

**Viscosity-Reducing and stabilizing liquid Formulations for High
Concentration Protein Formulations**

FIELD OF INVENTION

[0001] The present disclosure relates to a series of viscosity-reducing and stabilizing liquid formulations, meticulously tailored to significantly decrease the viscosity and increase the stability of high concentration biopharmaceuticals. The viscosity-reducing and stabilizing liquid formulations can be used in high concentration biopharmaceutical products and can bring considerable potential for enhancing the formulation stability and elevating the feasibility of high concentration biopharmaceutical products.

BACKGROUND OF INVENTION

[0002] Specific administration routes such as subcutaneously and intramuscularly and higher dosage requirements give the increasing demand for high concentration formulations of biopharmaceutical drugs. This surge in demand presents a significant challenge related to viscosity and stability. To address this issue effectively, there is a need to develop innovative solutions for reducing viscosity and enhancing the stability in high concentration formulations of biopharmaceuticals.

SUMMARY OF INVENTION

[0003] The present disclosure has an object to develop a novel series of viscosity-reducing and stabilizing liquid formulations meticulously tailored to significantly decrease the viscosity and enhance the stability of high concentration biopharmaceuticals. Compared with existing viscosity reduction strategies, the viscosity-reducing and stabilizing liquid formulations of the present application have better capacity of viscosity reduction and protein stabilization. The introduction of these innovative formulations as additives brings considerable potential for enhancing the formulation stability and elevating the feasibility of high concentration biopharmaceutical products.

[0004] In a first aspect, the present disclosure relates to a novel series of viscosity-reducing and stabilizing liquid formulations meticulously tailored to significantly decrease the viscosity of high concentration biopharmaceuticals and stabilize the biopharmaceuticals. The viscosity-reducing and stabilizing liquid formulations include:

- (a) Arginine (30-300 mM) and Niacin (30-300 mM); or
- (b) Histidine (30-300 mM) and Niacin (30-300 mM); or
- (c) Meglumine (30-300 mM) and Niacin (30-300 mM); or
- (d) Lysine (30-300 mM) and Niacin (30-300 mM); or
- 5 (e) Arginine·HCl (30-300 mM) and Niacinamide (30-300 mM); or
- (f) Histidine (30-300 mM) and Niacinamide (30-300 mM); or
- (g) Meglumine (30-300 mM) and Niacinamide (30-300 mM); or
- (h) Lysine·HCl (30-300 mM) and Niacinamide (30-300 mM).

[0005] In some embodiments, the viscosity-reducing and stabilizing liquid formulations can
10 be used to reduce viscosity and enhance the stability of a formulation comprising a protein agent.
In other embodiments, the viscosity-reducing and stabilizing liquid formulations can be used to
prepare a liquid formulation of a protein agent with high concentration of a protein agent, high
stability and with low viscosity, for example, less than 100 cP, preferably less than 50 cP, as
measured at 20°C.

15 [0006] In a second aspect, the present disclosure relates to a pharmaceutically acceptable
protein agent formulation, comprising:

- (i) one or more protein agents;
- (ii) a suitable buffer system;
- (iii) a viscosity-reducing and stabilizing liquid formulation, comprising:

- 20 (a) Arginine (30-300 mM) and Niacin (30-300 mM); or
- (b) Histidine (30-300 mM) and Niacin (30-300 mM); or
- (c) Meglumine (30-300 mM) and Niacin (30-300 mM); or
- (d) Lysine (30-300 mM) and Niacin (30-300 mM); or
- (e) Arginine·HCl (30-300 mM) and Niacinamide (30-300 mM); or
- 25 (f) Histidine (30-300 mM) and Niacinamide (30-300 mM); or
- (g) Meglumine (30-300 mM) and Niacinamide (30-300 mM); or
- (h) Lysine·HCl (30-300 mM) and Niacinamide (30-300 mM);

wherein the pharmaceutically acceptable protein agent formulation has a pH between about 4.5 and 7.5, increased stability, and a viscosity less than 100 cP, preferably less than 50 cP, as measured at 20 °C.

[0007] In some embodiments, the one or more protein agents have a molecular weight from about 50 kDa to about 250 kDa and at a concentration from about 10 mg/mL to about 300 mg/mL, preferably from about 100 mg/mL to about 300 mg/mL.

[0008] In some embodiments, the pharmaceutically acceptable protein agent formulation has a pH about 4.5 to 7.5, about 5.0 to 7.5, about 5.5 to 7.5, about 6.0 to 7.5, about 4.0 to 7.5, about 4.5 to 7.5, about 5.0 to 7.5, or about 6.0 to 7.5, or any pH value in a range of 4.5 to 7.5, for example, pH 4.5, 5.0, 5.5, 6.0, 6.5, 7.0 or 7.5.

[0009] In some embodiments, the buffer system may be selected from, but not limited to: histidine buffer, acetate buffer, citrate buffer, phosphate buffer, tris buffer, succinate buffer, and any combination thereof.

[0010] In some embodiments, the buffer system may be selected from:

- (1) histidine buffer at a concentration from about 5 mM to about 50 mM and at a pH 5.0 to 7.0;
- (2) acetate buffer at a concentration from about 5 mM to about 50 mM and at a pH 4.5 to 6.0;
- (3) citrate buffer at a concentration from about 5 mM to about 50 mM and at a pH 4.5 to 6.0;
- (4) phosphate buffer at a concentration from about 5 mM to about 50 mM and at a pH 6.5 to 7.5;
- (5) tris buffer at a concentration from about 5 mM to about 50 mM and at a pH 6.5 to 7.5; or
- (6) Succinate buffer at a concentration from about 5 mM to about 50 mM and at a pH 4.5 to 6.0.

[0011] In some embodiments, the pharmaceutically acceptable protein agent formulation is a high concentration formulation (e.g., at a concentration greater than 200 mg/mL) of protein agents with reduced viscosity and increased stability, including therapeutic agents. In an embodiment, the pharmaceutically acceptable protein agent formulation is a liquid formulation having a viscosity less than 100 cP, preferably less than 50 cP, as measured at 20 °C. As described in the following Examples, the viscosity is measured by VROC® initium one plus viscometer. In general, these formulations are suitable for parenteral administration, such as subcutaneous, intramuscular, or

intravenous administration (e.g., by injection, such as subcutaneous, intramuscular, or intravenous injection), and in many embodiments by parenteral administration that does not involve infusion and/or that is other than intravenous administration. In particular, in many embodiments, the present disclosure provides formulations suitable for administration by intravenous (IV),
5 subcutaneous (SC) and/or intramuscular (IM) injection. In many embodiments, provided formulations are suitable for administration via 18–32-gauge needles.

[0012] In some embodiments, the pharmaceutically acceptable protein agent formulation is in aqueous liquid form or a non-aqueous liquid form. In other embodiments, the pharmaceutically acceptable protein agent formulation can be lyophilized and reconstituted immediately prior to use.

10 **[0013]** In some embodiments, the pharmaceutically acceptable protein agent formulation has good stability during storage. The presence of the viscosity-reducing and stabilizing agent may significantly reduce the aggregation of the protein agent, for example, during preparation and/or storage.

[0014] Typically, the formulations are aqueous formulations. Most commercially available
15 mAb products administered by SC or IM injection are formulated in aqueous buffers, such as a phosphate, succinate or L-histidine buffer, with the addition of excipients and/or surfactants, such as maltose, mannitol, sucrose, lactose, trehalose, lactic acid, proline, arginine, EDTA, sorbitol, POLOXAMER® or POLYSORBATE® 80 (PS80 sorbitan monolaurate). These compounds act to improve overall solution stability.

20 **[0015]** In an embodiment, the protein agent is a therapeutic protein. The term “protein agent” also includes peptide or polypeptide. In another embodiment, the protein agent is an immunoglobulin, an antibody or antigen binding fragment thereof, or fusion protein, or antibody-drug conjugate (ADC), preferably a monoclonal antibody or antigen binding fragment thereof, for example, but not limited to Pembrolizumab, Adalimumab, Trastuzumab, Aflibercept, or
25 Rituximab.

[0016] In an embodiment, the protein agent is a fusion protein. In another embodiment, the protein agent is an antibody-drug conjugate (ADC).

[0017] In an embodiment, the pharmaceutically acceptable protein agent formulation further comprises other excipients or additives, for example, selected from: aggregation-reducing agents,

sugars or sugar alcohols, polysaccharides, stabilizers, hyaluronidase, buffering agents, preservatives, carriers, antioxidants, chelating agents, natural or synthetic polymers, cryoprotectants, lyoprotectants, surfactants, bulking agents, acidifying agents, ingredients to reduce injection site discomfort, antifoaming agents, alkalizing agents, vehicles, aggregation inhibitors, solubilizing agents, tonicity modifiers, or stabilizing agents and combinations thereof. It should be appreciated that the skilled person in the art can select suitable compounds or compositions for the other excipients or additives based on the desired properties of the final formulation.

[0018] In an embodiment, the aggregation-reducing agents are selected from the group consisting of nicotinic acid, caffeine citrate, caffeine nicotinate, caffeine, octyl- β -D-glucopyranoside, and n-dodecyl-P-D-maltoside and optionally in combination with one or more of arginine, tryptophan, histidine, proline, cysteine, β -alanine, Potassium Glutamate, Arginine Ethylester, lysine, aspartic acid, glutamic acid, glycine, DTPA (diethylenetriaminepentaacetic acid), EGTA (aminopolycarboxylic acid), EDTA (Ethylenediaminetetraacetic acid), hydroxy propyl beta (HP-Beta) cyclodextrins, hydroxy propyl gamma (HP-Gamma) cyclodextrins, sulfo-butyl ether (SBE) cyclodextrins, TMAO (trimethylamine N-oxide), trehalose, ethylene glycol, betaine, xylitol, sorbitol, 6-(N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino)hexanoic acid (NBD-X), methyl acetyl phosphate (MAP), citraconic anhydride, pyrophosphate and citrate.

[0019] In an embodiment, the tonicity modifiers are selected from the group consisting of arginine, cysteine, histidine, glycine, alkali salts such as sodium chloride, potassium chloride, sodium citrate, saccharides such as sucrose, glucose, dextrose, glycerin or mannitol and combinations thereof.

[0020] In an embodiment, the antioxidants are selected from the group consisting of glycine, lysine, EDTA, DTPA, sorbitol, mannitol, ascorbic acid, ascorbyl palmitate, butylated hydroxyanisole, butylated hydroxytoluene, hypophosphorous acid, monothioglycerol, propyl gallate, sodium bisulfite, sodium formaldehyde sulfoxylate, sodium metabisulfite, sodium thiosulfate, sulfur dioxide, tocopherol and combinations thereof.

