CLAIMS:

1. A modified PH20 polypeptide, comprising an amino acid replacement in an unmodified PH20 polypeptide, wherein:

the unmodified PH20 polypeptide consists of the sequence of amino acids set forth in any of SEQ ID NOS: 3, 7 and 32-66 or a sequence of amino acids having at least 95% sequence identity the sequence of amino acids set forth in any of SEQ ID NOS: 3, 7 and 32-66;

the amino acid replacement is at a position corresponding to a position selected from among 10, 12, 20, 22, 26, 34, 36, 46, 50, 52, 58, 68, 70, 74, 82, 83, 84, 86, 97, 127, 138, 142, 143, 144, 166, 169, 174, 193, 195, 196, 204, 205, 206, 213, 234, 237, 238, 240, 249, 261, 267, 277, 279, 291, 309, 310, 314, 315, 317, 318, 347, 367, 375, 376, 399, 401, 407, 416, 419, 421, 431, 433, 439, 440, 443 or 445 with reference to amino acid positions set forth in SEQ ID NO:3, with the proviso that if the modified PH20 polypeptide includes only a single amino acid replacement, the replacement does not correspond to amino acid replacements V12A, E249Q with reference to amino acid positions set forth in SEQ ID NO:3;

corresponding amino acid positions are identified by alignment of the PH20 polypeptide with the polypeptide set forth in SEQ ID NO. 3;

the modified PH20 polypeptide exhibits increased stability in the presence of a phenolic preservative(s) compared to the unmodified PH20 polypeptide not containing the amino acid replacement; and

increased stability is manifested as increased hyaluronidase activity in the presence of the phenolic preservative(s) compared to the hyaluronidase activity of the unmodified PH20 polypeptide not containing the amino acid replacement in the presence of the same phenolic preservative(s), and the activity is compared under the same conditions.

2. The modified PH20 polypeptide of claim 1, wherein the amino acid replacement is in a PH20 polypeptide that consists of the sequence of amino acids set forth in any of SEQ ID NOS: 3, 7 and 32-66.

3. The modified PH20 polypeptide of claim 1 or claim 2, wherein the phenolic preservative is selected from among one or more of phenol, metacresol (m-cresol), benzyl alcohol and a paraben.

4. The modified PH20 polypeptide of claim 3, wherein the preservative is a paraben that is methylparaben or propylparaben.

5. The modified PH20 polypeptide of any of claims 1-4, wherein the preservative is a phenolic preservative that is m-cresol, phenol, or m-cresol and phenol .

6. The modified PH20 polypeptide of any of claims 1-5, comprising at least one amino acid replacement selected from among replacement with:

G at a position corresponding to position 10; K at a position corresponding to position 12; S at a position corresponding to position 20; T at a position corresponding to position 22; M at a position corresponding to position 26; W at a position corresponding to position 34; N at a position corresponding to position 36; L at a position corresponding to position 46; M at a position corresponding to position 50; T at a position corresponding to position 52; S at a position corresponding to position 52; C at a position corresponding to position 58; K at a position corresponding to position 58; R at a position corresponding to position 58; N at a position corresponding to position 58; Y at a position corresponding to position 58; P at a position corresponding to position 58; H at a position corresponding to position 58; P at a position corresponding to position 68; V at a position corresponding to position 70; E at a

position corresponding to position 74; L at a position corresponding to position 82; N at a position corresponding to position 82; V at a position corresponding to position 83; Q at a position corresponding to position 83; S at a position corresponding to position 83; G at a position corresponding to position 83; N at a position corresponding to position 84; A at a position corresponding to position 86; K at a position corresponding to position 86; E at a position corresponding to position 97; L at a position corresponding to position 97; R at a position corresponding to position 127; R at a position corresponding to position 131; L at a position corresponding to position 138; K at a position corresponding to position 142; N at a position corresponding to position 142; P at a position corresponding to position 142; S at a position corresponding to position 142; T at a position corresponding to position 142; G at a position corresponding to position 143; K at a position corresponding to position 143; T at a position corresponding to position 144; Q at a position corresponding to position 166; T at a position corresponding to position 166; L at a position corresponding to position 169; G at a position corresponding to position 174; N at a position corresponding to position 174; Q at a position corresponding to position 193; T at a position corresponding to position 195; N at a position corresponding to position 195; E at a position corresponding to position 196; R at a position corresponding to position 196; P at a position corresponding to position 204; A at a position corresponding to position 205; E at a position corresponding to position 205; I at a position corresponding to position 206; A at a position corresponding to position 213; I at a position corresponding to position 219; M at a position corresponding to position 234; T at a position corresponding to position 237; H at a position corresponding to position 238; Q at a position corresponding to position 240; V at a position corresponding to position 249; A at a position corresponding to position 261; K at a position corresponding to position 261; T at a position corresponding to position 267; K at a position corresponding to position 277; H at a position corresponding to position 279; V at a position corresponding to position 279; V at a position corresponding to position 291; E at a position corresponding to position 309; Q at a position corresponding to position 310; Y at a position corresponding to position 314; Y at a position corresponding to position 315; N at a position corresponding to position 317; W at a position corresponding to position 317; D at a position corresponding to position 318; G at a position corresponding to position 347; A at a position corresponding to position 367; R at a position corresponding to position 375; R at a position corresponding to position 376; V at a position corresponding to position 399; E at a position corresponding to position 401; A at a position corresponding to position 407; L at a position corresponding to position 416; K at a position corresponding to position 419; H at a position corresponding to position 421; E at a position corresponding to position 431; T at a position corresponding to position 433; V at a position corresponding to position 433; C at a position corresponding to position 439; P at a position corresponding to position 440; G at a position corresponding to position 443; and N at a position corresponding to position 445, with reference to amino acid residue positions set forth in SEQ ID NO:3.

