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 ~~that comprises~~ three to six PEG moieties per ~~hyaluronidase~~ polypeptide.

2. The pharmaceutical composition of claim 1~~A PEGylated hyaluronidase that comprises three to six PEG moieties per hyaluronidase polypeptide~~, 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 ~~about~~ 91% amino acid sequence identity with a sequence of amino acids included in SEQ ID NO:1; and

~~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 ~~about~~ 91% sequence identity.

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

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

7. The ~~PEGylated hyaluronidase~~pharmaceutical composition of any of claims 1-6 ~~or claim 2~~, wherein the PEG moieties are branched.

8. The ~~PEGylated hyaluronidase~~pharmaceutical composition of any of claims 1-6 ~~or claim 2~~, 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. A pharmaceutical composition, comprising a PEGylated hyaluronidase of any of claims 1-8 and a pharmaceutical carrier.~~

~~10. A pharmaceutical composition, consisting essentially of polypeptides of claim 2 or claim 3.~~

~~11~~9. The pharmaceutical composition of any of claims 1-8 ~~claim 9 or claim 10~~, further comprising an active agent that is a therapeutic or cosmetic agent.

~~12~~10. The pharmaceutical composition of claim ~~11~~9, wherein the active agent is selected from a corticosteroid, a chemotherapeutic agent, an antibody, a botulinum toxin and an anti-microbial.

~~13~~11. The pharmaceutical composition of claim ~~11~~9 or claim ~~12~~10, wherein the agent is selected from among alclomethasones, algestones, beclomethasones, betamethasones, budesonides, clobetasols, clobetasones, clocortolones, cloprednols, corticosterones, cortisones and hydrocortisones, cortivazols, deflazacorts, desonides, desoximetasones, dexamethasones, ~~difluorosones~~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.

~~14~~12. The pharmaceutical composition of claim ~~13~~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.

~~15~~13. The pharmaceutical composition of claim ~~13~~11, wherein the agent is selected from among anti-cancer antibodies, insulins, interferons, pegylated interferons and chemotherapeutic agents

~~16~~14. Use of a ~~PEGylated hyaluronidase~~pharmaceutical composition of any of claims 1-~~8~~13 in the manufacture of a medicament for intravenous administration~~increasing the diffusion of a therapeutic substance or other molecule or macromolecular complex smaller than about 0.5 microns in diameter in a subject.~~

~~17. The use of claim 16, wherein the therapeutic substance or other molecule or macromolecular complex 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, or an organic molecule.~~

~~18. Use of a PEGylated hyaluronidase of any of claims 1-8 in the manufacture of a medicament for inducing liquefaction of vitreous humor to treat a disorder of a mammalian eye, wherein the PEGylated hyaluronidase is used in an amount effective to liquefy said vitreous humor.~~

~~19. A method of preparing a PEGylated hyaluronidase of any of claims 1-8, comprising reacting a hyaluronidase with a molar excess of a PEG reagent selected from among a PEG-succinimidyl butanoate, a PEG-succinimidyl methylbutanoate, a PEG-succinimidyl proprionate, a PEG-N-hydroxysuccinimide, a PEG-aldehyde, a PEG-carbonate, a PEG-propionaldehyde and a PEG-maleimide, to produce a hyaluronidase that has at least three PEG moieties.~~

~~20. The method of claim 19, wherein the PEG reagent is 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).~~

~~21. A PEGylated hyaluronidase produced by the method of claim 19 or 20.~~

~~22~~15. A combination, comprising: a pharmaceutical composition of any of claims 1-13; and a second composition comprising~~PEGylated hyaluronidase of any of claims 1-8 or 21 and~~ an active agent that is a therapeutic or cosmetic agent.

~~23~~16. The combination of claim ~~22~~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.

~~24~~18. The combination of claim ~~22~~17, wherein the ~~active~~ agent is selected from among alclomethasones, algestones, beclomethasones, betamethasones, budesonides, clobetasols, clobetasones, clocortolones, cloprednols, corticosterones, cortisones and hydrocortisones, cortivazols, deflazacorts, desonides, desoximetasones,

dexamethasones, ~~difluorosones~~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.

~~25~~19. The combination of claim ~~24~~18, wherein the ~~active~~ agent is selected from among hydrocortisone acetate, dexamethasone 21-phosphate, prednisolone 25-diethylamino-acetate, prednisolone sodium phosphate, triamcinolone acetonide, triamcinolone benetonide, and triamcinolone hexacetonide.

~~26~~20. The combination of claim ~~22~~15, wherein the ~~active~~ agent is selected from among anti-cancer antibodies, insulins, interferons, pegylated interferons and chemotherapeutic agents.

~~27~~21. The combination of claim ~~22~~15, wherein the ~~active~~ agent is an immunoglobulin.

~~28~~22. The combination of claim ~~22~~15, wherein the ~~active~~ agent is selected from among interferon-alphas and interferon betas.

~~29~~23. The combination of claim ~~22~~20, wherein the ~~active~~ agent is an insulin.

~~30. The combination of claim 22, wherein the active agent is a Pamidronates or a Zoledronates.~~

~~31~~24. The combination of claim ~~22~~20, wherein the ~~active~~ agent is selected from among Docetaxels, Doxorubicins; Doxorubicin liposomals; and bevacizumabs.

~~32~~25. A combination, comprising:

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

b) a blood modifier drug.

~~33~~26. The combination of claim ~~32~~25, wherein the blood modifier is selected from among antihemophilic factors, anti-inhibitor ~~coagulent~~coagulant complexes, antithrombin III, coagulation Factor V, coagulation Factor VIII, coagulation Factor IX~~s~~, 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 ~~drotecogin~~drotrecogin alfas; anticoagulants, dalteparins, ~~enoxaperins~~enoxaparins, heparins, and warfarins.

~~34~~27. ~~A~~The pharmaceutical composition of any of claims 1-13 further comprising~~:~~

~~a) PEGylated hyaluronidase of any of claims 1-8; and~~

~~b)~~ a blood modifier drug.

~~35~~28. The pharmaceutical composition of claim ~~34~~27, wherein the blood modifier is selected from among antihemophilic factors, anti-inhibitor ~~coagulent~~coagulant complexes, antithrombin III, coagulation Factor V, coagulation Factor VIII, coagulation Factor IX~~s~~, 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, ~~enoxaperins~~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.