[0021] In an embodiment, the lyoprotectants are selected from the group consisting of sucrose, lactose, trehalose, dextran, erythritol, arabitol, xylitol, sorbitol, maltose, lactulose, maltulose, glucitol, maltitol, lactitol, isomaltulose and mannitol; amino acids, such as arginine or histidine or

proline or glycine; lyotropic salts, such as magnesium sulfate; polyols, such as propylene glycol, glycerol, poly(ethylene glycol), or polypropylene glycol; gelatin, dextrans, modified starch, carboxymethyl cellulose and combinations thereof.

[0022] In some embodiments, the concentration of a protein agent in a high concentration, low-viscosity formulation may be at least about 10 mg/mL, 25 mg/mL, 50 mg/mL, 75 mg/mL, 100 mg/mL, 150 mg/mL, 200 mg/mL, 250 mg/mL, or 300 mg/mL. In some embodiments, the concentration may be within a range bounded by a lower limit and an upper limit, the upper limit being larger than the lower limit. In some embodiments, the lower limit may be about 10 mg/mL, about 25 mg/mL, about 50 mg/mL, about 75 mg/mL, about 100 mg/mL, about 150 mg/mL, about 200 mg/mL or about 250 mg/mL. In some embodiments, the upper limit may be about 200 mg/mL, about 250 mg/mL or about 300 mg/mL. In some embodiments, the range may be about 10 mg/mL to about 300 mg/mL. In some embodiments, the range may be about 10 mg/mL to about 250 mg/mL. In some embodiments, the range may be about 10 mg/mL to about 200 mg/mL. In some embodiments, the range may be about 25 mg/mL to about 300 mg/mL. In some embodiments, the range may be about 25 mg/mL to about 250 mg/mL. In some embodiments, the range may be about 25 mg/mL to about 200 mg/mL. In some embodiments, the range may be about 50 mg/mL to about 300 mg/mL. In some embodiments, the range may be about 50 mg/mL to about 250 mg/mL. In some embodiments, the range may be about 50 mg/mL to about 200 mg/mL. In some embodiments, the range may be about 75 mg/mL to about 300 mg/mL. In some embodiments, the range may be about 75 mg/mL to about 250 mg/mL. In some embodiments, the range may be about 75 mg/mL to about 200 mg/mL. In some embodiments, the range may be about 100 mg/mL to about 300 mg/mL. In some embodiments, the range may be about 100 mg/mL to about 250 mg/mL. In some embodiments, the range may be about 100 mg/mL to about 200 mg/mL. In some embodiments, the range may be about 150 mg/mL to about 300 mg/mL. In some embodiments, the range may be about 150 mg/mL to about 250 mg/mL. In some embodiments, the range may be about 150 mg/mL to about 200 mg/mL. In some embodiments, the range may be about 200 mg/mL to about 300 mg/mL. In some embodiments, the range may be about 200 mg/mL to about 250 mg/mL. In some embodiments the range may be about 250 mg/mL to about 300 mg/mL.

[0023] In a third aspect, the present disclosure relates to a method for reducing viscosity and increasing the stability of a formulation comprising a protein agent, comprising: adding a

viscosity-reducing amount of any one of the viscosity-reducing and stabilizing liquid formulations of the first aspect to the formulation comprising one or more protein agents, wherein the final formulation has a viscosity less than 100 cP, preferably less than 50 cP, as measured at 20 °C.

[0024] In an embodiment, the protein agent is a therapeutic protein. The term “protein agent” also includes peptide or polypeptide. In another embodiment, the protein agent is an immunoglobulin, an antibody or antigen binding fragment thereof, or fusion protein, or antibody-drug conjugate (ADC), preferably a monoclonal antibody or antigen binding fragment thereof, for example, but not limited to Pembrolizumab, Adalimumab, Trastuzumab, Aflibercept, or Rituximab. In a further embodiment, the protein agent is a fusion protein. In another embodiment, the protein agent is an antibody-drug conjugate (ADC).

[0025] In an embodiment, the protein agent is at a concentration from about 10 mg/mL to about 300 mg/mL in the formulation, for example, about 100 mg/mL to about 300 mg/mL, for example, about 100 mg/mL, about 150 mg/mL, about 200 mg/mL, about 250 mg/mL, or about 300 mg/mL.

[0026] In an embodiment, the formulation is administrated by parenteral administration, for example, subcutaneous, intramuscular, or intravenous administration.

[0027] In a fourth aspect, the present disclosure relates to a method for preparing a liquid formulation comprising a protein agent with high concentration of a protein agent, high stability and low viscosity, comprising:

- (i) dissolving the protein agent in a buffer; and
- (ii) adding any one of the viscosity-reducing and stabilizing liquid formulations of the first aspect; wherein the liquid formulation comprising a high concentration of protein agent has a viscosity less than 100 cP as measured at 20 °C.

[0028] In an embodiment, the buffer is selected from histidine buffer, acetate buffer, citrate buffer, phosphate buffer, tris buffer, succinate buffer, or any combination thereof. For example, the buffer is selected from:

- (1) histidine buffer at a concentration from about 5 mM to about 50 mM and at a pH 5.0 to 7.0;
- (2) acetate buffer at a concentration from about 5 mM to about 50 mM and at a pH 4.5 to 6.0;

- (3) citrate buffer at a concentration from about 5 mM to about 50 mM and at a pH 4.5 to 6.0;
- (4) phosphate buffer at a concentration from about 5 mM to about 50 mM and at a pH 6.5 to 7.5;
- (5) tris buffer at a concentration from about 5 mM to about 50 mM and at a pH 6.5 to 7.5; or
- (6) Succinate buffer at a concentration from about 5 mM to about 50 mM and at a pH 4.5 to 6.0.

5 **[0029]** In an embodiment, the protein agent is a therapeutic protein. The term “protein agent” also includes peptide or polypeptide. In another embodiment, the protein agent is an immunoglobulin, an antibody or antigen binding fragment thereof, or fusion protein, or antibody-drug conjugate (ADC), preferably a monoclonal antibody or antigen binding fragment thereof, for example, but not limited to Pembrolizumab, Adalimumab, Trastuzumab, Aflibercept, or
10 Rituximab. In a further embodiment, the protein agent is a fusion protein or an antibody-drug conjugate (ADC).

[0030] In some embodiments, the protein agent is present at a concentration within a range of about 10 mg/mL to about 300 mg/mL. Typically, the liquid protein agent formulation prepared according to this method is characterized by a viscosity that is lower than that of an otherwise
15 comparable formulation of the protein agent lacking the viscosity-reducing and stabilizing liquid formulation.

[0031] In some embodiments, the use of a viscosity-reducing and stabilizing liquid formulation reduces the viscosity of a protein agent formulation to a viscosity that, when measured at 20°C, may be less than 100 cP, preferably less than 50 cP, for example, about 95 cP, 90 cP, 85
20 cP, 80 cP, 75 cP, 70 cP, 65 cP, 60 cP, 55 cP, 50 cP, about 45 cP, 40 cP, 35 cP, 30 cP, 25 cP, 20 cP, 15 cP, or lower, or any value therein, for example, any value in the range of 0 to 100 cP, or preferably any value in the range of 0 to 50 cP.

[0032] In an embodiment, the liquid formulation comprising a protein agent is administrated by parenteral administration, for example, subcutaneous, intramuscular, or intravenous
25 administration.

[0033] In an embodiment, the liquid formulation comprising a protein agent has reduced protein aggregation during preparation and storage.

[0034] In a fifth aspect, the present disclosure relates to use of the liquid formulation comprising a protein agent for preventing or treating diseases in a subject.

[0035] In a sixth aspect, the present disclosure relates to use of any one of the viscosity-reducing and stabilizing liquid formulation as described in the first aspect for reducing viscosity and increasing the stability of a formulation comprising a protein agent at a high concentration, for example, about 10 mg/mL to about 300 mg/mL, preferably from about 100 mg/mL to about 300 mg/mL.

[0036] In a seventh aspect, the present disclosure relates to use of any one of the viscosity-reducing and stabilizing liquid formulation as described in the first aspect for preparing a liquid formulation comprising a protein agent with high concentration of a protein agent, high stability and low viscosity.

[0037] The foregoing and other features and advantages of the disclosure will become more apparent from the following detailed description of several embodiments.

DETAILED DESCRIPTION OF INVENTION

[0038] While the present disclosure may be embodied in many different forms, disclosed herein are specific illustrative embodiments thereof that exemplify the principles of the disclosure. It should be emphasized that the present disclosure is not limited to the specific embodiments illustrated. Moreover, any section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described.

[0039] DEFINITIONS

[0040] In order to better understand the disclosure, the definitions and explanations of the relevant terms are provided as follows.

[0041] Unless otherwise defined herein, scientific and technical terms used in connection with the present disclosure shall have the meanings that are commonly understood by those of ordinary skill in the art. Further, unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular. More specifically, as used in this specification and the appended claims, the singular forms “a,” “an” and “the” include plural referents unless the context clearly dictates otherwise. In this application, the use of “or” means “and/or” unless stated otherwise.

[0042] Throughout this disclosure, unless the context requires otherwise, the words “comprise”, “comprises” and “comprising” will be understood to imply the inclusion of a stated step or element or group of steps or elements but not the exclusion of any other step or element or group of steps or elements. By “consisting of” is meant including, and limited to, whatever follows the phrase “consisting of”. Thus, the phrase “consisting of” indicates that the listed elements are required or mandatory, and that no other elements may be present. By “consisting essentially of” is meant including any elements listed after the phrase, and limited to other elements that do not interfere with or contribute to the activity or action specified in the disclosure for the listed elements. Thus, the phrase “consisting essentially of” indicates that the listed elements are required or mandatory, but that other elements are optional and may or may not be present depending upon whether or not they affect the activity or action of the listed elements.

[0043] As used herein, the term “about” or “approximately” refers to a quantity, level, value, number, frequency, percentage, dimension, size, amount, weight, or length that varies by as much as 30, 25, 20, 15, 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1% to a reference quantity, level, value, number, frequency, percentage, dimension, size, amount, weight or length. In particular embodiments, the terms “about” or “approximately” when preceding a numerical value indicates the value plus or minus a range of 15%, 10%, 5%, or 1%. In general, those skilled in the art, familiar with the context, will appreciate the relevant degree of variance encompassed by “about” in that context.