7. The modified PH20 polypeptide of any of claims 1-6, comprising at least one amino acid replacement selected from among replacement with:

T at a position corresponding to position 52, K at a position corresponding to position 58, R at a position corresponding to position 58, V at a position corresponding to position 83, P at a position corresponding to position 204, M at a position corresponding to position 234, A at a position corresponding to position 261, Q at a position corresponding to position 310; and H at a position corresponding to position 421, with reference to amino acid residue positions set forth in SEQ ID NO:3.

8. The modified PH20 polypeptide of any of claims 1-7, comprising replacement with P at a position corresponding to position 204 in a PH20 polypeptide with reference to amino acid residue positions set forth in SEQ ID NO:3.

9. The modified polypeptide of claim 8, comprising replacement with P at a position corresponding to position 204 in a PH20 polypeptide and up to 5 additional amino acid replacements, wherein the amino acid replacement(s) is/are in an unmodified PH20 polypeptide that consists of the sequence of amino acids set forth in any of SEQ ID NOS: 3, 7 and 32-66.

10. The modified PH20 polypeptide of any of claims 1-9, comprising replacement with R at a position corresponding to position 58 in a PH20 polypeptide with reference to amino acid positions set forth in any of SEQ ID NOS: 3, 7 and 32-66.

11. A modified PH20 polypeptide of any of claims 1-10, comprising a sequence of amino acids set forth in any of SEQ ID NOS: 83, 88, 93, 94, 101, 144, 148, 158, 171, 175, 176, 177, 178, 180, 182, 183, 184, 185, 194, 221, 240, 259, 260, 261, 262, 263, 264, 268, 270, 272, 307, 309, 327, 334, 341, 351, 352, 353, 356, 357, 358, 359, 361, 424, 426, 430, 434, 436, 443, 444, 445, 446, 447, 449, 450, 451, 454, 461, 467, 480, 487, 489, 492, 504, 505, 509, 527, 544, 551, 576, 582, 589, 600, 603, 607, 612, 614, 647, 658, 683, 687, 733, 736, 741, 754, 763, 768, 781, 796, 797, 809, 818, 829 or 837, or a sequence of amino acids that exhibits at least 96% sequence identity to a sequence of amino acids set forth in any of SEQ ID NOS: 83, 88, 93, 94, 101, 144, 148, 158, 171, 175, 176, 177, 178, 180, 182, 183, 184, 185, 194, 221, 240, 259, 260, 261, 262, 263, 264, 268, 270, 272, 307, 309, 327, 334, 341, 351, 352, 353, 356, 357, 358, 359, 361, 424, 426, 430, 434, 436, 443, 444, 445, 446, 447, 449, 450, 451, 454, 461, 467, 480, 487, 489, 492, 504, 505, 509, 527, 544, 551, 576, 582, 589, 600, 603, 607, 612, 614, 647, 658, 683, 687, 733, 736, 741, 754, 763, 768, 781, 796, 797, 809, 818, 829 or 837, and that contains the amino acid replacement.

12. The modified PH20 polypeptide of any of claims 1-11, comprising replacement with P at a position corresponding to position 204 in a PH20 polypeptide with reference to amino acid residue positions set forth in SEQ ID NO:3.

13. A modified PH20 polypeptide, comprising replacement with P at a position corresponding to position 204 in a PH20 polypeptide, wherein the amino acid replacement(s)is in an unmodified PH20 polypeptide that consists of the sequence of amino acids set forth in any of SEQ ID NOS: 3, 32-66, 69 and 72, or a sequence of amino acids that has at least 95 % sequence identity to any of SEQ ID NOS:3, 7, 69, 72 or 32-66, with the proviso that the modified polypeptide contains the amino acid replacement corresponding to F204P.

14. A modified PH20 polypeptide, comprising replacement with P at a position corresponding to position 204 in a PH20 polypeptide, wherein the amino acid replacement(s)is in an unmodified PH20 polypeptide that comprises the sequence of amino acids set forth in SEQ ID NO. 41.

15. A modified PH20 polypeptide that has only the replacement with P at a position corresponding to position 204 in a PH20 polypeptide, wherein the amino acid replacement(s)is in an unmodified PH20 polypeptide that consists of the sequence of amino acids set forth in any of SEQ ID NOS: 3, 32-66, 69 and 72.

16. The modified PH20 polypeptide of any of claims 1-15, comprising up to 10 amino acid modifications selected from among amino acid replacements, insertions and deletions.

17. The modified PH20 polypeptide of claim 15, comprising up to 5 amino acid modifications selected from among amino acid replacements, insertions and deletions.

18. The modified PH20 polypeptide of any of claims 1-15, comprising up to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 , 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48,49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90 or more amino acid replacements.

19. The modified PH20 polypeptide of any of claims 1-18 that is modified by one or more of glycosylation, sialation, albumination, farnysylation, carboxylation, hydroxylation, phosphorylation, conjugation to a polymer, conjugation to a multimerization domain, conjugation to a toxin, conjugation to a detectable label or conjugation to a drug

20. The modified PH20 polypeptide of claim 19, wherein the PH20 polypeptide is conjugated to a polymer that is dextran or PEG.

