Many of these are ovine or bovine forms, which can be immunogenic for treatment of humans. Improved hyaluronan-degrading enzymes, such as hyaluronidases, and compositions thereof that can be used for treatment are needed.

SUMMARY

Provided is a modified PH20 polypeptide, comprising one or more amino acid replacements in an unmodified PH20 polypeptide, wherein:

the unmodified PH20 polypeptide consists of the sequence of amino acids set forth in SEQ ID NO: 3, 7 or 32-66;

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(s);

the amino acid replacement(s) confer(s) the increased hyaluronidase activity;

the modified PH20 polypeptide comprises up to 10 amino acid replacement(s) compared to the unmodified PH20 polypeptide not containing the replacement(s); and

the only amino acid replacement(s) is/are at a position corresponding to a position selected from among 1, 15, 24, 27, 29, 30, 31, 32, 33, 37, 39, 48, 63, 67, 69, 71, 72, 73, 75, 87, 92, 93, 94, 118, 120, 135, 141, 147, 148, 150, 151, 152, 155, 156, 163, 164, 165, 170, 198, 209, 212, 215, 219, 233, 236, 247, 257, 259, 260, 263, 269, 271, 272, 276, 278, 282, 293, 305, 308, 313, 320, 324, 325, 326, 328, 353, 359, 371, 377, 380, 389, 392, 395, 405, 409, 410, 418, 425, 436, 437, 438, 441, 442, 446 or 447 with reference to amino acid positions set forth in SEQ ID NO:3, wherein corresponding amino acid positions are identified by alignment of the PH20 polypeptide with the polypeptide having the sequence of amino acids 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 replacement N219A with reference to amino acid positions set forth in SEQ ID NO:3.

Provided is a modified PH20 polypeptide, comprising one or more amino acid replacements in an unmodified PH20 polypeptide, wherein:

the unmodified PH20 polypeptide consists of the sequence of amino acids set forth in SEQ ID NO: 3, 7 or 32-66;

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(s);

the amino acid replacement(s) confer(s) the increased hyaluronidase activity;

the modified PH20 polypeptide comprises up to 10 amino acid replacement(s) compared to the unmodified PH20 polypeptide not containing the replacement(s); and

the only amino acid replacement(s) is/are at a position corresponding to a position selected from among replacement with:

E at a position corresponding to position 12; E at a position corresponding to position 26; K at a position corresponding to position 26; R at a position corresponding to position 46; Q at a position corresponding to position 52; Q at a

position corresponding to position 58; H at a position corresponding to position 68; Q at a position corresponding to position 68; 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; 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; G at a position corresponding to position 84; R at a position corresponding to position 84; G at a position corresponding to position 97; H at a position corresponding to position 127; N at a position corresponding to position 127; G at a position corresponding to position 131; V at a position corresponding to position 131; R at a position corresponding to position 142; 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; R at a position corresponding to position 166; Y at a position corresponding to position 166; K at a position corresponding to position 174; K at a position corresponding to position 206; M at a position corresponding to position 213; N at a position corresponding to position 213; E at a position corresponding to position 237; S at a position corresponding to position 238; N at a position corresponding to position 261; R at a position corresponding to position 277; T at a position corresponding to position 277; 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; 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; S at a position corresponding to position 347; M at a position corresponding to position 399; T at a position corresponding to position 399; W at a position corresponding to position 399; D at a position corresponding to position 407; Q at a position corresponding to position 407; F at a position corresponding to position 419; I at a position corresponding to position 419; R at a position corresponding to position 419; S at a position corresponding to position 419; K 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; A at a position corresponding to position 431; H 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; V at a position corresponding to position 439; H at a position corresponding to position 440; R at a

position corresponding to position 440; A at a position corresponding to position 443; M at a position corresponding to position 443; and/or with P at a position corresponding to position 445, with reference to amino acid positions set forth in SEQ ID NO:3.

Provided is a nucleic acid molecule, encoding a modified PH20 polypeptide as described herein.

Provided is a vector, comprising the nucleic acid molecule as decribed above.

Provided is an isolated cell, comprising the vector as described above.

Provided is a modified PH20 polypeptide that is produced by the cell as described herein.

Provided is a method of producing a modified PH20 polypeptide, comprising:

introducing the nucleic acid of claim 20 or the vector as described above 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.

Provided is a pharmaceutical composition, comprising a modified PH20 polypeptide as described herein.

Provided is a pharmaceutical composition as described above for use in treating a hyaluronan-associated disease or disorder.

Provided is a pharmaceutical composition as described above for use in delivering a therapeutic agent to a subject.

Provided is a pharmaceutical composition as described above for treating an excess of glycosaminoglycans; for treating a tumor; for treating glycosaminoglycan accumulation in the brain; for treating a cardiovascular disorder; for treating an ophthalmic disorder; for treating pulmonary disease; for increasing penetration of chemotherapeutic agents into solid tumors; for treating cellulite; for treating a proliferative disorder; or for increasing bioavailability of drugs and other therapeutic agents.