[0044] The term “viscosity,” as generally used herein, refers to the resistance of a substance (typically a liquid) to flow. Viscosity is related to the concept of shear force; it can be understood as the effect of different layers of the fluid exerting shearing force on each other, or on other surfaces, as they move against each other. Viscosity can be “kinematic” or “absolute”. There are several measures of viscosity. The units of viscosity are Ns/m, also known as Pascal-seconds (Pa-s). Viscosity may be measured by using, for example, a viscometer at a given shear rate or multiple shear rates. An “extrapolated zero-shear” viscosity can be determined by creating a best fit line of the four highest-shear points on a plot of absolute viscosity versus shear rate, and linearly extrapolating viscosity back to zero-shear. Alternatively, for a Newtonian fluid, viscosity can be determined by averaging viscosity values at multiple shear rates. Viscosity can also be measured using a microfluidic viscometer at single or multiple shear rates (also called flow rates), wherein

absolute viscosity is derived from a change in pressure as a liquid flow through a channel. Viscosity equals shear stress over shear rate.

[0045] As generally used herein, the term "absolute viscosity" is sometimes called "dynamic viscosity" or "simple viscosity," is the product of kinematic viscosity and fluid density. Absolute
5 viscosity is expressed in units of centipoise (cP). The SI unit of absolute viscosity is the milli Pascal-second (mPa-s), where 1 cP = 1 mPa-s.

[0046] As used herein, the term "viscosity-reducing agent" refers to a compound or a composition which acts to reduce the viscosity of a solution relative to the viscosity of a solution absent of a viscosity-reducing agent. The viscosity-reducing agent may be a single compound, or
10 may be a mixture of two or more compounds. When the viscosity-reducing agent is a mixture of two or more compounds, the listed concentration refers to each individual agent, unless otherwise specified. Particularly, when the viscosity-reducing agent is a mixture of two or more compounds, it is referred to as "viscosity-reducing formulation" in the context of the disclosure. The viscosity-reducing formulation of the present disclosure has a capacity of stabilizing a liquid formulation of
15 a protein agent, and thus it is also known as "the viscosity-reducing and stabilizing formulation".

[0047] As used herein, the term "administration" typically refers to the administration of a composition to a subject or system to achieve delivery of an agent that is, or is included in, the composition. Those of ordinary skill in the art will be aware of a variety of routes that may, in appropriate circumstances, be utilized for administration to a subject, for example a human. For
20 example, in some embodiments, administration may be ocular, oral, parenteral, topical, etc. In some particular embodiments, administration may be bronchial (e.g., by bronchial instillation), buccal, dermal (which may be or comprise, for example, one or more of topical to the dermis, intradermal, interdermal, transdermal, etc.), enteral, intra-arterial, intradermal, intragastric, intramedullary, intramuscular, intranasal, intraperitoneal, intrathecal, intravenous, intraventricular,
25 within a specific organ (e.g., intrahepatic), mucosal, nasal, oral, rectal, subcutaneous, sublingual, topical, tracheal (e.g., by intratracheal instillation), vaginal, vitreal, etc. In some embodiments, administration may involve only a single dose. In some embodiments, administration may involve application of a fixed number of doses. In some embodiments, administration may involve dosing that is intermittent (e.g., a plurality of doses separated in time) and/or periodic (e.g., individual

doses separated by a common period of time) dosing. In some embodiments, administration may involve continuous dosing (e.g., perfusion) for at least a selected period of time.

[0048] In general, the term "agent", as used herein, may be used to refer to a compound or entity of any chemical class including, for example, a polypeptide, nucleic acid, saccharide, lipid, small molecule, metal, or combination or complex thereof. In appropriate circumstances, as will be clear from context to those skilled in the art, the term may be utilized to refer to an entity that is or comprises a cell or organism, or a fraction, extract, or component thereof. Alternatively, or additionally, as context will make clear, the term may be used to refer to a natural product in that it is found in and/or is obtained from nature. In some instances, again as will be clear from context, the term may be used to refer to one or more entities that are man-made in that they are designed, engineered, and/or produced through action of the hand of man and/or are not found in nature. In some embodiments, an agent may be utilized in isolated or pure form; in some embodiments, an agent may be utilized in crude form. In some embodiments, potential agents may be provided as collections or libraries, for example that may be screened to identify or characterize active agents within them. In some cases, the term "agent" may refer to a compound or entity that is or comprises a polymer; in some cases, the term may refer to a compound or entity that comprises one or more polymeric moieties. In some embodiments, the term "agent" may refer to a compound or entity that is not a polymer and/or is substantially free of any polymer and/or of one or more particular polymeric moieties. In some embodiments, the term may refer to a compound or entity that lacks or is substantially free of any polymeric moiety.

[0049] The term "protein aggregation," as generally used herein, refers to a biological phenomenon in which mis-folded proteins aggregate (i.e., accumulate and clump together) either intra- or extracellularly. These protein aggregates are often correlated with diseases. In fact, protein aggregates have been implicated in a wide variety of disease known as amyloidosis, including ALS, Alzheimer's, Parkinson's and prion disease. This aggregation can be 'native,' in which the protein structure is maintained and the aggregation is largely reversible, or 'non-native,' where denaturation and structural changes mean this effect is largely irreversible. Aggregates may continue to grow and form over a wide size range, including up to and beyond the formation of visible particles, and ultimately this leads to precipitation.

[0050] The term "protein aggregation preventer/aggregation inhibitor," as generally used herein, means an inhibitor which is capable of preventing formation of additional protein aggregate in a protein-containing solution. Thus, inhibition can encompass preventing an increase in the amount of protein aggregate in a protein formulation or solution. Prevention is measured by comparing the amount of aggregate present in a protein-containing solution that comprises at least one inhibitor of insoluble aggregate formation with the amount of aggregate present in a protein-containing solution that does not comprise at least one inhibitor of insoluble aggregate formation and is measured by either using Size-Exclusion chromatography or dynamic light scattering techniques.

10 [0051] The term "aggregation-reducing agent," as generally used herein, means an agent for decreasing the amount of protein aggregate in a protein-containing solution. Thus, reducing can encompass decreasing the amount of protein aggregate in a protein formulation or solution. Decreasing is measured by comparing the amount of aggregate present in a protein-containing solution that comprises at least one reducer of insoluble aggregate formation with the amount of aggregate present in a protein-containing solution that does not comprise at least one reducer of insoluble aggregate formation and is measured by either using Size-Exclusion chromatography or dynamic light scattering techniques.

[0052] As generally used herein, the term "formulation" refers to a combination of a therapeutic protein (e.g., a therapeutic antibody or antibody fragments thereof) and one or more ingredients or excipients. Examples of excipients are described in the Handbook of Pharmaceutical Excipients, published jointly by the American Pharmaceutical Association and the Pharmaceutical Society of Great Britain. As used herein, "formulations" include "Therapeutic Protein formulations." Furthermore, "formulations" include "Therapeutic High Protein Concentration" and "Antibody or fragments thereof formulations" and "monoclonal antibody formulations."

25 [0053] As generally used herein, the term "fusion protein" refers to a protein that is created from two different genes encoding for two separate proteins. Fusion proteins are generally produced through recombinant DNA techniques known to those skilled in the art. Two proteins (or protein fragments) are fused together covalently and exhibit properties from both parent proteins.

[0054] As used herein, the term "liquid formulation" refers to a protein formulation that is either supplied in an acceptable pharmaceutical diluent or one that is reconstituted in an acceptable pharmaceutical diluent prior to administration to the patient.

[0055] As generally used herein, the term "pharmaceutically acceptable salts" refers to salts prepared from pharmaceutically acceptable non-toxic acids and bases, including inorganic acids and bases, and organic acids and bases. Suitable non-toxic acids include inorganic and organic acids such as acetic, benzenesulfonic, benzoic, camphorsulfonic, citric, ethanesulfonic, fumaric, gluconic, glutamic, hydrobromic, hydrochloric, isethionic, lactic, maleic, malic, mandelic, methanesulfonic, mucic, nitric, pamoic, pantothenic, phosphoric, succinic, sulfuric, tartaric acid, p-toluenesulfonic acid and the like. Suitable positively charged counterions include sodium, potassium, lithium, calcium and magnesium.

[0056] As used herein, the term "pharmaceutical composition" refers to a composition in which an active agent is formulated together with one or more pharmaceutically acceptable carriers. In some embodiments, the active agent is present in unit dose amount appropriate for administration in a therapeutic regimen that shows a statistically significant probability of achieving a predetermined therapeutic effect when administered to a relevant population. In some embodiments, a pharmaceutical composition may be specially formulated for administration in solid or liquid form, including those adapted for the following: oral administration, for example, drenches (aqueous or non-aqueous solutions or suspensions), tablets, e.g., those targeted for buccal, sublingual, and systemic absorption, boluses, powders, granules, pastes for application to the tongue; parenteral administration, for example, by subcutaneous, intramuscular, intravenous or epidural injection as, for example, a sterile solution or suspension, or sustained-release formulation; topical application, for example, as a cream, ointment, or a controlled-release patch or spray applied to the skin, lungs, or oral cavity; intravaginally or intrarectally, for example, as a pessary, cream, or foam; sublingually; ocularly; transdermally; or nasally, pulmonary, and to other mucosal surfaces.

[0057] As used herein, the term "pharmaceutically acceptable carrier" means a pharmaceutically-acceptable material, composition or vehicle, such as a liquid or solid filler, diluent, excipient, or solvent encapsulating material, involved in carrying or transporting the subject compound from one organ, or portion of the body, to another organ, or portion of the body.

Each carrier must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not injurious to the patient. Some examples of materials which can serve as pharmaceutically-acceptable carriers include: sugars, such as lactose, glucose and sucrose; starches, such as corn starch and potato starch; cellulose, and its derivatives, such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; powdered tragacanth; malt; gelatin; talc; excipients, such as cocoa butter and suppository waxes; oils, such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; glycols, such as propylene glycol; polyols, such as glycerin, sorbitol, mannitol and polyethylene glycol; esters, such as ethyl oleate and ethyl laurate; agar; buffering agents, such as magnesium hydroxide and aluminum hydroxide; alginic acid; pyrogen-free water; isotonic saline; Ringer's solution; ethyl alcohol; pH buffered solutions; polyesters, polycarbonates and/or poly anhydrides; and other non-toxic compatible substances employed in pharmaceutical formulations.

[0058] As generally used herein, the term "stability" or "physical stability" refers to the ability of a protein formulation to resist physical deterioration, such as aggregation. A formulation that is physically stable forms only an acceptable percentage of irreversible aggregates (e.g., dimers, trimers, or other aggregates) of the bioactive protein agent. The presence of aggregates may be assessed in a number of ways, including by measuring the average particle size of the proteins in the formulation by means of dynamic light scattering. A formulation is considered physically stable if less than about 5% irreversible aggregates are formed after 24 months at 4°C. Acceptable levels of aggregated contaminants ideally would be less than about 2%. Level as low as about 0.2% is achievable, although approximately 1% is more typical.