21. A nucleic acid molecule, encoding a modified PH20 polypeptide of any of claims 1-19.

22. A vector, comprising the nucleic acid molecule of claim 21.

23. A cell, comprising the vector of claim 22.

24. A method of producing a modified PH20 polypeptide, comprising:

introducing the nucleic acid of claim 25 or the vector of claim 26 into a cell capable of incorporating N-linked sugar moieties into the polypeptide;

culturing the cell under conditions whereby an encoded modified PH20 polypeptide is produced and secreted by the cell; and

recovering the expressed polypeptide.

25. A pharmaceutical composition, comprising a modified PH20 polypeptide of any of claims 1-20, and a pharmaceutically acceptable excipient.

26. The pharmaceutical composition of claim 25, comprising at least one phenolic preservative.

27. The pharmaceutical composition of claim 26, wherein the preservative(s) is(are) selected from among phenol, metacresol (m-cresol), benzyl alcohol, and a paraben.

28. The pharmaceutical composition of any of claims 25-27, comprising a therapeutically active agent.

29. The pharmaceutical composition of claim 28, wherein the therapeutic agent is a polypeptide, a protein, a nucleic acid, a drug, a small molecule or an organic molecule.

30. The pharmaceutical composition of claim 28, wherein the therapeutically active agent is selected from among a chemotherapeutic agent, an analgesic agent, an anti-inflammatory agent, an antimicrobial agent, an amoebicidal agent, a trichomonacidal agent, an anti-parkinson agent, an anti-malarial agent, an anticonvulsant agent, an anti-depressant agent, and antiarthritics agent, an anti-fungal agent, an antihypertensive agent, an antipyretic agent, an anti-parasite agent, an antihistamine agent, an alpha-adrenergic agonist agent, an alpha blocker agent, an anesthetic agent, a bronchial dilator agent, a biocide agent, a bactericide agent, a bacteriostat 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, a 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 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, or a sleep inducer.

31. The pharmaceutical composition of claim 28, wherein the therapeutic agent is selected from among an antibody, an Immune Globulin, a cytokine, a chemotherapeutic agent, a coagulation factor and an insulin.

32. The pharmaceutical composition of claim 28, wherein the therapeutic agent is an insulin that is a fast-acting insulin.

33. A pharmaceutical composition of any of claims 25-32 for use in treating a hyaluronan-associated disease or disorder, for use in treating a disease or condition associated with an excess of glycosaminoglycans, for use in delivering a therapeutic drug, or for use in increasing penetration of chemotherapeutic agents into solid tumors..

34. The pharmaceutical composition of claim 33, wherein the use is for treating a tumor; for treating glycosaminoglycan accumulation in the brain, for treating a cardiovascular disorder; for treating an ophthalmic disorder; for treating a pulmonary disease; for treating cellulite; for treating a proliferative disorder, for treating elevated interstitial fluid pressure, for treating disc pressure or for treating edema.

35. A pharmaceutical composition of claim 30 for use in treating diabetes, wherein the composition comprises an insulin.

CLAIMS:

1. A modified PH20 polypeptide, comprising an amino acid replacement in an unmodified PH20 polypeptide, wherein:

the unmodified PH20 polypeptide consists of the sequence of amino acids set forth in any of SEQ ID NOS: 3, 7 and 32-66;

the amino acid replacement is at a position corresponding to a position selected from among 10, 12, 20, 22, 26, 34, 36, 46, 50, 52, 58, 68, 70, 74, 82, 83, 84, 86, 97, 127, 138, 142, 143, 144, 166, 169, 174, 193, 195, 196, 204, 205, 206, 213, 234, 237, 238, 240, 249, 261, 267, 277, 279, 291, 309, 310, 314, 315, 317, 318, 347, 367, 375, 376, 399, 401, 407, 416, 419, 421, 431, 433, 439, 440, 443 or 445 with reference to amino acid positions set forth in SEQ ID NO:3, with the proviso that if the modified PH20 polypeptide includes only a single amino acid replacement, the replacement does not correspond to amino acid replacements V12A, E249Q with reference to amino acid positions set forth in SEQ ID NO:3;

corresponding amino acid positions are identified by alignment of the PH20 polypeptide with the polypeptide set forth in SEQ ID NO. 3;

the modified PH20 polypeptide exhibits increased stability in the presence of a phenolic preservative(s) compared to the unmodified PH20 polypeptide not containing the amino acid replacement; and

increased stability is manifested as increased hyaluronidase activity in the presence of the phenolic preservative(s) compared to the hyaluronidase activity of the unmodified PH20 polypeptide not containing the amino acid replacement in the presence of the same phenolic preservative(s), and the activity is compared under the same conditions.

2. The modified PH20 polypeptide of claim 1, wherein the amino acid replacement is in a PH20 polypeptide that consists of the sequence of amino acids set forth in SEQ ID NO: 3.

3. The modified PH20 polypeptide of claim 1 or claim 2, wherein the phenolic preservative is selected from among one or more of phenol, metacresol (m-cresol), benzyl alcohol and a paraben.

4. The modified PH20 polypeptide of claim 3, wherein the preservative is a paraben that is methylparaben or propylparaben.

5. The modified PH20 polypeptide of any of claims 1-4, wherein the preservative is a phenolic preservative that is m-cresol, phenol, or m-cresol and phenol.

