

alter a property, such as, but not limited to, half-life and pharmacokinetics. The modification includes linking directly or indirectly via a linker, such as covalently or by other stable linkage, a polymer, such as dextran, a pegylation or sialation moiety, or other such polymers, such as natural or sugar polymers. In the exemplary embodiments herein, the hyaluronan degrading enzyme is pegylated.

In one aspect, there is provided a method of identifying a subject for treatment of a tumor with a modified hyaluronidase, comprising:

- a) measuring the expression or level of hyaluronan in a biopsy of a tumor previously obtained from a subject; and
- b) selecting a subject in which hyaluronan is expressed in at least 30% of the tumoral area of the tumor biopsy, thereby identifying the subject from whom the sample was obtained as a subject for treatment with the modified hyaluronidase, wherein modification of the hyaluronidase is conjugation to a polymer.

Provided herein are methods for treating a disease or condition in which a hyaluronidase substrate accumulates, and methods for treating a hyaluronan-associated disease or condition. Such methods include administering a soluble hyaluronidase that is modified by conjugation to a polymer. Also provided herein are compositions containing a soluble hyaluronidase in an amount sufficient for maintaining a plasma level of the hyaluronidase enzyme in plasma at a level of at least 3 U/mL for at least a week, and combinations containing such compositions. The soluble hyaluronidase in the compositions and combinations provided herein is conjugated to a polymer.

Provided herein are methods for treating a disease or condition in which a hyaluronidase substrate accumulates. The methods involve administering a soluble hyaluronidase enzyme to a subject more than once a week for a predetermined number of weeks in an amount sufficient to maintain a pharmacologically active level of the hyaluronidase in the plasma of at least about or 3 U/mL to prevent resynthesis of the substrate to levels prior to treatment. The hyaluronidase enzyme used in the methods is modified by conjugation to a polymer, and the predetermined number of weeks is more than one week. In some examples, the predetermined number of weeks

is at least two weeks, such as two weeks, three weeks, or four weeks. Exemplary hyaluronidase substrates that accumulate in the condition or disease being treated include hyaluronan. In one example, the hyaluronan expression in a sample from the subject is measured prior to treatment.

In some examples of the methods for treating a disease or condition in which a hyaluronidase substrate accumulates, after the predetermined number of weeks, administration is discontinued for a first predetermined period of time, such as at least one week, and then resumed for at least one week. For example, administration can be discontinued for one week, two weeks, three weeks or four weeks, and then resumed