[0059] As generally used herein, the term "plasticizing" refers to the use of a plasticizer, e.g., lanolin, ethanol, to make a formulation comprising a therapeutic protein in a solution that becomes viscous after it is injected subcutaneously, forming a matrix. The resulting high viscosity matrix is adhesive, biodegradable and biocompatible. The therapeutic protein is then released in a controlled manner from the matrix.

[0060] As generally used herein, the term "reduced-viscosity formulation (of a protein agent)" refers to a liquid formulation with a high concentration of a high-molecular-weight protein, such as a mAb, or a low-molecular-weight protein that is modified by the presence of one or more

additives to lower the viscosity, as compared to a corresponding formulation that does not contain the viscosity-reducing additive(s).

[0061] The term “drug” as used herein refers to any cytotoxic molecule which has an antitumor effect and at least one substituted group or a partial structure allowing connection to a linker structure. The drug may kill cancer cells and/or inhibit growth, proliferation, or metastasis of cancer cells, thereby reducing, alleviating, or eliminating one or more symptoms of a disease or disorder.

[0062] An "immunoglobulin " or "native antibody" is a tetrameric glycoprotein. In a naturally-occurring immunoglobulin, each tetramer is composed of two identical pairs of polypeptide chains, each pair having one "light" (about 25 kDa) and one "heavy" chain (about 50-70 kDa). The amino-terminal portion of each chain includes a "variable" ("V") region of about 100 to 110 or more amino acids which are primarily responsible for antigen recognition. The carboxy-terminal portion of each chain defines an invariable region primarily responsible for effector function. The four chains are arranged in a classic "Y" model. The bottom "leg" of the "Y" is called the Fc region and is used to anchor the antibody within cell membranes, and is also used to bind macrophage cells and thus activate complementation. The two "arms" at the top of the "Y" are called Fab regions. Each Fab region contains an invariable region (at the junction of the Fab and the Fc regions) and a variable region (which extends to the tip of the "Y" or Fc region). Each variable region contains identical antigen-binding sites (at regions within the variable regions called "hypervariable" regions) at each tip of the "Y". The term "hypervariable" region refers to amino acid residues from a complementarity-determining region or CDR (i.e., residues 24-34 (CDRL1), 50-56 (CDRL2) and 89-97 (CDRL3) in the light chain variable domain and 31-35 (CDRH1), 50-65 (CDRH2) and 95- 102 (CDRH3) in the heavy chain variable domain as described by Kabat et al., Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991)). "Framework" or FR residues are the remaining variable region residues other than the hypervariable region residues. Each Fab region has one antigen-binding site, and the complete antibody molecule therefore has two antigen-binding sites (i.e., is "bivalent"). The two antigen-binding sites on a naturally occurring antibody are identical to each other, and therefore the antibody is specific for one antigen (i.e., is "monospecific").

[0063] Immunoglobulins can be assigned to different classes depending on the amino acid sequence of the invariable domain of their heavy chains. Heavy chains are classified as mu (μ), delta (Δ), gamma (γ), alpha (α), and epsilon (ϵ), and define the antibody's isotype as IgM, IgD, IgG, IgA, and IgE, respectively. Typically, IgG, IgE and IgD occur as monomers, while IgA can occur as not only a monomer, but also a dimer or trimer, and IgM can occur as a pentamer. Several of the above may be further divided into subclasses or isotypes, e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2. Different isotypes have different effector functions; for example, IgG1 and IgG3 isotypes have antibody-dependent cellular cytotoxicity (ADCC) activities. Human light chains are classified as kappa (κ) and lambda (λ) light chains. Within light and heavy chains, the variable and invariable regions are joined by a "J" region of about 12 or more amino acids, with the heavy chain additionally encompassing a "D" region of about 10 more amino acids (See generally, Fundamental Immunology, Ch. 7 (Paul, W., ed., 2nd ed. Raven Press, N.Y. (1989)).

[0064] "Antibody fragments" comprise a portion of a full-length antibody, generally the antigen binding or variable region thereof. Examples of antibody fragments include Fab, Fab', F(ab')₂, and Fv fragments; diabodies; linear antibodies; minibodies (Olafsen et al. (2004) Protein Eng. Design & Sel. 17(4):315-323), fragments produced by a Fab expression library, anti-idiotypic (anti-Id) antibodies, CDR (complementary determining region), and epitope -binding fragments of any described herein which immunospecifically bind to cancer cell antigens, viral antigens or microbial antigens, single-chain antibody molecules; and multispecific antibodies formed from antibody fragments.

[0065] The following examples are provided to better illustrate the claimed invention and are not to be interpreted as limiting the scope of the invention. All specific compositions, materials, and methods described below, in whole or in part, fall within the scope of the present invention. These specific compositions, materials, and methods are not intended to limit the invention, but merely to illustrate specific embodiments falling within the scope of the invention. One skilled in the art may develop equivalent compositions, materials, and methods without the exercise of inventive capacity and without departing from the scope of the invention. It will be understood that many variations can be made in the procedures herein described while still remaining within the bounds of the present invention. It is the intention of the inventors that such variations are included within the scope of the invention.

EXAMPLES

[0066] Now the present disclosure will be illustrated in detail with reference to the following examples. However, those skilled in the art should understand that, the following examples are only provided for illustration, but not intended to limit the present disclosure in any way.

5 **Example 1: Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab solutions in various buffers at 20°C.**

[0067] This example tested the viscosity reducing effect of viscosity-reducing and stabilizing formulations of the present application on Pembrolizumab solutions.

[0068] **Materials and Methods**

10 [0069] Pembrolizumab (Keytruda®) is a commercially available mAb. In this example, it was produced by WuXi Biologics based on its sequence sourced from Drug Bank (DB09037). The recombinant cell culture fermentation was harvested by centrifugation, and the resulting filtrate pool was loaded onto a Protein A column. The target protein was eluted at pH 3.8 and subsequently neutralized to pH 5.5 using 1 M Tris base. The eluate then underwent depth filtration and was
15 passed through a 0.2 µm filter. The intermediate filtration pool was loaded onto an AEX (Anion Exchange) column in flow-through mode. Following this step, the AEX flow-through pool was further processed on a CEX (Cation Exchange) column, and the target protein was eluted using a linear gradient elution. The CEX eluate was subsequently concentrated to a concentration of 40 g/L and diafiltrated over six dia-volumes to exchange the buffer to a final composition of a buffer
20 concentration within 5-50 mM using histidine, acetate, citrate, phosphate, tris or succinate buffer system at a pH between 4.5 and 7.5, respectively. Through formulation exchange, Pembrolizumab was transferred into test groups, encompassing with the component concentration varied from 30 mM to 300 mM, incorporating one of the viscosity-reducing and stabilizing formulations, shown in Tables 1-18. Furthermore, there was a control group (i.e., positive control) comprising 25 mM
25 phosphate buffer at pH 6.0, with 81.2 mM Nicotinic acid and 29.4 mM Tryptophan (matching the lead formulation, 25 mM phosphate buffer at pH 6.0 along with 10 mg/mL Nicotinic acid (acid form) and 6 mg/mL Tryptophan, from Examples 14 and 16-21 in WO2018211517). An additional control group solely consisted of MilliQ water and the protein as blank control. The formulation containing Pembrolizumab was subsequently concentrated to 100-300 mg/mL (e.g., 100, 200, or

300 mg/mL) using an Eppendorf centrifuge with a concentration variation of 3%. To ascertain Pembrolizumab's concentration in the groups, absorbance at 280 nm combined with SE-UPLC was gauged against corresponding buffers containing a viscosity-reducing and stabilizing formulation for excipient-containing samples, and absorbance at 280 nm was measured for the protein solution without a viscosity-reducing and stabilizing formulation. For Pembrolizumab without excipients, the buffer alone (i.e., devoid of excipients) served as a blank for protein concentration calculation. The extinction coefficient was measured at $1.42 \text{ (mg/mL)}^{-1} \cdot \text{cm}^{-1}$.

[0070] The viscosity of samples was measured by VROC® initium one plus viscometer (Rheosense) at 20°C. For samples with a viscosity exceeding 1000 cP, viscosity was measured using a TA rheometer.

[0071] As shown in Tables 1-18, the data demonstrated the viscosity-reducing efficacy of the viscosity-reducing and stabilizing formulations of the present application on Pembrolizumab in different buffers: histidine (pH 5.0 to 7.0), acetate (pH 4.5 to 6.0), citrate (pH 4.5 to 6.0), phosphate (pH 6.5 to 7.5), Tris (pH 6.5 to 7.5), and succinate (pH 4.5 to 6.0) buffer. As for Pembrolizumab at a concentration from 100 to 300 mg/mL, the tested viscosity-reducing and stabilizing formulations exhibited superior viscosity reduction when compared to the reference lead formulation from WO2018211517 and excipient-free samples.