6. The modified PH20 polypeptide of any of claims 1-5, comprising at least one amino acid replacement selected from among replacement with:

G at a position corresponding to position 10; K at a position corresponding to position 12; S at a position corresponding to position 20; T at a position corresponding to position 22; M at a position corresponding to position 26; W at a position corresponding to position 34; N at a position

corresponding to position 36; L at a position corresponding to position 46; M at a position corresponding to position 50; T at a position corresponding to position 52; S at a position corresponding to position 52; C at a position corresponding to position 58; K at a position corresponding to position 58; R at a position corresponding to position 58; N at a position corresponding to position 58; Y at a position corresponding to position 58; P at a position corresponding to position 58; H at a position corresponding to position 58; P at a position corresponding to position 68; V at a position corresponding to position 70; E at a position corresponding to position 74; L at a position corresponding to position 82; N at a position corresponding to position 82; V at a position corresponding to position 83; Q at a position corresponding to position 83; S at a position corresponding to position 83; G at a position corresponding to position 83; N at a position corresponding to position 84; A at a position corresponding to position 86; K at a position corresponding to position 86; E at a position corresponding to position 97; L at a position corresponding to position 97; R at a position corresponding to position 127; R at a position corresponding to position 131; L at a position corresponding to position 138; K at a position corresponding to position 142; N at a position corresponding to position 142; P at a position corresponding to position 142; S at a position corresponding to position 142; T at a position corresponding to position 142; G at a position corresponding to position 143; K at a position corresponding to position 143; T at a position corresponding to position 144; Q at a position corresponding to position 166; T at a position corresponding to position 166; L at a position corresponding to position 169; G at a position corresponding to position 174; N at a position corresponding to position 174; Q at a position corresponding to position 193; T at a position corresponding to position 195; N at a position corresponding to position 195; E at a position corresponding to position 196; R at a position corresponding to position 196; P at a position corresponding to position 204; A at a position corresponding to position 205; E at a position corresponding to position 205; I at a position corresponding to position 206; A at a position corresponding to position 213; I at a position corresponding to position 219; M at a position corresponding to position 234; T at a position corresponding to position 237; H at a position corresponding to position 238; Q at a position corresponding to position 240; V at a position corresponding to position 249; A at a position corresponding to position 261; K at a position corresponding to position 261; T at a position corresponding to position 267; K at a position corresponding to position 277; H at a position corresponding to position 279; V at a position corresponding to position 279; V at a position corresponding to position 291; E at a position corresponding to position 309; Q at a position corresponding to position 310; Y at a position corresponding to position 314; Y at a position corresponding to position 315; N at a position corresponding to position 317; W at a position corresponding to position 317; D at a position corresponding to position 318; G at a position corresponding to position 347; A at a position corresponding to position 367; R at a position corresponding to position 375; R at a position corresponding to position 376; V at a position corresponding to position 399; E at a position corresponding to position 401; A at a position corresponding to position 407; L at a position corresponding to position 416; K at a position corresponding to position 419; H at a position corresponding to position 421; E at a position corresponding to position 431; T at a position corresponding to position 433; V at a position

corresponding to position 433; C at a position corresponding to position 439; P at a position corresponding to position 440; G at a position corresponding to position 443; and N at a position corresponding to position 445, with reference to amino acid residue positions set forth in SEQ ID NO:3.

7. The modified PH20 polypeptide of any of claims 1-6, comprising at least one amino acid replacement selected from among replacement with:

T at a position corresponding to position 52, K at a position corresponding to position 58, R at a position corresponding to position 58, V at a position corresponding to position 83, P at a position corresponding to position 204, M at a position corresponding to position 234, A at a position corresponding to position 261, Q at a position corresponding to position 310; and H at a position corresponding to position 421, with reference to amino acid residue positions set forth in SEQ ID NO:3.

8. The modified PH20 polypeptide of any of claims 1-7, comprising replacement with P at a position corresponding to position 204 in a PH20 polypeptide with reference to amino acid residue positions set forth in SEQ ID NO:3.

9. A modified polypeptide of claim 8, comprising replacement with P at a position corresponding to position 204 in a PH20 polypeptide and up to 5 additional amino acid replacements, wherein the amino acid replacement(s) is/are in an unmodified PH20 polypeptide that consists of the sequence of amino acids set forth in SEQ ID NO: 3.

10. The modified PH20 polypeptide of any of claims 1-7, comprising replacement with R at a position corresponding to position 58 in a PH20 polypeptide with reference to amino acid positions set forth in SEQ ID NO:3.

11. A modified PH20 polypeptide of any of claims 1-10, comprising a sequence of amino acids set forth in any of SEQ ID NOS: 83, 88, 93, 94, 101, 144, 148, 158, 171, 175, 176, 177, 178, 180, 182, 183, 184, 185, 194, 221, 240, 259, 260, 261, 262, 263, 264, 268, 270, 272, 307, 309, 327, 334, 341, 351, 352, 353, 356, 357, 358, 359, 361, 424, 426, 430, 434, 436, 443, 444, 445, 446, 447, 449, 450, 451, 454, 461, 467, 480, 487, 489, 492, 504, 505, 509, 527, 544, 551, 576, 582, 589, 600, 603, 607, 612, 614, 647, 658, 683, 687, 733, 736, 741, 754, 763, 768, 781, 796, 797, 809, 818, 829 or 837, or a sequence of amino acids that exhibits at least 75%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity to a sequence of amino acids set forth in any of SEQ ID NOS: 83, 88, 93, 94, 101, 144, 148, 158, 171, 175, 176, 177, 178, 180, 182, 183, 184, 185, 194, 221, 240, 259, 260, 261, 262, 263, 264, 268, 270, 272, 307, 309, 327, 334, 341, 351, 352, 353, 356, 357, 358, 359, 361, 424, 426, 430, 434, 436, 443, 444, 445, 446, 447, 449, 450, 451, 454, 461, 467, 480, 487, 489, 492, 504, 505, 509, 527, 544, 551, 576, 582, 589, 600, 603, 607, 612, 614, 647, 658, 683, 687, 733, 736, 741, 754, 763, 768, 781, 796, 797, 809, 818, 829 or 837, and that contains the amino acid replacement.