Provided are modified PH20 polypeptides that have an altered property or properties compared to the PH20 polypeptide that do not have the modification(s). The modifications include amino acid replacement, deletion and/or insertions. Detailed structure/function of virtually each amino acid in a PH20 polypeptide is provided herein, as well as the identification of residues and loci that contribute to alteration of a property, such as stability in particular conditions, is provided. Hence, provided are modified PH20 polypeptides that contain one or more amino acid replacements that result in a PH20 polypeptide that retains

activity and/or exhibits increased or altered stability under a variety of conditions. Activity retained can be, for example, hyaluronidase activity that is as least about 40% or more of the PH20 polypeptide that does not include the replacement. Exemplary modifications are amino acid replacements. For purposes herein, amino acid replacements are denoted by the single amino acid letter followed by the corresponding amino acid position in SEQ ID NO:3 in which the replacement occurs. Single amino acid abbreviations for amino acid residues are well known to a skilled artisan (*see e.g.* Table 1), and are used herein throughout the description and examples. For example, 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 means that the replacement encompasses F204P in a PH20 polypeptide set forth in SEQ ID NO:3, or the same replacement at the corresponding position in another PH20 polypeptide.

Provided are modified PH20 polypeptides that contain at least one amino acid replacement in a PH20 polypeptide, whereby the modified PH20 polypeptide exhibits increased stability compared to the PH20 polypeptide not containing the amino acid replacement. Increased stability can be manifested as increased resistance to one or more protein conditions that are denaturing to proteins. The stability of modified and unmodified PH20 is compared under the same conditions. Exemplary protein denaturation (or denaturing, used interchangeably herein) conditions include, but are not limited to, elevated temperature greater than 30 °C or about 30 °C, agitation, low salt, including essentially or substantially or no salt, and presence of excipients that tend to denature proteins. Exemplary of such excipients are antiadherent(s), binder(s), coating(s), filler(s) and diluent(s), flavor(s), color(s), lubricant(s), glidant(s), preservative(s), detergent(s), sorbent(s) and combinations thereof.

CLAIMS:

1. A modified PH20 polypeptide, comprising one or more amino acid replacements in an unmodified PH20 polypeptide, wherein:

the unmodified PH20 polypeptide consists of the sequence of amino acids set forth in SEQ ID NO: 3, 7 or 32-66;

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(s);

the amino acid replacement(s) confer(s) the increased hyaluronidase activity;

the modified PH20 polypeptide comprises up to 10 amino acid replacement(s) compared to the unmodified PH20 polypeptide not containing the replacement(s); and

the only amino acid replacement(s) is/are at a position corresponding to a position selected from among 1, 15, 24, 27, 29, 30, 31, 32, 33, 37, 39, 48, 63, 67, 69, 71, 72, 73, 75, 87, 92, 93, 94, 118, 120, 135, 141, 147, 148, 150, 151, 152, 155, 156, 163, 164, 165, 170, 198, 209, 212, 215, 219, 233, 236, 247, 257, 259, 260, 263, 269, 271, 272, 276, 278, 282, 293, 305, 308, 313, 320, 324, 325, 326, 328, 353, 359, 371, 377, 380, 389, 392, 395, 405, 409, 410, 418, 425, 436, 437, 438, 441, 442, 446 or 447 with reference to amino acid positions set forth in SEQ ID NO:3, wherein corresponding amino acid positions are identified by alignment of the PH20 polypeptide with the polypeptide having the sequence of amino acids 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 replacement N219A with reference to amino acid positions set forth in SEQ ID NO:3.

2. The modified PH20 polypeptide of claim 1, 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; V at a position corresponding to position 15; E at a position corresponding to position 24; H at a position corresponding to position 24; 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; F at a position corresponding to position 48; H at a position corresponding to position 48; N at a position corresponding to position 48; W at a position corresponding to position 63; V at a position corresponding to position 67; 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; 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; 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; 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; 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; 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 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; R at a position corresponding to position 170; D at a position corresponding to position 198; N at a position corresponding to position 212; 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; R at a position corresponding to position 236; 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 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; 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; 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; K at a position corresponding to position 313; R at a position corresponding to

position 313; 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; 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; G at a position corresponding to position 405; 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; K at a position corresponding to position 425; 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; F at a position corresponding to position 441; R at a position corresponding to position 442; 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.