Table 1 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 5 mM Histidine buffer, at pH 5.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	458.5
300	30 mM Histidine and 30 mM Niacin	549.6
300	30 mM Meglumine and 30 mM Niacin	357.5
300	30 mM Lysine and 30 mM Niacin	405.6
300	30 mM Arginine·HCl and 30 mM Niacinamide	154.6
300	30 mM Histidine and 30 mM Niacinamide	239.3
300	30 mM Meglumine and 30 mM Niacinamide	389.7
300	30 mM Lysine·HCl and 30 mM Niacinamide	196.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	30 mM Arginine and 30 mM Niacin	39.2
200	30 mM Histidine and 30 mM Niacin	47.8
200	30 mM Meglumine and 30 mM Niacin	44.8
200	30 mM Lysine and 30 mM Niacin	35.6
200	30 mM Arginine·HCl and 30 mM Niacinamide	28.4
200	30 mM Histidine and 30 mM Niacinamide	30.4
200	30 mM Meglumine and 30 mM Niacinamide	46.5
200	30 mM Lysine·HCl and 30 mM Niacinamide	37.4
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	30 mM Arginine and 30 mM Niacin	6.9
100	30 mM Histidine and 30 mM Niacin	7.5
100	30 mM Meglumine and 30 mM Niacin	7.7
100	30 mM Lysine and 30 mM Niacin	5.9
100	30 mM Arginine·HCl and 30 mM Niacinamide	3.5
100	30 mM Histidine and 30 mM Niacinamide	4.5
100	30 mM Meglumine and 30 mM Niacinamide	7.8
100	30 mM Lysine·HCl and 30 mM Niacinamide	4.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Table 2 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 20 mM Histidine buffer, pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	364.8
300	140 mM Histidine and 140 mM Niacin	412.5
300	140 mM Meglumine and 140 mM Niacin	308.9
300	140 mM Lysine and 140 mM Niacin	367.8
300	70 mM Arginine·HCl and 140 mM Niacinamide	88.9
300	140 mM Histidine and 140 mM Niacinamide	116.4
300	140 mM Meglumine and 140 mM Niacinamide	230.8
300	70 mM Lysine·HCl and 140 mM Niacinamide	147.9
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	140 mM Arginine and 140 mM Niacin	33.2
200	140 mM Histidine and 140 mM Niacin	35.0
200	140 mM Meglumine and 140 mM Niacin	31.8
200	140 mM Lysine and 140 mM Niacin	34.5
200	70 mM Arginine·HCl and 140 mM Niacinamide	18.0
200	140 mM Histidine and 140 mM Niacinamide	19.8
200	140 mM Meglumine and 140 mM Niacinamide	30.3
200	70 mM Lysine·HCl and 140 mM Niacinamide	24.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	140 mM Arginine and 140 mM Niacin	7.2
100	140 mM Histidine and 140 mM Niacin	7.8
100	140 mM Meglumine and 140 mM Niacin	7.3
100	140 mM Lysine and 140 mM Niacin	6.7
100	70 mM Arginine·HCl and 140 mM Niacinamide	4.6
100	140 mM Histidine and 140 mM Niacinamide	4.8
100	140 mM Meglumine and 140 mM Niacinamide	6.8
100	70 mM Lysine·HCl and 140 mM Niacinamide	5.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Table 3 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 50 mM Histidine buffer, at pH 7.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	273.6
300	300 mM Histidine and 300 mM Niacin	309.4
300	300 mM Meglumine and 300 mM Niacin	231.7
300	300 mM Lysine and 300 mM Niacin	276.0
300	140 mM Arginine·HCl and 300 mM Niacinamide	66.7
300	300 mM Histidine and 300 mM Niacinamide	87.3
300	300 mM Meglumine and 300 mM Niacinamide	173.1
300	140 mM Lysine·HCl and 300 mM Niacinamide	110.9
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	300 mM Arginine and 300 mM Niacin	24.9
200	300 mM Histidine and 300 mM Niacin	26.3
200	300 mM Meglumine and 300 mM Niacin	23.9
200	300 mM Lysine and 300 mM Niacin	25.9
200	140 mM Arginine·HCl and 300 mM Niacinamide	13.5
200	300 mM Histidine and 300 mM Niacinamide	14.8
200	300 mM Meglumine and 300 mM Niacinamide	22.7
200	140 mM Lysine·HCl and 300 mM Niacinamide	18.6
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	300 mM Arginine and 300 mM Niacin	5.4
100	300 mM Histidine and 300 mM Niacin	5.8
100	300 mM Meglumine and 300 mM Niacin	5.5
100	300 mM Lysine and 300 mM Niacin	5.0
100	140 mM Arginine·HCl and 300 mM Niacinamide	3.5
100	300 mM Histidine and 300 mM Niacinamide	3.6
100	300 mM Meglumine and 300 mM Niacinamide	5.1
100	140 mM Lysine·HCl and 300 mM Niacinamide	3.8
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Table 4 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 5 mM Acetate buffer, pH 4.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	462.1
300	30 mM Histidine and 30 mM Niacin	553.3
300	30 mM Meglumine and 30 mM Niacin	360.2
300	30 mM Lysine and 30 mM Niacin	410.4
300	30 mM Arginine·HCl and 30 mM Niacinamide	158.9
300	30 mM Histidine and 30 mM Niacinamide	242.7
300	30 mM Meglumine and 30 mM Niacinamide	392.5
300	30 mM Lysine·HCl and 30 mM Niacinamide	198.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	30 mM Arginine and 30 mM Niacin	40.1
200	30 mM Histidine and 30 mM Niacin	48.2
200	30 mM Meglumine and 30 mM Niacin	45.5
200	30 mM Lysine and 30 mM Niacin	36.3
200	30 mM Arginine·HCl and 30 mM Niacinamide	29.7
200	30 mM Histidine and 30 mM Niacinamide	31.2
200	30 mM Meglumine and 30 mM Niacinamide	47.9
200	30 mM Lysine·HCl and 30 mM Niacinamide	38.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	30 mM Arginine and 30 mM Niacin	7.1
100	30 mM Histidine and 30 mM Niacin	7.8
100	30 mM Meglumine and 30 mM Niacin	7.6
100	30 mM Lysine and 30 mM Niacin	6.3
100	30 mM Arginine·HCl and 30 mM Niacinamide	3.8
100	30 mM Histidine and 30 mM Niacinamide	4.8
100	30 mM Meglumine and 30 mM Niacinamide	8.0
100	30 mM Lysine·HCl and 30 mM Niacinamide	5.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Table 5 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 20 mM Acetate buffer, at pH 5.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	360.2
300	140 mM Histidine and 140 mM Niacin	408.0
300	140 mM Meglumine and 140 mM Niacin	304.5
300	140 mM Lysine and 140 mM Niacin	365.0
300	70 mM Arginine·HCl and 140 mM Niacinamide	87.0
300	140 mM Histidine and 140 mM Niacinamide	114.2
300	140 mM Meglumine and 140 mM Niacinamide	228.0
300	70 mM Lysine·HCl and 140 mM Niacinamide	145.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	140 mM Arginine and 140 mM Niacin	32.0
200	140 mM Histidine and 140 mM Niacin	34.0
200	140 mM Meglumine and 140 mM Niacin	30.0
200	140 mM Lysine and 140 mM Niacin	33.0
200	70 mM Arginine·HCl and 140 mM Niacinamide	17.0
200	140 mM Histidine and 140 mM Niacinamide	18.5
200	140 mM Meglumine and 140 mM Niacinamide	29.0
200	70 mM Lysine·HCl and 140 mM Niacinamide	24.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	140 mM Arginine and 140 mM Niacin	6.5
100	140 mM Histidine and 140 mM Niacin	7.5
100	140 mM Meglumine and 140 mM Niacin	7.0
100	140 mM Lysine and 140 mM Niacin	6.3
100	70 mM Arginine·HCl and 140 mM Niacinamide	4.4
100	140 mM Histidine and 140 mM Niacinamide	4.6
100	140 mM Meglumine and 140 mM Niacinamide	6.5
100	70 mM Lysine·HCl and 140 mM Niacinamide	4.8
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Table 6 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 50 mM Acetate buffer, at pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	287.2
300	300 mM Histidine and 300 mM Niacin	324.9
300	300 mM Meglumine and 300 mM Niacin	243.2
300	300 mM Lysine and 300 mM Niacin	290.4
300	140 mM Arginine·HCl and 300 mM Niacinamide	70.0
300	300 mM Histidine and 300 mM Niacinamide	91.4
300	300 mM Meglumine and 300 mM Niacinamide	184.2
300	140 mM Lysine·HCl and 300 mM Niacinamide	116.6
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	300 mM Arginine and 300 mM Niacin	26.2
200	300 mM Histidine and 300 mM Niacin	27.9
200	300 mM Meglumine and 300 mM Niacin	25.0
200	300 mM Lysine and 300 mM Niacin	28.4
200	140 mM Arginine·HCl and 300 mM Niacinamide	14.2
200	300 mM Histidine and 300 mM Niacinamide	17.0
200	300 mM Meglumine and 300 mM Niacinamide	23.4
200	140 mM Lysine·HCl and 300 mM Niacinamide	19.4
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	300 mM Arginine and 300 mM Niacin	5.7
100	300 mM Histidine and 300 mM Niacin	6.1
100	300 mM Meglumine and 300 mM Niacin	6.0
100	300 mM Lysine and 300 mM Niacin	5.5
100	140 mM Arginine·HCl and 300 mM Niacinamide	3.9
100	300 mM Histidine and 300 mM Niacinamide	4.1
100	300 mM Meglumine and 300 mM Niacinamide	5.8
100	140 mM Lysine·HCl and 300 mM Niacinamide	4.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Table 7 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 5 mM Citrate buffer, at pH 4.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	466.0
300	30 mM Histidine and 30 mM Niacin	558.2
300	30 mM Meglumine and 30 mM Niacin	365.0
300	30 mM Lysine and 30 mM Niacin	415.8
300	30 mM Arginine·HCl and 30 mM Niacinamide	162.5
300	30 mM Histidine and 30 mM Niacinamide	246.9
300	30 mM Meglumine and 30 mM Niacinamide	396.8
300	30 mM Lysine·HCl and 30 mM Niacinamide	200.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	30 mM Arginine and 30 mM Niacin	41.5
200	30 mM Histidine and 30 mM Niacin	49.0
200	30 mM Meglumine and 30 mM Niacin	46.3
200	30 mM Lysine and 30 mM Niacin	37.8
200	30 mM Arginine·HCl and 30 mM Niacinamide	30.4
200	30 mM Histidine and 30 mM Niacinamide	32.0
200	30 mM Meglumine and 30 mM Niacinamide	48.7
200	30 mM Lysine·HCl and 30 mM Niacinamide	39.5
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	30 mM Arginine and 30 mM Niacin	7.3
100	30 mM Histidine and 30 mM Niacin	7.9
100	30 mM Meglumine and 30 mM Niacin	7.5
100	30 mM Lysine and 30 mM Niacin	6.5
100	30 mM Arginine·HCl and 30 mM Niacinamide	4.0
100	30 mM Histidine and 30 mM Niacinamide	5.0
100	30 mM Meglumine and 30 mM Niacinamide	6.4
100	30 mM Lysine·HCl and 30 mM Niacinamide	5.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Table 8 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 20 mM Citrate buffer, pH 5.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	394.4
300	140 mM Histidine and 140 mM Niacin	433.8
300	140 mM Meglumine and 140 mM Niacin	288.2
300	140 mM Lysine and 140 mM Niacin	321.9
300	70 mM Arginine·HCl and 140 mM Niacinamide	124.5
300	140 mM Histidine and 140 mM Niacinamide	185.3
300	140 mM Meglumine and 140 mM Niacinamide	333.5
300	70 mM Lysine·HCl and 140 mM Niacinamide	156.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	140 mM Arginine and 140 mM Niacin	33.5
200	140 mM Histidine and 140 mM Niacin	36.4
200	140 mM Meglumine and 140 mM Niacin	30.9
200	140 mM Lysine and 140 mM Niacin	30.3
200	70 mM Arginine·HCl and 140 mM Niacinamide	22.5
200	140 mM Histidine and 140 mM Niacinamide	24.3
200	140 mM Meglumine and 140 mM Niacinamide	30.6
200	70 mM Lysine·HCl and 140 mM Niacinamide	27.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	140 mM Arginine and 140 mM Niacin	5.4
100	140 mM Histidine and 140 mM Niacin	6.1
100	140 mM Meglumine and 140 mM Niacin	5.3
100	140 mM Lysine and 140 mM Niacin	5.1
100	70 mM Arginine·HCl and 140 mM Niacinamide	3.0
100	140 mM Histidine and 140 mM Niacinamide	3.5
100	140 mM Meglumine and 140 mM Niacinamide	5.3
100	70 mM Lysine·HCl and 140 mM Niacinamide	4.3
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Table 9 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 50 mM Citrate buffer, at pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	290.5
300	300 mM Histidine and 300 mM Niacin	328.7
300	300 mM Meglumine and 300 mM Niacin	245.0
300	300 mM Lysine and 300 mM Niacin	293.6
300	140 mM Arginine·HCl and 300 mM Niacinamide	72.5
300	300 mM Histidine and 300 mM Niacinamide	93.8
300	300 mM Meglumine and 300 mM Niacinamide	188.5
300	140 mM Lysine·HCl and 300 mM Niacinamide	118.0
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	300 mM Arginine and 300 mM Niacin	26.8
200	300 mM Histidine and 300 mM Niacin	28.3
200	300 mM Meglumine and 300 mM Niacin	25.5
200	300 mM Lysine and 300 mM Niacin	29.1
200	140 mM Arginine·HCl and 300 mM Niacinamide	14.5
200	300 mM Histidine and 300 mM Niacinamide	17.5
200	300 mM Meglumine and 300 mM Niacinamide	24.0
200	140 mM Lysine·HCl and 300 mM Niacinamide	20.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	300 mM Arginine and 300 mM Niacin	5.8
100	300 mM Histidine and 300 mM Niacin	6.3
100	300 mM Meglumine and 300 mM Niacin	6.2
100	300 mM Lysine and 300 mM Niacin	5.7
100	140 mM Arginine·HCl and 300 mM Niacinamide	4.2
100	300 mM Histidine and 300 mM Niacinamide	4.4
100	300 mM Meglumine and 300 mM Niacinamide	6.0
100	140 mM Lysine·HCl and 300 mM Niacinamide	4.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Table 10 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 5 mM Phosphate buffer, pH 6.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	484.0