12. A modified PH20 polypeptide, comprising at least one amino acid replacement in a PH20 polypeptide, wherein:

the unmodified PH20 polypeptide consists of the sequence of amino acids set forth in any of SEQ ID NOS: 3, 7 and 32-66;

the replacement is at a position corresponding to one or more of positions 1, 12, 15, 24, 26, 27, 29, 30, 31, 32, 33, 37, 39, 46, 48, 52, 58, 63, 67, 68, 69, 70, 71, 72, 73, 74, 75, 84, 86, 87, 92, 93, 94, 97, 118, 120, 127, 131, 135, 141, 142, 147, 148, 150, 151, 152, 155, 156, 163, 164, 165, 166, 169, 170, 174, 198, 206, 209, 212, 213, 215, 219, 233, 234, 236, 238, 247, 257, 259, 260, 261, 263, 269, 271, 272, 276, 277, 278, 282, 291, 293, 305, 308, 309, 310, 313, 315, 317, 318, 320, 324, 325, 326, 328, 347, 353, 359, 371, 377, 380, 389, 392, 395, 399, 405, 407, 409, 410, 418, 419, 421, 425, 431, 433, 436, 437, 438, 439, 440, 441, 442, 443, 445, 446 and 447 with reference to amino acid positions set forth in SEQ ID NO:3, with the proviso that:

if the modified PH20 polypeptide includes only a single amino acid replacement, the replacement does not correspond to amino acid replacements V12A, N131A or E249Q with reference to amino acid positions set forth in SEQ ID NO:3; and

if the modified PH20 polypeptide includes only two amino acid replacements the replacements do not correspond to amino acid replacements N131A/N219A with reference to amino acid positions set forth in SEQ ID NO:3;

corresponding amino acid positions are identified by alignment of the PH20 polypeptide with the polypeptide set forth in SEQ ID NO:3; and

the modified PH20 polypeptide exhibits increased hyaluronidase activity that is at least 120% of the hyaluronidase activity compared to the unmodified PH20 polypeptide not containing the amino acid replacement.

13. The modified PH20 polypeptide of claim 12, comprising at least one amino acid replacement selected from among replacement with:

histidine (H) at a position corresponding to position 1; Q at a position corresponding to position 1; E at a position corresponding to position 12; T at a position corresponding to position 12; V at a position corresponding to position 15; E at a position corresponding to position 24; H at a position corresponding to position 24; E at a position corresponding to position 26; K at a position corresponding to position 26; K at a position corresponding to position 27; R at a position corresponding to position 27; E at a position corresponding to position 29; I at a position corresponding to position 29; L at a position corresponding to position 29; M at a position corresponding to position 29; P at a position corresponding to position 29; S at a position corresponding to position 29; V at a position corresponding to position 29; G at a position corresponding to position 30; H at a position corresponding to position 30; K at a position corresponding to position 30; M at a position corresponding to position 30; R at a position corresponding to position 30; S at a position corresponding to position 30; A at a position corresponding to position 31; C at a position corresponding to position 31; H at a position

corresponding to position 31; I at a position corresponding to position 31; K at a position corresponding to position 31; L at a position corresponding to position 31; P at a position corresponding to position 31; R at a position corresponding to position 31; S at a position corresponding to position 31; T at a position corresponding to position 31; V at a position corresponding to position 31; F at a position corresponding to position 32; G at a position corresponding to position 32; H at a position corresponding to position 32; W at a position corresponding to position 33; F at a position corresponding to position 37; N at a position corresponding to position 39; T at a position corresponding to position 39; R at a position corresponding to position 46; F at a position corresponding to position 48; H at a position corresponding to position 48; N at a position corresponding to position 48; Q at a position corresponding to position 52; K at a position corresponding to position 58; Q at a position corresponding to position 58; W at a position corresponding to position 63; V at a position corresponding to position 67; H at a position corresponding to position 68; Q at a position corresponding to position 68; A at a position corresponding to position 69; C at a position corresponding to position 69; F at a position corresponding to position 69; G at a position corresponding to position 69; I at a position corresponding to position 69; L at a position corresponding to position 69; M at a position corresponding to position 69; P at a position corresponding to position 69; R at a position corresponding to position 69; W at a position corresponding to position 69; Y at a position corresponding to position 69; A at a position corresponding to position 70; C at a position corresponding to position 70; F at a position corresponding to position 70; G at a position corresponding to position 70; H at a position corresponding to position 70; K at a position corresponding to position 70; L at a position corresponding to position 70; N at a position corresponding to position 70; P at a position corresponding to position 70; R at a position corresponding to position 70; S at a position corresponding to position 70; T at a position corresponding to position 70; V at a position corresponding to position 70; R at a position corresponding to position 71; S at a position corresponding to position 71; M at a position corresponding to position 72; Q at a position corresponding to position 72; H at a position corresponding to position 73; L at a position corresponding to position 73; W at a position corresponding to position 73; A at a position corresponding to position 74; C at a position corresponding to position 74; G at a position corresponding to position 74; N at a position corresponding to position 74; P at a position corresponding to position 74; R at a position corresponding to position 74; S at a position corresponding to position 74; V at a position corresponding to position 74; W at a position corresponding to position 74; F at a position corresponding to position 75; L at a position corresponding to position 75; R at a position corresponding to position 75; T at a position corresponding to position 75; G at a position corresponding to position 84; R at a position corresponding to position 84; A at a position corresponding to position 86; C at a position corresponding to position 87; T at a position corresponding to position 87; Y at a position corresponding to position 87; C at a position corresponding to position 92; I at a position corresponding to position 93; L at a position corresponding to position 93; R at a position corresponding to position 93; T at a position corresponding to position 93; R at a position corresponding to position 94; G at a position corresponding to position 97; Q at a position