3. A modified PH20 polypeptide, comprising one or more amino acid replacements in an unmodified PH20 polypeptide, wherein:

the unmodified PH20 polypeptide consists of the sequence of amino acids set forth in SEQ ID NO: 3, 7 or 32-66;

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(s);

the amino acid replacement(s) confer(s) the increased hyaluronidase activity;

the modified PH20 polypeptide comprises up to 10 amino acid replacement(s) compared to the unmodified PH20 polypeptide not containing the replacement(s); and

the only amino acid replacement(s) is/are at a position corresponding to a position selected from among replacement with:

E at a position corresponding to position 12; E at a position corresponding to position 26; K at a position corresponding to position 26; R at a position corresponding to position 46; Q at a position corresponding to position 52; Q at a position corresponding to position 58; H at a position corresponding to position 68; Q at a position corresponding to position 68; 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; 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; G at a position corresponding to position 84; R at a position corresponding to position 84; G at a position corresponding to position 97; H at a position corresponding to position 127; N at a position corresponding to position 127; G at a position corresponding to position 131; V at a position corresponding to position 131; R at a position corresponding to position 142; 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; R at a position corresponding to position 166; Y at a position corresponding to position 166; K at a position corresponding to position 174; K at a position corresponding to position 206; M at a position corresponding to position 213; N at a position corresponding to position 213; E at a position corresponding to position 237; S at a position corresponding to position 238; N at a position corresponding to position 261; R at a position corresponding to position 277; T at a position corresponding to position 277; 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; 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; S at a position corresponding to position 347; M at a position corresponding to position 399; T at a position corresponding to position 399; W at a position corresponding to position 399; D at a position corresponding to position 407; Q at a position corresponding to position 407; F at a position corresponding to position 419; I at a position corresponding to position 419; R at a position corresponding to position 419; S at a position corresponding to position 419; K 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; A at a position corresponding to position 431; H 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; V at a position corresponding to position 439; H at a position corresponding to position 440; R at a position corresponding to position 440; A at a position corresponding to position 443; M at a position corresponding to position 443; and/or with P at a position corresponding to position 445, with reference to amino acid positions set forth in SEQ ID NO:3.

4. The modified PH20 polypeptide of claim 1 or claim 2, comprising a sequence of amino acids set forth in any of SEQ ID NOS:

73, 78, 91, 95, 96, 105, 106, 108, 109, 111, 112, 113, 115, 117, 118, 119, 120, 123-126, 128-136, 139-141, 149, 154, 155, 164, 165, 167, 191, 192, 196, 197, 199-205, 207, 208, 225, 226, 228, 229, 231, 233, 237, 253, 254, 256, 257, 277, 283, 293, 295, 296, 298, 300, 303, 316, 318, 321, 322, 338-340, 344, 348, 367, 369, 371, 377, 384-388, 394, 398, 399, 401, 406-408, 410, 412, 414, 416, 431, 448, 459, 465, 469, 478, 479, 482, 493, 497, 501, 503, 507, 508, 510-512, 514, 518, 522, 523, 537-543, 545, 558, 559, 561, 563-566, 569, 572, 574, 594, 596, 618-620, 624-634, 637, 640-644, 652, 657, 675, 695, 698, 699, 700, 712, 717, 725, 738, 748-750, 757, 775, 799-801, 807, 822, 825, 844, 847, 851 and 853, or a sequence of amino acids that exhibits at least 97% sequence identity to a sequence of amino acids set forth in any of 73, 78, 91, 95, 96, 105, 106, 108, 109, 111, 112, 113, 115, 117, 118, 119, 120, 123-126, 128-136, 139-141, 149, 154, 155, 164, 165, 167, 191, 192, 196, 197, 199-205, 207, 208,

225, 226, 228, 229, 231, 233, 237, 253, 254, 256, 257, 277, 283, 293, 295, 296, 298, 300, 303, 316, 318, 321, 322, 338-340, 344, 348, 367, 369, 371, 377, 384-388, 394, 398, 399, 401, 406-408, 410, 412, 414, 416, 431, 448, 459, 465, 469, 478, 479, 482, 493, 497, 501, 503, 507, 508, 510-512, 514, 518, 522, 523, 537-543, 545, 558, 559, 561, 563-566, 569, 572, 574, 594, 596, 618-620, 624-634, 637, 640-644, 652, 657, 675, 695, 698, 699, 700, 712, 717, 725, 738, 748-750, 757, 775, 799-801, 807, 822, 825, 844, 847, 851 and 853 and that contains the amino acid replacement.

5. The modified PH20 polypeptide of claim 3, comprising a sequence of amino acids set forth in any of SEQ ID NOS:

86, 89, 99, 100, 159, 173, 181, 193, 195, 209-220, 238, 239, 242, 247-252, 267, 269, 277, 308, 324, 325, 330, 335, 355, 419, 421-423, 425, 428, 435, 455, 456, 462, 463, 484, 490, 506, 531, 533, 579, 581-583, 585, 587, 588, 602, 605, 606, 609, 613, 648, 731, 732, 734, 742, 746, 760, 762, 764, 765, 769, 771-773, 779, 782, 786-789, 794, 795, 814, 816, 819, 826, 830 and 838, or a sequence of amino acids that exhibits at least 97% sequence identity to a sequence of amino acids set forth in any of 86, 89, 99, 100, 159, 173, 181, 193, 195, 209-220, 238, 239, 242, 247-252, 267, 269, 277, 308, 324, 325, 330, 335, 355, 419, 421-423, 425, 428, 435, 455, 456, 462, 463, 484, 490, 506, 531, 533, 579, 581-583, 585, 587, 588, 602, 605, 606, 609, 613, 648, 731, 732, 734, 742, 746, 760, 762, 764, 765, 769, 771-773, 779, 782, 786-789, 794, 795, 814, 816, 819, 826, 830 and 838 and that contains the amino acid replacement.