300	30 mM Histidine and 30 mM Niacin	589.0
300	30 mM Meglumine and 30 mM Niacin	375.6
300	30 mM Lysine and 30 mM Niacin	433.4
300	30 mM Arginine·HCl and 30 mM Niacinamide	162.4
300	30 mM Histidine and 30 mM Niacinamide	257.4
300	30 mM Meglumine and 30 mM Niacinamide	419.6
300	30 mM Lysine·HCl and 30 mM Niacinamide	207.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	30 mM Arginine and 30 mM Niacin	41.2
200	30 mM Histidine and 30 mM Niacin	50.5
200	30 mM Meglumine and 30 mM Niacin	48.4
200	30 mM Lysine and 30 mM Niacin	38.5
200	30 mM Arginine·HCl and 30 mM Niacinamide	30.5
200	30 mM Histidine and 30 mM Niacinamide	32.8
200	30 mM Meglumine and 30 mM Niacinamide	49.9
200	30 mM Lysine·HCl and 30 mM Niacinamide	39.9
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	30 mM Arginine and 30 mM Niacin	7.3
100	30 mM Histidine and 30 mM Niacin	8.0
100	30 mM Meglumine and 30 mM Niacin	7.3
100	30 mM Lysine and 30 mM Niacin	6.4
100	30 mM Arginine·HCl and 30 mM Niacinamide	3.8
100	30 mM Histidine and 30 mM Niacinamide	4.9
100	30 mM Meglumine and 30 mM Niacinamide	7.4
100	30 mM Lysine·HCl and 30 mM Niacinamide	5.3
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Table 11 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 20 mM Phosphate buffer, at pH 7.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	394.4
300	140 mM Histidine and 140 mM Niacin	439.4
300	140 mM Meglumine and 140 mM Niacin	333.5
300	140 mM Lysine and 140 mM Niacin	412.5
300	70 mM Arginine·HCl and 140 mM Niacinamide	99.5
300	140 mM Histidine and 140 mM Niacinamide	130.5
300	140 mM Meglumine and 140 mM Niacinamide	248.4
300	70 mM Lysine·HCl and 140 mM Niacinamide	159.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	140 mM Arginine and 140 mM Niacin	36.0
200	140 mM Histidine and 140 mM Niacin	39.2
200	140 mM Meglumine and 140 mM Niacin	34.3
200	140 mM Lysine and 140 mM Niacin	38.7
200	70 mM Arginine·HCl and 140 mM Niacinamide	20.2
200	140 mM Histidine and 140 mM Niacinamide	22.2
200	140 mM Meglumine and 140 mM Niacinamide	32.7
200	70 mM Lysine·HCl and 140 mM Niacinamide	27.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	140 mM Arginine and 140 mM Niacin	7.8
100	140 mM Histidine and 140 mM Niacin	7.7
100	140 mM Meglumine and 140 mM Niacin	6.2
100	140 mM Lysine and 140 mM Niacin	7.5
100	70 mM Arginine·HCl and 140 mM Niacinamide	5.0
100	140 mM Histidine and 140 mM Niacinamide	5.4
100	140 mM Meglumine and 140 mM Niacinamide	7.6
100	70 mM Lysine·HCl and 140 mM Niacinamide	5.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Table 12 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 50 mM Phosphate buffer, at pH 7.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	287.4
300	300 mM Histidine and 300 mM Niacin	326.2
300	300 mM Meglumine and 300 mM Niacin	244.3
300	300 mM Lysine and 300 mM Niacin	295.7
300	140 mM Arginine·HCl and 300 mM Niacinamide	70.5
300	300 mM Histidine and 300 mM Niacinamide	93.8
300	300 mM Meglumine and 300 mM Niacinamide	182.5
300	140 mM Lysine·HCl and 300 mM Niacinamide	116.4
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	300 mM Arginine and 300 mM Niacin	26.2
200	300 mM Histidine and 300 mM Niacin	28.3
200	300 mM Meglumine and 300 mM Niacin	25.3
200	300 mM Lysine and 300 mM Niacin	27.7
200	140 mM Arginine·HCl and 300 mM Niacinamide	14.2
200	300 mM Histidine and 300 mM Niacinamide	16.0
200	300 mM Meglumine and 300 mM Niacinamide	24.0
200	140 mM Lysine·HCl and 300 mM Niacinamide	19.6
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	300 mM Arginine and 300 mM Niacin	5.7
100	300 mM Histidine and 300 mM Niacin	6.3
100	300 mM Meglumine and 300 mM Niacin	5.9
100	300 mM Lysine and 300 mM Niacin	5.4
100	140 mM Arginine·HCl and 300 mM Niacinamide	3.7
100	300 mM Histidine and 300 mM Niacinamide	3.9
100	300 mM Meglumine and 300 mM Niacinamide	5.4
100	140 mM Lysine·HCl and 300 mM Niacinamide	4.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Table 13 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 5 mM Tris buffer, at pH 6.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	469.0
300	30 mM Histidine and 30 mM Niacin	572.5
300	30 mM Meglumine and 30 mM Niacin	366.0
300	30 mM Lysine and 30 mM Niacin	412.2
300	30 mM Arginine·HCl and 30 mM Niacinamide	157.4
300	30 mM Histidine and 30 mM Niacinamide	242.6
300	30 mM Meglumine and 30 mM Niacinamide	401.5
300	30 mM Lysine·HCl and 30 mM Niacinamide	198.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	30 mM Arginine and 30 mM Niacin	40.4
200	30 mM Histidine and 30 mM Niacin	48.7
200	30 mM Meglumine and 30 mM Niacin	45.0
200	30 mM Lysine and 30 mM Niacin	36.0
200	30 mM Arginine·HCl and 30 mM Niacinamide	28.7
200	30 mM Histidine and 30 mM Niacinamide	31.0
200	30 mM Meglumine and 30 mM Niacinamide	47.0
200	30 mM Lysine·HCl and 30 mM Niacinamide	38.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	30 mM Arginine and 30 mM Niacin	7.2
100	30 mM Histidine and 30 mM Niacin	7.9
100	30 mM Meglumine and 30 mM Niacin	7.0
100	30 mM Lysine and 30 mM Niacin	6.2
100	30 mM Arginine·HCl and 30 mM Niacinamide	3.6
100	30 mM Histidine and 30 mM Niacinamide	4.7
100	30 mM Meglumine and 30 mM Niacinamide	8.0
100	30 mM Lysine·HCl and 30 mM Niacinamide	5.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Table 14 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 20 mM Tris buffer, pH 7.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	394.0
300	140 mM Histidine and 140 mM Niacin	419.0
300	140 mM Meglumine and 140 mM Niacin	334.6
300	140 mM Lysine and 140 mM Niacin	402.0
300	70 mM Arginine·HCl and 140 mM Niacinamide	95.6
300	140 mM Histidine and 140 mM Niacinamide	123.3
300	140 mM Meglumine and 140 mM Niacinamide	238.9
300	70 mM Lysine·HCl and 140 mM Niacinamide	154.0
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	140 mM Arginine and 140 mM Niacin	36.0
200	140 mM Histidine and 140 mM Niacin	38.4
200	140 mM Meglumine and 140 mM Niacin	33.5
200	140 mM Lysine and 140 mM Niacin	37.5
200	70 mM Arginine·HCl and 140 mM Niacinamide	19.4
200	140 mM Histidine and 140 mM Niacinamide	21.6
200	140 mM Meglumine and 140 mM Niacinamide	31.0
200	70 mM Lysine·HCl and 140 mM Niacinamide	26.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	140 mM Arginine and 140 mM Niacin	7.5
100	140 mM Histidine and 140 mM Niacin	6.3
100	140 mM Meglumine and 140 mM Niacin	7.9
100	140 mM Lysine and 140 mM Niacin	7.2
100	70 mM Arginine·HCl and 140 mM Niacinamide	4.8
100	140 mM Histidine and 140 mM Niacinamide	5.2
100	140 mM Meglumine and 140 mM Niacinamide	7.3
100	70 mM Lysine·HCl and 140 mM Niacinamide	5.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Table 15 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 50 mM Tris buffer, at pH 7.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	276.5
300	300 mM Histidine and 300 mM Niacin	313.6
300	300 mM Meglumine and 300 mM Niacin	234.2
300	300 mM Lysine and 300 mM Niacin	279.7
300	140 mM Arginine·HCl and 300 mM Niacinamide	67.5
300	300 mM Histidine and 300 mM Niacinamide	89.5
300	300 mM Meglumine and 300 mM Niacinamide	174.8
300	140 mM Lysine·HCl and 300 mM Niacinamide	111.7
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	300 mM Arginine and 300 mM Niacin	25.0
200	300 mM Histidine and 300 mM Niacin	27.0
200	300 mM Meglumine and 300 mM Niacin	24.5
200	300 mM Lysine and 300 mM Niacin	26.3
200	140 mM Arginine·HCl and 300 mM Niacinamide	13.9
200	300 mM Histidine and 300 mM Niacinamide	15.6
200	300 mM Meglumine and 300 mM Niacinamide	22.9
200	140 mM Lysine·HCl and 300 mM Niacinamide	19.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	300 mM Arginine and 300 mM Niacin	5.6
100	300 mM Histidine and 300 mM Niacin	6.0
100	300 mM Meglumine and 300 mM Niacin	5.7
100	300 mM Lysine and 300 mM Niacin	5.1
100	140 mM Arginine·HCl and 300 mM Niacinamide	3.6
100	300 mM Histidine and 300 mM Niacinamide	3.7
100	300 mM Meglumine and 300 mM Niacinamide	5.2
100	140 mM Lysine·HCl and 300 mM Niacinamide	3.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Table 16 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 5 mM Succinate buffer, pH 4.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	470.2
300	30 mM Histidine and 30 mM Niacin	564.5
300	30 mM Meglumine and 30 mM Niacin	370.2
300	30 mM Lysine and 30 mM Niacin	420.6
300	30 mM Arginine·HCl and 30 mM Niacinamide	165.8
300	30 mM Histidine and 30 mM Niacinamide	250.3
300	30 mM Meglumine and 30 mM Niacinamide	400.5
300	30 mM Lysine·HCl and 30 mM Niacinamide	202.4
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	30 mM Arginine and 30 mM Niacin	42.8
200	30 mM Histidine and 30 mM Niacin	50.2
200	30 mM Meglumine and 30 mM Niacin	47.1
200	30 mM Lysine and 30 mM Niacin	38.5
200	30 mM Arginine·HCl and 30 mM Niacinamide	31.0
200	30 mM Histidine and 30 mM Niacinamide	33.1
200	30 mM Meglumine and 30 mM Niacinamide	49.5
200	30 mM Lysine·HCl and 30 mM Niacinamide	40.2
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	30 mM Arginine and 30 mM Niacin	7.5
100	30 mM Histidine and 30 mM Niacin	7.2
100	30 mM Meglumine and 30 mM Niacin	7.8
100	30 mM Lysine and 30 mM Niacin	6.7
100	30 mM Arginine·HCl and 30 mM Niacinamide	4.3
100	30 mM Histidine and 30 mM Niacinamide	5.2
100	30 mM Meglumine and 30 mM Niacinamide	6.6
100	30 mM Lysine·HCl and 30 mM Niacinamide	5.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Table 17 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 20 mM Succinate buffer, at pH 5.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	398.6
300	140 mM Histidine and 140 mM Niacin	438.2
300	140 mM Meglumine and 140 mM Niacin	290.7
300	140 mM Lysine and 140 mM Niacin	324.5
300	70 mM Arginine·HCl and 140 mM Niacinamide	127.0
300	140 mM Histidine and 140 mM Niacinamide	187.6
300	140 mM Meglumine and 140 mM Niacinamide	337.1
300	70 mM Lysine·HCl and 140 mM Niacinamide	158.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	140 mM Arginine and 140 mM Niacin	34.1
200	140 mM Histidine and 140 mM Niacin	37.2
200	140 mM Meglumine and 140 mM Niacin	31.5
200	140 mM Lysine and 140 mM Niacin	31.0
200	70 mM Arginine·HCl and 140 mM Niacinamide	23.1
200	140 mM Histidine and 140 mM Niacinamide	25.0
200	140 mM Meglumine and 140 mM Niacinamide	31.2
200	70 mM Lysine·HCl and 140 mM Niacinamide	27.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	140 mM Arginine and 140 mM Niacin	6.0
100	140 mM Histidine and 140 mM Niacin	6.3
100	140 mM Meglumine and 140 mM Niacin	5.5
100	140 mM Lysine and 140 mM Niacin	5.2
100	70 mM Arginine·HCl and 140 mM Niacinamide	3.2
100	140 mM Histidine and 140 mM Niacinamide	3.6
100	140 mM Meglumine and 140 mM Niacinamide	5.6
100	70 mM Lysine·HCl and 140 mM Niacinamide	4.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Table 18 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Pembrolizumab in 50 mM Succinate buffer, at pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	285.6
300	300 mM Histidine and 300 mM Niacin	322.1
300	300 mM Meglumine and 300 mM Niacin	240.4
300	300 mM Lysine and 300 mM Niacin	287.8
300	140 mM Arginine·HCl and 300 mM Niacinamide	68.5
300	300 mM Histidine and 300 mM Niacinamide	90.0
300	300 mM Meglumine and 300 mM Niacinamide	182.7
300	140 mM Lysine·HCl and 300 mM Niacinamide	115.4
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	976.4
300	Water (Blank)	1958.3
200	300 mM Arginine and 300 mM Niacin	25.6
200	300 mM Histidine and 300 mM Niacin	27.2
200	300 mM Meglumine and 300 mM Niacin	24.6
200	300 mM Lysine and 300 mM Niacin	27.6
200	140 mM Arginine·HCl and 300 mM Niacinamide	13.8
200	300 mM Histidine and 300 mM Niacinamide	16.8
200	300 mM Meglumine and 300 mM Niacinamide	22.9
200	140 mM Lysine·HCl and 300 mM Niacinamide	19.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	51.1
200	Water (blank)	150.7
100	300 mM Arginine and 300 mM Niacin	5.5
100	300 mM Histidine and 300 mM Niacin	6.0
100	300 mM Meglumine and 300 mM Niacin	5.9
100	300 mM Lysine and 300 mM Niacin	5.4
100	140 mM Arginine·HCl and 300 mM Niacinamide	3.7
100	300 mM Histidine and 300 mM Niacinamide	3.9
100	300 mM Meglumine and 300 mM Niacinamide	5.5
100	140 mM Lysine·HCl and 300 mM Niacinamide	4.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	8.1
100	Water (blank)	11.3