corresponding to position 118; F at a position corresponding to position 120; V at a position corresponding to position 120; Y at a position corresponding to position 120; H at a position corresponding to position 127; N at a position corresponding to position 127; G at a position corresponding to position 131; R at a position corresponding to position 131; V at a position corresponding to position 131; D at a position corresponding to position 135; G at a position corresponding to position 135; R at a position corresponding to position 135; H at a position corresponding to position 141; Y at a position corresponding to position 141; R at a position corresponding to position 142; R at a position corresponding to position 147; V at a position corresponding to position 147; K at a position corresponding to position 148; G at a position corresponding to position 150; K at a position corresponding to position 151; L at a position corresponding to position 151; M at a position corresponding to position 151; Q at a position corresponding to position 151; R at a position corresponding to position 151; R at a position corresponding to position 152; G at a position corresponding to position 155; K at a position corresponding to position 155; D at a position corresponding to position 156; A at a position corresponding to position 163; E at a position corresponding to position 163; K at a position corresponding to position 163; R at a position corresponding to position 163; M at a position corresponding to position 164; D at a position corresponding to position 165; N at a position corresponding to position 165; A at a position corresponding to position 166; F at a position corresponding to position 166; H at a position corresponding to position 166; L at a position corresponding to position 166; Q at a position corresponding to position 166; R at a position corresponding to position 166; T at a position corresponding to position 166; Y at a position corresponding to position 166; L at a position corresponding to position 169; R at a position corresponding to position 170; K at a position corresponding to position 174; D at a position corresponding to position 198; K at a position corresponding to position 206; L at a position corresponding to position 206; N at a position corresponding to position 212; M at a position corresponding to position 213; N at a position corresponding to position 213; M at a position corresponding to position 215; S at a position corresponding to position 219; K at a position corresponding to position 233; R at a position corresponding to position 233; M at a position corresponding to position 234; R at a position corresponding to position 236; E at a position corresponding to position 237; S at a position corresponding to position 238; I at a position corresponding to position 247; T at a position corresponding to position 257; P at a position corresponding to position 259; Y at a position corresponding to position 260; K at a position corresponding to position 261; N at a position corresponding to position 261; K at a position corresponding to position 263; R at a position corresponding to position 263; A at a position corresponding to position 269; L at a position corresponding to position 271; M at a position corresponding to position 271; T at a position corresponding to position 272; D at a position corresponding to position 276; S at a position corresponding to position 276; Y at a position corresponding to position 276; K at a position corresponding to position 277; R at a position corresponding to position 277; T at a position corresponding to position 277; H at a position corresponding to position 278; K at a position corresponding to position 278; N at a position corresponding to position 278; R at a position corresponding to position 278; S at a position corresponding to position 278; T at a position corresponding to position 278; Y at a position

corresponding to position 278; M at a position corresponding to position 282; V at a position corresponding to position 291; A at a position corresponding to position 293; C at a position corresponding to position 293; F at a position corresponding to position 293; M at a position corresponding to position 293; P at a position corresponding to position 293; Q at a position corresponding to position 293; V at a position corresponding to position 293; E at a position corresponding to position 305; G at a position corresponding to position 308; N at a position corresponding to position 308; E at a position corresponding to position 309; L at a position corresponding to position 309; N at a position corresponding to position 309; Q at a position corresponding to position 309; R at a position corresponding to position 309; T at a position corresponding to position 309; A at a position corresponding to position 310; G at a position corresponding to position 310; K at a position corresponding to position 313; R at a position corresponding to position 313; H at a position corresponding to position 315; I at a position corresponding to position 317; K at a position corresponding to position 317; R at a position corresponding to position 317; M at a position corresponding to position 318; H at a position corresponding to position 320; K at a position corresponding to position 320; R at a position corresponding to position 320; R at a position corresponding to position 324; A at a position corresponding to position 325; D at a position corresponding to position 325; E at a position corresponding to position 325; G at a position corresponding to position 325; H at a position corresponding to position 325; K at a position corresponding to position 325; M at a position corresponding to position 325; N at a position corresponding to position 325; Q at a position corresponding to position 325; S at a position corresponding to position 325; V at a position corresponding to position 326; I at a position corresponding to position 328; K at a position corresponding to position 328; L at a position corresponding to position 328; S at a position corresponding to position 328; Y at a position corresponding to position 328; G at a position corresponding to position 347; S at a position corresponding to position 347; V at a position corresponding to position 353; T at a position corresponding to position 359; R at a position corresponding to position 371; P at a position corresponding to position 377; T at a position corresponding to position 377; W at a position corresponding to position 380; Y at a position corresponding to position 380; K at a position corresponding to position 389; M at a position corresponding to position 392; R at a position corresponding to position 395; M at a position corresponding to position 399; T at a position corresponding to position 399; W at a position corresponding to position 399; G at a position corresponding to position 405; D at a position corresponding to position 407; Q at a position corresponding to position 407; A at a position corresponding to position 409; Q at a position corresponding to position 409; T at a position corresponding to position 410; P at a position corresponding to position 418; F at a position corresponding to position 419; I at a position corresponding to position 419; K at a position corresponding to position 419; R at a position corresponding to position 419; S at a position corresponding to position 419; H at a position corresponding to position 421; K at a position corresponding to position 421; N at a position corresponding to position 421; Q at a position corresponding to position 421; R at a position corresponding to position 421; S at a position corresponding to position 421; K at a position corresponding to position 425; A at a position corresponding to position 431; H at a position corresponding to position 431; K at a position