6. The modified PH20 polypeptide of any of claims 1-5, wherein the modified PH20 polypeptide exhibits at least 98% amino acid sequence identity to the sequence of amino acids set forth in SEQ ID NO: 3.

7. The modified PH20 polypeptide of any of claims 1-6, 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: 7 or 32-66.

8. The modified PH20 polypeptide of any of claims 1-6, wherein the amino acid replacement is in an unmodified PH20 polypeptide that consists of the sequence of amino acids set forth in SEQ ID NO: 3.

9. The modified PH20 polypeptide of any of claims 1-8, wherein the modified PH20 polypeptide exhibits at least 2.0-fold of the hyaluronidase activity compared to the PH20 polypeptide not containing the amino acid replacement.

10. The modified PH20 polypeptide of any of claims 1-8, wherein the modified PH20 polypeptide exhibits at least 130%, 135%, 140%, 145%, 150%, 160%, 170%, 180%, 200%, 250%, 300%, 350%, 400%, 500%, 1500%, 2000%, 3000%, 4000%, 5000% or more of the hyaluronidase activity of the unmodified PH20 polypeptide not containing the amino acid replacement(s).

11. The modified PH20 polypeptide of any of claims 1-10 that is substantially purified or isolated.

12. The modified PH20 polypeptide of any of claims 1-11 that is further modified by modification selected from among glycosylation, sialation, albumination, farnysylation, carboxylation, hydroxylation and phosphorylation.

13. The modified PH20 polypeptide of claim 12, wherein the modified PH20 polypeptide is glycosylated, whereby the polypeptide comprises at least an N-acetylglucosamine moiety linked to each of at least three asparagine (N) residues.

14. The modified PH20 polypeptide of claim 13, wherein the three asparagine residues correspond to amino acid residues 200, 333 and 358 of SEQ ID NO:3.

15. The modified PH20 polypeptide of any of claims 1-14 that is further modified by conjugation to a polymer.

16. The modified PH20 polypeptide of claim 15, wherein the polymer is dextran or PEG.

17. The modified PH20 polypeptide of any of claims 1-16, wherein the modified PH20 polypeptide is conjugated to a moiety selected from among a multimerization domain, toxin, detectable label or drug.

18. The modified PH20 polypeptide of claim 17, wherein the modified PH20 polypeptide is conjugated to an Fc domain.

19. The modified PH20 polypeptide of any of claims 1-18, comprising up to 5 amino acid replacements.

20. A nucleic acid molecule, encoding a modified PH20 polypeptide of any of claims 1-14.

21. A vector, comprising the nucleic acid molecule of claim 20.

22. The vector of claim 21 that is a eukaryotic or a prokaryotic vector.

23. The vector of claim 21 or claim 22 that is a mammalian vector or a viral vector.

24. The vector of claim 23 that is a viral vector, wherein the viral vector is an adenovirus vector, a retrovirus vector or a vaccinia virus vector.

25. An isolated cell, comprising the vector of any of claims 21-24.

26. The cell of claim 25 that is a mammalian cell.

27. The cell of claim 26, wherein the mammalian cell is a Chinese Hamster Ovary (CHO) cell.

28. The cell of claim 25 that is a eukaryotic cell.

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

introducing the nucleic acid of claim 20 or the vector of any of claims 21-24 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.

30. The method of claim 29, wherein the nucleic acid is operably linked to a promoter.

31. The method of claim 29 or claim 30, wherein the cell is a eukaryotic cell.

32. The method of any of claims 29-31, wherein the cell is a mammalian cell.

33. The method of any of claims 29-32, wherein the cell is a Chinese hamster ovary (CHO) cell.

34. A pharmaceutical composition, comprising a modified PH20 polypeptide of any of claims 1-19.

35. The pharmaceutical composition of claim 34, comprising a therapeutically active agent.

36. The pharmaceutical composition of claim 35, wherein the therapeutic agent is formulated with the composition or in a separate composition.

37. The pharmaceutical composition of claim 35 or claim 36, wherein the therapeutic agent is a polypeptide, a protein, a nucleic acid, a drug, a small molecule or an organic molecule.

38. The pharmaceutical composition of any of claims 34-37, 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.

39. The pharmaceutical composition of any of claims 34-38, wherein the therapeutic agent is selected from among an antibody, an Immune Globulin, a cytokine, a chemotherapeutic agent, a coagulation factor and an insulin.