Example 2: Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab solutions in various buffers at 20°C

[0072] This example tested the viscosity reducing effect of viscosity-reducing and stabilizing formulations of the present application on Adalimumab solutions.

5 [0073] **Materials and Methods**

[0074] Adalimumab (Humira®) is a commercially available mAb. In this example, it was produced by WuXi Biologics based on its sequence sourced from Drug Bank (DB00051). The recombinant cell culture fermentation was harvested by centrifugation, and the resulting filtrate pool was loaded onto a Protein A column. The target protein was eluted at pH 3.8 and subsequently
10 neutralized to pH 5.5 using 1 M Tris base. The eluate then underwent depth filtration and was passed through a 0.2 µm filter. The intermediate filtration pool was loaded onto an AEX (Anion Exchange) column in flow-through mode. Following this step, the AEX flow-through pool was further processed on a CEX (Cation Exchange) column, and the target protein was eluted using a linear gradient elution. The CEX eluate was subsequently concentrated to a concentration of 40
15 g/L and diafiltrated over six dia-volumes to exchange the buffer to a final composition of a buffer concentration within 5-50 mM using histidine, acetate, citrate, phosphate, tris or succinate buffer system at a pH between 4.5 and 7.5, respectively. Through formulation exchange, Adalimumab was transferred into test groups, encompassing with the component concentration varied from 30 mM to 300 mM, incorporating one of the viscosity-reducing and stabilizing formulations, shown
20 in Tables 19-36. Furthermore, there was a control group (i.e., positive control) comprising 25 mM phosphate buffer at pH 6.0, with 81.2 mM Nicotinic acid and 29.4 mM Tryptophan (matching the lead formulation 25 mM phosphate buffer at pH 6.0 along with 10 mg/mL Nicotinic acid (acid form) and 6 mg/mL Tryptophan from Examples 14 and 16-21 in WO2018211517). An additional control group solely consisted of MilliQ water and the protein as blank control. The formulation
25 containing Adalimumab was subsequently concentrated to 100-300 mg/mL (e.g., 100, 200, or 300 mg/mL) using an Eppendorf centrifuge with a concentration variation of 3%. To ascertain Adalimumab's concentration in the groups, absorbance at 280 nm combined with SE-UPLC was gauged against corresponding buffers containing a viscosity-reducing and stabilizing formulation for excipient-containing samples, and absorbance at 280 nm was measured for the protein solution
30 without a viscosity-reducing and stabilizing formulation. For Adalimumab without excipients, the

buffer alone (i.e., devoid of excipients) served as a blank for protein concentration calculation. The extinction coefficient was measured at $1.40 \text{ (mg/mL)}^{-1} \cdot \text{cm}^{-1}$.

[0075] The viscosity of samples was measured by VROC® initium one plus viscometer (Rheosense) at 20°C. For samples with a viscosity exceeding 1000 cP, viscosity was measured
5 using a TA rheometer.

[0076] As shown in Tables 19-36, the data demonstrated the viscosity-reducing efficacy of viscosity-reducing and stabilizing formulations of the present application on Adalimumab in different buffers: histidine (pH 5.0 to 7.0), acetate (pH 4.5 to 6.0), citrate (pH 4.5 to 6.0), phosphate (pH 6.5 to 7.5), Tris (pH 6.5 to 7.5), and succinate (pH 4.5 to 6.0) buffer. As for Adalimumab at a
10 concentration from 100 to 300 mg/mL, the tested viscosity-reducing and stabilizing formulations exhibited superior viscosity reduction when compared to the reference lead formulation from WO2018211517 and excipient-free samples.