corresponding to position 431; Q at a position corresponding to position 431; R at a position corresponding to position 431; S at a position corresponding to position 431; V at a position corresponding to position 431; L at a position corresponding to position 433; R at a position corresponding to position 433; T at a position corresponding to position 433; V at a position corresponding to position 433; K at a position corresponding to position 436; I at a position corresponding to position 437; M at a position corresponding to position 437; T at a position corresponding to position 438; V at a position corresponding to position 439; H at a position corresponding to position 440; R at a position corresponding to position 440; F at a position corresponding to position 441; R at a position corresponding to position 442; A at a position corresponding to position 443; M at a position corresponding to position 443; M at a position corresponding to position 445; P at a position corresponding to position 445; A at a position corresponding to position 446; D at a position corresponding to position 447; N at a position corresponding to position 447; and/or with Q at a position corresponding to position 447, with reference to amino acid positions set forth in SEQ ID NO:3.

14. The modified PH20 polypeptide of claim 12 or 13, comprising at least one amino acid replacement at an amino acid position corresponding to a position selected from among 24, 29, 31, 48, 58, 69, 70, 75, 84, 97, 165, 166, 271, 278, 317, 320, 325 and 326 with reference to positions set forth in SEQ ID NO:3, wherein corresponding amino acid positions are identified by alignment of the PH20 polypeptide with the polypeptide set forth in SEQ ID NO:3.

15. A modified PH20 polypeptide of any of claims 12-14, comprising a sequence of amino acids set forth in any of SEQ ID NOS: 73, 78, 86, 89, 91, 95, 96, 99, 100, 105, 106, 108, 109, 111-113, 115, 117-120, 122-126, 128-136, 139-142, 149, 154, 155, 159, 164, 165, 167, 173, 178, 181, 191-193, 195-197, 199-205, 207-222, 225, 226, 228, 229, 231, 233, 237-239, 242, 247-254, 256, 257, 267, 269, 270, 277, 283, 285, 293, 295, 296, 298, 300, 303, 308, 316, 318, 321, 322, 324, 325, 330, 334, 335, 338-340, 344, 348, 355, 367, 369, 371, 377, 384-388, 394, 398, 399, 401, 406-408, 410, 412, 414, 416, 419, 421-426, 428, 430, 431, 435, 448, 455, 456, 459, 462, 463, 465, 469, 478-480, 482, 484, 490, 493, 497, 501, 503, 505-508, 510-512, 514, 518, 522, 523, 527, 531, 533, 537-543, 545, 551, 558, 559, 561, 563-566, 569, 572, 574, 576, 579, 581-583, 585, 587, 588, 594, 596, 602, 605, 606, 609, 613, 618-620, 624-634, 637, 640, 641, 643, 644, 647, 648, 652, 657, 675, 695, 698, 699, 700, 712, 717, 725, 731, 732, 734, 738, 742, 746, 748-750, 757, 760, 762-765, 768-773, 775, 779, 782, 783, 786-789, 794-797, 799-801, 807, 814, 816, 819, 822, 825, 826, 830, 836, 838, 844, 847, 851 or 853, or a sequence of amino acids that exhibits at least 75%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity to a sequence of amino acids set forth in any of SEQ ID NOS: 73, 78, 86, 89, 91, 95, 96, 99, 100, 105, 106, 108, 109, 111-113, 115, 117-120, 122-126, 128-136, 139-142, 149, 154, 155, 159, 164, 165, 167, 173, 178, 181, 191-193, 195-197, 199-205, 207-222, 225, 226, 228, 229, 231, 233, 237-239, 242, 247-254, 256, 257, 267, 269, 270, 277, 283, 285, 293, 295, 296, 298, 300, 303, 308, 316, 318, 321, 322, 324, 325, 330, 334, 335, 338-340, 344, 348, 355, 367, 369, 371, 377, 384-388, 394, 398, 399, 401, 406-408, 410, 412, 414, 416, 419, 421-426, 428, 430, 431, 435, 448, 455, 456, 459, 462, 463, 465, 469, 478-480, 482, 484, 490, 493, 497, 501, 503, 505-508, 510-512, 514, 518, 522, 523, 527, 531, 533, 537-543, 545, 551, 558, 559, 561, 563-566, 569, 572, 574, 576, 579, 581-583, 585, 587, 588, 594, 596, 602,

605, 606, 609, 613, 618-620, 624-634, 637, 640, 641, 643, 644, 647, 648, 652, 657, 675, 695, 698, 699, 700, 712, 717, 725, 731, 732, 734, 738, 742, 746, 748-750, 757, 760, 762-765, 768-773, 775, 779, 782, 783, 786-789, 794-797, 799-801, 807, 814, 816, 819, 822, 825, 826, 830, 836, 838, 844, 847, 851 or 853, and that contains the amino acid replacement.