40. The pharmaceutical composition of claim 35, wherein the therapeutic agent is selected from among Adalimumabs, Agalsidase Betas, Alefacepts, Ampicillins, Anakinras, Antipoliomyelitic Vaccines, Anti-Thymocytes, Azithromycins, Becaplermins, Caspofungins, Cefazolins, Cefepimes, Cefotetans, Ceftazidimes, Ceftriaxones, Cetuximabs, Cilastatins, Clavulanic Acids, Clindamycins, Darbepoetin Alfas, Daclizumabs, Diphtheria, Diphtheria antitoxins, Diphtheria Toxoids, Efalizumabs, Epinephrines, Erythropoietin Alphas, Etanercepts, Filgrastims, Fluconazoles, Follicle-Stimulating Hormones, Follitropin Alphas, Follitropin Betas, Fosphenytoins, Gadodiamides, Gadopentetates, Gatifloxacins, Glatiramers, GM-CSF's, Goserelins, Goserelin acetates, Granisetrons, Haemophilus Influenza B's, Haloperidols, Hepatitis vaccines, Hepatitis A Vaccines, Hepatitis B Vaccines, Ibritumomab Tiuxetans, Ibritumomabs, Tiuxetans, Immunoglobulins, Hemophilus influenza vaccines, Influenza Virus Vaccines, Infliximabs, Insulin lispro, 75% neutral protamine lispro (NPL)/25% insulin lispro, 50% neutral protamine Hagedorn (NPH)/ 50% regular insulin, 70% NPH/30% regular insulin; Regular insulin, NPH insulin, Ultra insulin, Ultralente insulin, and Insulin Glargines, Interferons, Interferon alpha, Interferon Betas, Interferon Gammas, Interferon alpha-2a, Interferon alpha 2-b, Interferon Alphacon, Interferon alpha-n, Interferon Betas, Interferon Beta-1a's, Interferon Gammas, Interferon alpha-con, Iodixanols, Iohexols, Iopamidols, Ioversols, Ketorolacs, Laronidases, Levofloxacins, Lidocaines, Linezolids, Lorazepams, Measles Vaccines, Measles virus, Mumps viruses, Measles-Mumps-Rubella Virus Vaccines, Rubella vaccines, Medroxyprogesterones, Meropenems, Methylprednisolones, Midazolams, Morphines, Octreotides, Omalizumabs, Ondansetrons, Palivizumabs, Pantoprazoles, Pegaspargases, Pegfilgrastims, Peg-Interferon Alpha-2a's, Peg-Interferon Alpha-2b's, Pegvisomants, Pertussis vaccines, Piperacillins, Pneumococcal Vaccines and Pneumococcal Conjugate Vaccines, Promethazines, Reteplases, Somatropins, Sulbactams, Sumatriptans, Tazobactams, Tenecteplases, Tetanus Purified Toxoids,

