Peg-Interferon Alfa-2a, Peg-Interferon Alfa-2b, Pegvisomant, Pertussis vaccine, Piperacillin, Pneumococcal Vaccine and Pneumococcal Conjugate Vaccine, Promethazine, Reteplase, Somatropin, Sulbactam, Sumatriptan, Tazobactam, Tenecteplase, Tetanus Purified Toxoid, Ticarcillin, Tositumomab, Triamcinolone Acetonide, Vancomycin and Varicella vaccine.

17. The pharmaceutical composition of claim 10, wherein the agent is an antibiotic agent or combination of agents selected from among Aminoglycosides; Amphenicols; Ansamycins; Carbacephems; Carbapenems; Cephalosporins or Cephems; Cephamycins; Clavams; Cyclic lipopeptides; Diaminopyrimidines; Ketolides; Lincosamides; Macrolides; Monobactams; Nitrofurans; Oxacephems; Oxazolidinones; Penems, thienamycins and miscellaneous beta-lactams; Penicillins; Polypeptides antibiotics; Quinolones; Sulfonamides; Sulfones; Tetracyclines; and other antibiotics (such as Clofoctols, Fusidic acids, Hexedines, Methenamines, Nitrofurantoins Nitroxolines, Ritipenems, Taurolidines, Xibomols).

18. The pharmaceutical composition of claim 10, wherein the agent is an anticancer agent or combination of agents selected from among Aclacinomycins, Actinomycins, Adriamycins, Ancitabines, Anthramycins, Azacitidines, Azaserines, 6-Azauridines, Bisantrenes, Bleomycins, Cactinomycins, Carmofurs, Carmustines, Carubicins, Carzinophilins, Chromomycins, Cisplatins, Cladribines, Cytarabines, Dactinomycins, Daunorubicins, Denopterins, 6-Diazo-5-Oxo-L-Norleucines, Doxifluridines, Doxorubicins, Edatrexates, Emitefurs, Enocitabines, Fepirubicins, Fludarabines, Fluorouracils, Gemcitabines, Idarubicins, Loxuridines, Menogarils, 6- Mercaptopurines, Methotrexates, Mithramycins, Mitomycins, Mycophenolic Acids, Nogalamycins, Olivomycines, Peplomycins, Pirarubicins, Piritreximes, Plicamycins, Porfiromycins, Pteropterins, Puromycins, Retinoic Acids, Streptonigrins, Streptozocins, Tagafurs, Tamoxifens, Thiamiprines, Thioguanines, Triamcinolones, Trimetrexates, Tubercidins, Vinblastines, Vincristines, Zinostatins, and Zorubicins.

19. A pharmaceutical composition of any of claims 1-9 for use in treating cancer.

20. A pharmaceutical composition for the use of claim 19, wherein the cancer is an invasive tumor.

21. The pharmaceutical composition of any of claims 1-9 for use in treating a disorder of the mammalian eye by inducing liquefaction of vitreous humor; for use in treating disorders involving an excess of glycosaminoglycans by removal of glycosaminoglycans; or for use in treating a mammal who has had a stroke or other CNS injury by ameliorating the consequences of the stroke or other CNS injury.

22. The pharmaceutical composition of claim 10, wherein the agent is an antibody.

23. The pharmaceutical composition of claim 10, wherein the agent is a monoclonal antibody.