16. A modified PH20 polypeptide, comprising an amino acid replacement in a PH20 polypeptide, wherein:

the unmodified PH20 polypeptide consists of the sequence of amino acids set forth in any of SEQ ID NOS: 3, 7 and 32-66

the at least one amino replacement(s) is at an amino acid position corresponding to a position selected from among 1, 2, 3, 4, 5, 6, 8, 9, 10, 11, 12, 13, 14, 15, 20, 22, 23, 24, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 54, 58, 59, 60, 61, 63, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 77, 79, 81, 82, 83, 84, 85, 86, 87, 89, 90, 91, 92, 93, 94, 96, 97, 98, 99, 102, 103, 104, 105, 106, 107, 108, 110, 114, 117, 118, 119, 120, 122, 124, 125, 127, 128, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 186, 192, 193, 195, 196, 197, 198, 200, 202, 204, 205, 206, 208, 209, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 224, 226, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 242, 245, 247, 248, 251, 253, 255, 256, 257, 258, 259, 260, 261, 263, 264, 265, 266, 267, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 297, 298, 300, 301, 302, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 320, 321, 323, 324, 325, 326, 327, 328, 331, 334, 335, 338, 339, 342, 343, 347, 348, 349, 351, 353, 356, 357, 358, 359, 360, 361, 367, 368, 369, 371, 373, 374, 375, 376, 377, 378, 379, 380, 381, 383, 385, 387, 388, 389, 391, 392, 393, 394, 395, 396, 397, 398, 399, 401, 403, 404, 405, 406, 407, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 425, 426, 427, 428, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446 and 447 with reference to amino acid positions set forth in SEQ ID NO:3 or 7, with the proviso that if the modified PH20 polypeptide contains an amino acid replacement at a position corresponding to position 13, 47, 131, or 219 the replacement is not replacement with an Alanine (A);

corresponding amino acid positions are identified by alignment of the PH20 polypeptide with the polypeptide set forth in SEQ ID NO:3; and

the modified PH20 polypeptide exhibits at least 40% of the hyaluronidase activity of the PH20 polypeptide not containing the amino acid replacement, and the activity is compared under the same conditions.

17. A modified PH20 polypeptide of claim 17, comprising the sequence of amino acids set forth in any of SEQ ID NOS: 73-855 or a sequence of amino acids that exhibits at least 75%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity to a sequence of amino acids set forth in any of SEQ ID NOS: 73-855 and contains the amino acid replacement.

18. The modified PH20 polypeptide of any of claims 1-17, comprising up to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 , 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48,49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90 or more amino acid replacements.

19. The modified PH20 polypeptide of any of claims 1-18 that is modified by glycosylation, sialation, albumination, farnysylation, carboxylation, hydroxylation, phosphorylation, conjugation to a polymer, conjugation to a multimerization domain, conjugation to a toxin, conjugation to a detectable label or conjugation to a drug

20. The modified PH20 polypeptide of claim 19 wherein the PH20 polypeptide is conjugated to dextran or PEG.

21 A nucleic acid molecule, encoding a modified PH20 polypeptide of any of claims 1-19.

22. A vector, comprising the nucleic acid molecule of claim 21.

23. A cell, comprising the vector of claim 22.

24. A method of producing a modified PH20 polypeptide, comprising:

introducing the nucleic acid of claim 25 or the vector of claim 26 into a cell capable of incorporating N-linked sugar moieties into the polypeptide;

culturing the cell under conditions whereby an encoded modified PH20 polypeptide is produced and secreted by the cell; and

recovering the expressed polypeptide.

25. A pharmaceutical composition, comprising a modified PH20 polypeptide of any of claims 1-23, and a pharmaceutically acceptable excipient.

26. The pharmaceutical composition of claim 25, comprising at least one phenolic preservative.

27. The pharmaceutical composition of claim 26, wherein the preservative(s) is(are) selected from among phenol, metacresol (m-cresol), benzyl alcohol, and a paraben.

28. The pharmaceutical composition of any of claims 25-27, comprising a therapeutically active agent.

29. The pharmaceutical composition of claim 28, wherein the therapeutic agent is a polypeptide, a protein, a nucleic acid, a drug, a small molecule or an organic molecule.

30. The pharmaceutical composition of claim 28, wherein the therapeutically active agent is selected from among a chemotherapeutic agent, an analgesic agent, an anti-inflammatory agent, an antimicrobial agent, an amoebicidal agent, a trichomonacidal agent, an anti-parkinson agent, an anti-malarial agent, an anticonvulsant agent, an anti-depressant agent, and antiarthritics agent, an anti-

fungal agent, an antihypertensive agent, an antipyretic agent, an anti-parasite agent, an antihistamine agent, an alpha-adrenergic agonist agent, an alpha blocker agent, an anesthetic agent, a bronchial dilator agent, a biocide agent, a bactericide agent, a bacteriostat 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, a 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 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, or a sleep inducer.

31. The pharmaceutical composition of claim 28, wherein the therapeutic agent is selected from among an antibody, an Immune Globulin, a cytokine, a chemotherapeutic agent, a coagulation factor and an insulin.

32. The pharmaceutical composition of claim 28, wherein the therapeutic agent is an insulin that is a fast-acting insulin.

33. A pharmaceutical composition of any of claims 25-32 for use in treating a hyaluronan-associated disease or disorder, for use in treating a disease or condition associated with an excess of glycosaminoglycans, for ue in delivering a therapeutic drug, or for use in increasing penetration of chemotherapeutic agents into solid tumors..

34. The pharmaceutical composition of claim 33, wherein the use is for treating a tumor; for treating glycosaminoglycan accumulation in the brain, for treating a cardiovascular disorder; for treating an ophthalmic disorder; for treating a pulmonary disease; for treating cellulite; for treating a proliferative disorder, for treating elevated interstitial fluid pressure, for treating disc pressure or for treating edema.

35. A pharmaceutical composition of claim 30 for use in treating diabetes, wherein the composition comprises an insulin.