Ticarcillins, Tositumomabs, Triamcinolones, Triamcinolone Acetonides, Triamcinolone hexacetonides, Vancomycins, Varicella Zoster immunoglobulins, Varicella vaccines, other vaccines, Alemtuzumabs, Alitretinoins, Allopurinols, Altretamines, Amifostines, Anastrozoles, Arsenics, Arsenic Trioxides, Asparaginases, Bacillus Calmette-Guerin (BCG) vaccines, BCG Live, Bexarotenes, Bleomycins, Busulfans, Busulfan intravenous, Busulfan orals, Calusterones, Capecitabines, Carboplatins, Carmustines, Carmustines with Polifeprosans, Celecoxibs, Chlorambucils, Cisplatins, Cladribines, Cyclophosphamides, Cytarabines, Cytarabine liposomals, Dacarbazines, Dactinomycins, Daunorubicin liposomals, Daunorubicins, Daunomycins, Denileukin Diftitoxes, Dexrazoxanes, Docetaxels, Doxorubicins, Doxorubicin liposomals, Dromostanolone propionates, Elliott's B Solutions, Epirubicins, Epoetin alfas, Estramustines, Etoposides, Etoposide phosphates, Etoposide VP-16s, Exemestanes, Floxuridines, Fludarabines, Fluorouracils, 5-Fluorouracils, Fulvestrants, Gemcitabines, Gemtuzumabs, Ozogamicins, Gemtuzumab ozogamicins, Hydroxyureas, Idarubicins, Ifosfamides, Imatinib mesylates, Irinotecans, Letrozoles, Leucovorins, Levamisoles, Lomustines, CCNUs, Mechlorethamines, Nitrogen mustards, Megestrols, Megestrol acetates, Melphalans, L-PAMs, Mercaptopurines, 6-Mercaptopurines, Mesnas, Methotrexates, Methoxsalens, Mitomycins, Mitomycin C's, Mitotanes, Mitoxantrones, Nandrolones, Nandrolone Phenpropionates, Nofetumomabs, Oprelvekins, Oxaliplatins, Paclitaxels, Pamidronates, Pegademases, Pentostatins, Pipobromans, Plicamycins, Mithramycins, Porfimers, Porfimer sodiums, Procarbazines, Quinacrines, Rasburicases, Rituximabs, Sargramostims, Streptozocins, Talcs, Tamoxifens, Temozolomides, Teniposides, Testolactones, Thioguanines, 6-Thioguanines, Triethylenethiophosphoramides (Thiotepas), Topotecans, Toremifenes, Trastuzumabs, Tretinoins, Uracil Mustards, Valrubicins, Vinblastines, Vincristines, Vinorelbines, Zoledronates, Acivicins, Aclarubicins, Acodazoles, Acronines, Adozelesins, Aldesleukins, Retinoic Acids, Alitretinoins, 9-Cis-Retinoic Acids, Alvocidibs, Ambazones, Ambomycins, Ametantrones, Aminoglutethimides, Amsacrines, Anaxirones, Ancitabines, Anthramycins, Apaziquones, Argimesnas, Asperlins, Atrimustines, Azacitidines, Azetepas, Azotomycins, Banoxantrones, Batabulins, Batimastats, Benaxibines, Bendamustines, Benzodepas, Bicalutamides, Bietaserpines, Biricodars, Bisantrenes, Bisnafide Dimesylates, Bizelesins, Bortezomibs, Brequinars, Bropirimines, Budotitanes, Cactinomycins, Canertinibs, Caracemides, Carbetimers, Carboquones, Carmofurs, Carubicins, Carzelesins, Cedefingols, Cemadotins, Chlorambucils, Cioteronels, Cirolemycins, Clanfenurs, Clofarabines, Crisnatols, Decitabines, Dexniguldipines, Dexormaplatins, Dezaguanines, Diaziquones, Dibrospidiums, Dienogests, Dinalins, Disermolides, Dofequidars, Doxifluridines, Droloxifenes, Duazomycins, Ecomustines, Edatrexates, Edotecarins, Eflomithines, Elacridars, Elinafides, Elsamitrucins, Emitefurs, Enloplatins, Enpromates, Enzastaurins, Epipropidines, Eptaloprosts, Erbulozoles, Esorubicins, Etanidazoles, Etoglucids, Etoprines, Exisulinds, Fadrozoles, Fazarabines, Fenretinides, Fluoxymesterones, Flurocitabines, Fosquidones, Fostriecins, Fotretamines, Galarubicins, Galocitabines, Geroquinols, Gimatecans, Gimeracils, Gloxazones, Glufosfamides, Ilmofosines, Ilomastats, Imexons, Improsulfans, Indisulams, Inproquones, Interleukins, Interleukin-2s, recombinant Interleukins, Intoplicines, Iobenguanes, Iproplatins, Irsogladines, Ixabepilones, Ketotrexates, L-Alanosines, Lanreotides, Lapatinibs, Ledoxantrones, Leuprolides, Leuprorelins, Lexacalcitols, Liarozoles, Lobaplatins, Lometrexols, Lonafarnibs, Losoxantrones, Lurtotecans, Mafosfamides, Mannosulfans, Marimastats, Masoprocols, Maytansines, Mechlorethamines, Melengestrols, Melphalans, Menogarils, Mepitiostanes, Metesinds, Metomidates, Metoprines, Meturedepas, Miboplatins, Miproxifenes, Misonidazoles, Mitindomides, Mitocarcins, Mitocromins, Mitoflaxones, Mitogillins, Mitoguazones, Mitomalcins, Mitonafides, Mitoquidones, Mitospers, Mitozolomides, Mivobulins, Mizoribines, Mofarotenes, Mopidamols, Mubritinibs,

Mycophenolic Acids, Nedaplatins, Neizarabines, Nemorubicins, Nitracrines, Nocodazoles, Nogalamycins, Nolatrexeds, Nortopixantrones, Ormaplatins, Ortataxels, Oteracils, Oxisurans, Oxophenarsines, Patupilones, Peldesines, Peliomycins, Pelitrexols, Pemetrexeds, Pentamustines, Peplomycins, Perfosfamides, Perifosines, Picoplatins, Pinafides, Piposulfans, Pirfenidones, Piroxantrones, Pixantrones, Plevitrexeds, Plomestanes, Porfiromycins, Prednimustines, Propamidines, Prospidiums, Pumitepas, Puromycins, Pyrazofurins, Ranimustines, Riboprines, Ritrosulfans, Rogletimides, Roquinimexs, Rufocromomycins, Sabarubicins, Safingols, Satraplatins, Sebriplatins, Semustines, Simtrazenes, Sizofirans, Sobuzoxanes, Sorafenibs, Sparfosates, Sparfosic Acids, Sparsomycins, Spirogermaniums, Spiromustines, Spiroplatins, Squalamines, Streptonigrins, Streptovarycins, Sufosfamides, Sulofenurs, Tacedinalines, Talisomycins, Tallimustines, Tariquidars, Tauromustines, Tecogalans, Tegafurs, Teloxantrones, Temoporfins, Teroxirones, Thiamiprines, Tiamiprines, Tiazofurins, Tilomisoles, Tilorones, Timcodars, Timonacics, Tirapazamines, Topixantrones, Trabectedins, Ecteinascidin 743, Trestolones, Triciribines, Trilostanes, Trimetrexates, Triplatin Tetranitrates, Triptorelins, Trofosfamides, Tubulozoles, Ubenimexs, Uredepas, Valspodars, Vapreotides, Verteporfins, Vinblastines, Vindesines, Vinepidines, Vinflunines, Vinformides, Vinglycinates, Vinleucinols, Vinleurosines, Vinrosidines, Vintriptols, Vinzolidines, Vorozoles, Xanthomycin A's, Guamecyclines, Zeniplatins, Zilascorbs [2-H], Zinostatins, Zorubicins, Zosuquidars, Acetazolamides, Acyclovirs, Adipiodones, Alatrofloxacins, Alfentanils, Allergenic extracts, Alpha 1-proteinase inhibitors, Alprostadils, Amikacins, Amino acids, Aminocaproic acids, Aminophyllines, Amitriptylines, Amobarbitals, Amrinones, Analgesics, Anti-poliomyelitic vaccines, Anti-rabic serums, Anti-tetanus immunoglobulins, tetanus vaccines, Antithrombin IIIs, Antivenom serums, Argatrobans, Arginines, Ascorbic acids, Atenolols, Atracuriums, Atropines, Aurothioglucoses, Azathioprines, Aztreonams, Bacitracins, Baclofens, Basiliximabs, Benzoic acids, Benztropines, Betamethasones, Biotins, Bivalirudins, Botulism antitoxins, Bretyliums, Bumetanides, Bupivacaines, Buprenorphines, Butorphanols, Calcitonins, Calcitriols, Calciums, Capreomycins, Carboprosts, Carnitines, Cefamandoles, Cefoperazones, Cefotaximes, Cefoxitins, Ceftizoximes, Cefuroximes, Chloramphenicols, Chloroprocaines, Chloroquines, Chlorothiazides, Chlorpromazines, Chondroitinsulfuric acids, Choriogonadotropin alfas, Chromiums, Cidofovirs, Cimetidines, Ciprofloxacins, Cisatracuriums, Clonidines, Codeines, Colchicines, Colistins, Collagens, Corticorelin ovine triflutates, Corticotrophins, Cosyntropins, Cyanocobalamins, Cyclosporines, Cysteines, Dacliximabs, Dalfopristins, Dalteparins, Danaparoids, Dantrolenes, Deferoxamines, Desmopressins, Dexamethasones, Dexmedetomidines, Dexpanthenols, Dextrans, Iron dextrans, Diatrizoic acids, Diazepams, Diazoxides, Dicyclomines, Digibinds, Digoxins, Dihydroergotamines, Diltiazems, Diphenhydramines, Dipyridamoles, Dobutamines, Dopamines, Doxacuriums, Doxaprams, Doxercalciferols, Doxycyclines, Droperidols, Dyphyllines, Edetic acids, Edrophoniums, Enalaprilats, Ephedrines, Epoprostenols, Ergocalciferols, Ergonovines, Ertapenems, Erythromycins, Esmolols, Estradiols, Estrogenics, Ethacrynic acids, Ethanolamines, Ethanols, Ethiodized oils, Etidronic acids, Etomidates, Famotidines, Fenoldopams, Fentanyls, Flumazenils, Fluoresceins, Fluphenazines, Folic acids, Fomepizoles, Fomivirsens, Fondaparinuxs, Foscarnets, Fosphenytoins, Furosemides, Gadoteridols, Gadoversetamides, Ganciclovirs, Gentamicins, Glucagons, Glucoses, Glycines, Glycopyrrolates, Gonadorelins, Gonadotropin chorionics, Haemophilus B polysaccharides, Hemins, Herbals, Histamines, Hydralazines, Hydrocortisones, Hydromorphones, Hydroxocobalamins, Hydroxyzines, Hyoscyamines, Ibutilides, Imiglucerases, Indigo carmines, Indomethacins, Iodides, Iopromides, Iothalamic acids, Ioxaglic acids, Ioxilans, Isoniazids, Isoproterenols, Japanese encephalitis vaccines, Kanamycins, Ketamines, Labetalols, Lepirudins, Levobupivacaines, Levothyroxines, Lincomycins, Liothyronines,

Luteinizing hormones, Lyme disease vaccines, Mangafodipirs, Manthtols, Meningococcal polysaccharide vaccines, Meperidines, Mepivacaines, Mesoridazines, Metaraminols, Methadones, Methocarbamols, Methohexitals, Methyldopates, Methylergonovines, Metoclopramides, Metoprolols, Metronidazoles, Minocyclines, Mivacuriums, Morrhuic acids, Moxifloxacins, Muromonab-CD3s, Mycophenolate mofetils, Nafcillins, Nalbuphines, Nalmefenes, Naloxones, Neostigmines, Niacinamides, Nicardipines, Nitroglycerins, Nitroprussides, Norepinephrines, Orphenadrines, Oxacillins, Oxymorphones, Oxytetracyclines, Oxytocins, Pancuroniums, Panthenols, Pantothenic acids, Papaverines, Peginterferon alpha 2As, Penicillin Gs, Pentamidines, Pentazocines, Pentobarbitals, Perflutrens, Perphenazines, Phenobarbitals, Phentolamines, Phenylephrines, Phenytoins, Physostigmines, Phytonadiones, Polymyxin, Pralidoximes, Prilocaines, Procainamides, Procaines, Prochlorperazines, Progesterones, Propranolols, Pyridostigmine hydroxides, Pyridoxines, Quinidines, Quinupristins, Rabies immunoglobulins, Rabies vaccines, Ranitidines, Remifentanils, Riboflavins, Rifampins, Ropivacaines, Samariums, Scopolamines, Seleniums, Sermorelins, Sincalides, Somatrems, Spectinomycins, Streptokinases, Streptomycins, Succinylcholines, Sufentanils, Sulfamethoxazoles, Tacrolimuses, Terbutalines, Teriparatides, Testosterones, Tetanus antitoxins, Tetracaines, Tetradecyl sulfates, Theophyllines, Thiamines, Thiethylperazines, Thiopentals, Thyroid stimulating hormones, Tinzaparins, Tirofibans, Tobramycins, Tolazolines, Tolbutamides, Torsemides, Tranexamic acids, Treprostinils, Trifluoperazines, Trimethobenzamides, Trimethoprims, Tromethamines, Tuberculins, Typhoid vaccines, Urofollitropins, Urokinases, Valproic acids, Vasopressins, Vecuroniums, Verapamils, Voriconazoles, Warfarins, Yellow fever vaccines, Zidovudines, Zincs, Ziprasidone hydrochlorides, Aclacinomycins, Actinomycins, Adriamycins, Azaserines, 6-Azauridines, Carzinophilins, Chromomycins, Denopterins, 6 Diazo 5 Oxo-L-Norleucines, Enocitabines, Floxuridines, Olivomycins, Pirarubicins, Piritreximes, Pteropterins, Tegafurs, Tubercidins, Alteplases, Arcitumomabs, bevacizumabs, Botulinum Toxin Type A's, Botulinum Toxin Type B's, Capromab Pendetides, Daclizumabs, Dornase alphas, Drotrecogin alphas, Imciromab Pentetates, Iodine-131's, an antibiotic agent; an angiogenesis inhibitor; anti-cataract and anti-diabetic retinopathy substances; carbonic anhydrase inhibitors; mydriatics; photodynamic therapy agents; prostaglandin analogs; growth factor; anti-neoplastics; anti-metabolites; anti-viral; amebicides and anti-protozoals; anti-tuberculosis and anti-leprotic; antitoxins and antivenins; antihemophilic factor, anti-inhibitor coagulant complex, antithrombin III, coagulations Factor V, coagulation Factor IX, plasma protein fraction, von Willebrand factor; antiplatelet agent a colony stimulating factor (CSF); an erythropoiesis stimulator; hemostatics and albumins; Immune Globulins; thrombin inhibitors; anticoagulants; a steroidal anti-inflammatory drug selected from among alclometasones, algestones, beclomethasones, betamethasones, budesonides, clobetasols, clobetasones, clocortolones, cloprednols, corticosterones, cortisones, 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; Docosenoid, prostaglandins, prostaglandin analogs, antiprostaglandins and prostaglandin precursors; miotics, cholinergics and anti-cholinesterase; and anti-allergenics.

41. A pharmaceutical composition of any of claims 34-40 for use in treating a hyaluronan-associated disease or disorder.

42. A pharmaceutical composition of any of claims 34-40 for use in delivering a therapeutic agent to a subject.

43. A pharmaceutical composition of any of claims 34-40 for treating an excess of glycosaminoglycans; for treating a tumor; for treating glycosaminoglycan accumulation in the brain; for treating a cardiovascular disorder; for treating an ophthalmic disorder; for treating pulmonary disease; for increasing penetration of chemotherapeutic agents into solid tumors; for treating cellulite; for treating a proliferative disorder; or for increasing bioavailability of drugs and other therapeutic agents.

44. The pharmaceutical composition of claim 41, wherein the hyaluronan-associated disease or condition is an inflammatory disease or a tumor or cancer.

45. The pharmaceutical composition of claim 44, wherein the tumor is a solid tumor.

46. The pharmaceutical composition of any of claims 42-44, wherein the hyaluronan-associated disease or condition is selected from among a late-stage cancer, metastatic cancers and undifferentiated cancers.

47. The pharmaceutical composition of any of claims 42-46, wherein the hyaluronan-associated disease or condition is selected from among ovarian cancer, in situ carcinoma (ISC), squamous cell carcinoma (SCC), prostate cancer, pancreatic cancer, non-small cell lung cancer, breast cancer and colon cancer.