Table 19 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 5 mM Histidine buffer, at pH 5.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	412.7
300	30 mM Histidine and 30 mM Niacin	494.2
300	30 mM Meglumine and 30 mM Niacin	321.9
300	30 mM Lysine and 30 mM Niacin	344.8
300	30 mM Arginine·HCl and 30 mM Niacinamide	131.6
300	30 mM Histidine and 30 mM Niacinamide	215.4
300	30 mM Meglumine and 30 mM Niacinamide	350.2
300	30 mM Lysine·HCl and 30 mM Niacinamide	176.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	30 mM Arginine and 30 mM Niacin	27.4
200	30 mM Histidine and 30 mM Niacin	31.8
200	30 mM Meglumine and 30 mM Niacin	31.4
200	30 mM Lysine and 30 mM Niacin	24.9
200	30 mM Arginine·HCl and 30 mM Niacinamide	20.5
200	30 mM Histidine and 30 mM Niacinamide	21.3
200	30 mM Meglumine and 30 mM Niacinamide	36.9
200	30 mM Lysine·HCl and 30 mM Niacinamide	26.2
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	30 mM Arginine and 30 mM Niacin	2.9
100	30 mM Histidine and 30 mM Niacin	2.7
100	30 mM Meglumine and 30 mM Niacin	2.8
100	30 mM Lysine and 30 mM Niacin	2.6
100	30 mM Arginine·HCl and 30 mM Niacinamide	1.8
100	30 mM Histidine and 30 mM Niacinamide	2.4
100	30 mM Meglumine and 30 mM Niacinamide	2.5
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Table 20 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 20 mM Histidine buffer, pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	380.3
300	140 mM Histidine and 140 mM Niacin	454.1
300	140 mM Meglumine and 140 mM Niacin	295.8
300	140 mM Lysine and 140 mM Niacin	317.5
300	70 mM Arginine·HCl and 140 mM Niacinamide	121.0
300	140 mM Histidine and 140 mM Niacinamide	198.5
300	140 mM Meglumine and 140 mM Niacinamide	322.7
300	70 mM Lysine·HCl and 140 mM Niacinamide	162.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	140 mM Arginine and 140 mM Niacin	25.2
200	140 mM Histidine and 140 mM Niacin	30.0
200	140 mM Meglumine and 140 mM Niacin	29.0
200	140 mM Lysine and 140 mM Niacin	22.9
200	70 mM Arginine·HCl and 140 mM Niacinamide	18.9
200	140 mM Histidine and 140 mM Niacinamide	19.6
200	140 mM Meglumine and 140 mM Niacinamide	34.0
200	70 mM Lysine·HCl and 140 mM Niacinamide	24.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	140 mM Arginine and 140 mM Niacin	2.8
100	140 mM Histidine and 140 mM Niacin	2.5
100	140 mM Meglumine and 140 mM Niacin	2.6
100	140 mM Lysine and 140 mM Niacin	2.4
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.7
100	140 mM Histidine and 140 mM Niacinamide	2.2
100	140 mM Meglumine and 140 mM Niacinamide	2.3
100	70 mM Lysine·HCl and 140 mM Niacinamide	2.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Table 21 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 50 mM Histidine buffer, at pH 7.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	363.0
300	300 mM Histidine and 300 mM Niacin	435.5
300	300 mM Meglumine and 300 mM Niacin	284.1
300	300 mM Lysine and 300 mM Niacin	303.5
300	140 mM Arginine·HCl and 300 mM Niacinamide	116.0
300	300 mM Histidine and 300 mM Niacinamide	189.2
300	300 mM Meglumine and 300 mM Niacinamide	308.2
300	140 mM Lysine·HCl and 300 mM Niacinamide	155.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	300 mM Arginine and 300 mM Niacin	24.1
200	300 mM Histidine and 300 mM Niacin	29.0
200	300 mM Meglumine and 300 mM Niacin	28.0
200	300 mM Lysine and 300 mM Niacin	22.0
200	140 mM Arginine·HCl and 300 mM Niacinamide	18.1
200	300 mM Histidine and 300 mM Niacinamide	18.8
200	300 mM Meglumine and 300 mM Niacinamide	33.0
200	140 mM Lysine·HCl and 300 mM Niacinamide	23.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	300 mM Arginine and 300 mM Niacin	1.8
100	300 mM Histidine and 300 mM Niacin	2.2
100	300 mM Meglumine and 300 mM Niacin	2.1
100	300 mM Lysine and 300 mM Niacin	2.5
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.8
100	300 mM Histidine and 300 mM Niacinamide	2.4
100	300 mM Meglumine and 300 mM Niacinamide	2.7
100	140 mM Lysine·HCl and 300 mM Niacinamide	2.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Table 22 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 5 mM Acetate buffer, pH 4.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	432.5
300	30 mM Histidine and 30 mM Niacin	528.4
300	30 mM Meglumine and 30 mM Niacin	337.5
300	30 mM Lysine and 30 mM Niacin	369.4
300	30 mM Arginine·HCl and 30 mM Niacinamide	137.5
300	30 mM Histidine and 30 mM Niacinamide	229.5
300	30 mM Meglumine and 30 mM Niacinamide	374.7
300	30 mM Lysine·HCl and 30 mM Niacinamide	188.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	30 mM Arginine and 30 mM Niacin	28.8
200	30 mM Histidine and 30 mM Niacin	33.9
200	30 mM Meglumine and 30 mM Niacin	33.6
200	30 mM Lysine and 30 mM Niacin	26.7
200	30 mM Arginine·HCl and 30 mM Niacinamide	21.9
200	30 mM Histidine and 30 mM Niacinamide	22.8
200	30 mM Meglumine and 30 mM Niacinamide	39.4
200	30 mM Lysine·HCl and 30 mM Niacinamide	27.9
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	30 mM Arginine and 30 mM Niacin	3.1
100	30 mM Histidine and 30 mM Niacin	2.8
100	30 mM Meglumine and 30 mM Niacin	3.0
100	30 mM Lysine and 30 mM Niacin	2.8
100	30 mM Arginine·HCl and 30 mM Niacinamide	1.9
100	30 mM Histidine and 30 mM Niacinamide	2.5
100	30 mM Meglumine and 30 mM Niacinamide	2.7
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Table 23 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 20 mM Acetate buffer, at pH 5.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	391.1
300	140 mM Histidine and 140 mM Niacin	479.8
300	140 mM Meglumine and 140 mM Niacin	305.4
300	140 mM Lysine and 140 mM Niacin	335.1
300	70 mM Arginine·HCl and 140 mM Niacinamide	124.3
300	140 mM Histidine and 140 mM Niacinamide	204.5
300	140 mM Meglumine and 140 mM Niacinamide	342.5
300	70 mM Lysine·HCl and 140 mM Niacinamide	171.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	140 mM Arginine and 140 mM Niacin	26.0
200	140 mM Histidine and 140 mM Niacin	31.0
200	140 mM Meglumine and 140 mM Niacin	29.7
200	140 mM Lysine and 140 mM Niacin	23.6
200	70 mM Arginine·HCl and 140 mM Niacinamide	19.5
200	140 mM Histidine and 140 mM Niacinamide	20.2
200	140 mM Meglumine and 140 mM Niacinamide	35.0
200	70 mM Lysine·HCl and 140 mM Niacinamide	24.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	140 mM Arginine and 140 mM Niacin	2.9
100	140 mM Histidine and 140 mM Niacin	2.6
100	140 mM Meglumine and 140 mM Niacin	2.7
100	140 mM Lysine and 140 mM Niacin	2.5
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.8
100	140 mM Histidine and 140 mM Niacinamide	2.3
100	140 mM Meglumine and 140 mM Niacinamide	2.4
100	70 mM Lysine·HCl and 140 mM Niacinamide	2.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Table 24 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 50 mM Acetate buffer, at pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	374.0
300	300 mM Histidine and 300 mM Niacin	450.0
300	300 mM Meglumine and 300 mM Niacin	293.0
300	300 mM Lysine and 300 mM Niacin	315.0
300	140 mM Arginine·HCl and 300 mM Niacinamide	119.5
300	300 mM Histidine and 300 mM Niacinamide	195.0
300	300 mM Meglumine and 300 mM Niacinamide	318.5
300	140 mM Lysine·HCl and 300 mM Niacinamide	161.0
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	300 mM Arginine and 300 mM Niacin	24.8
200	300 mM Histidine and 300 mM Niacin	30.0
200	300 mM Meglumine and 300 mM Niacin	29.4
200	300 mM Lysine and 300 mM Niacin	22.6
200	140 mM Arginine·HCl and 300 mM Niacinamide	18.6
200	300 mM Histidine and 300 mM Niacinamide	19.2
200	300 mM Meglumine and 300 mM Niacinamide	34.0
200	140 mM Lysine·HCl and 300 mM Niacinamide	23.9
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	300 mM Arginine and 300 mM Niacin	2.9
100	300 mM Histidine and 300 mM Niacin	2.6
100	300 mM Meglumine and 300 mM Niacin	2.7
100	300 mM Lysine and 300 mM Niacin	2.5
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.8
100	300 mM Histidine and 300 mM Niacinamide	2.3
100	300 mM Meglumine and 300 mM Niacinamide	2.4
100	140 mM Lysine·HCl and 300 mM Niacinamide	2.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Table 25 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 5 mM Citrate buffer, at pH 4.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	404.5
300	30 mM Histidine and 30 mM Niacin	484.0
300	30 mM Meglumine and 30 mM Niacin	316.3
300	30 mM Lysine and 30 mM Niacin	338.1
300	30 mM Arginine·HCl and 30 mM Niacinamide	129.4
300	30 mM Histidine and 30 mM Niacinamide	211.0
300	30 mM Meglumine and 30 mM Niacinamide	343.2
300	30 mM Lysine·HCl and 30 mM Niacinamide	172.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	30 mM Arginine and 30 mM Niacin	26.9
200	30 mM Histidine and 30 mM Niacin	31.1
200	30 mM Meglumine and 30 mM Niacin	30.8
200	30 mM Lysine and 30 mM Niacin	24.4
200	30 mM Arginine·HCl and 30 mM Niacinamide	20.1
200	30 mM Histidine and 30 mM Niacinamide	20.9
200	30 mM Meglumine and 30 mM Niacinamide	36.2
200	30 mM Lysine·HCl and 30 mM Niacinamide	25.7
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	30 mM Arginine and 30 mM Niacin	2.8
100	30 mM Histidine and 30 mM Niacin	2.6
100	30 mM Meglumine and 30 mM Niacin	2.7
100	30 mM Lysine and 30 mM Niacin	2.5
100	30 mM Arginine·HCl and 30 mM Niacinamide	1.8
100	30 mM Histidine and 30 mM Niacinamide	2.3
100	30 mM Meglumine and 30 mM Niacinamide	2.4
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Table 26 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 20 mM Citrate buffer, pH 5.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	372.5
300	140 mM Histidine and 140 mM Niacin	445.0
300	140 mM Meglumine and 140 mM Niacin	290.5
300	140 mM Lysine and 140 mM Niacin	311.5
300	70 mM Arginine·HCl and 140 mM Niacinamide	118.6
300	140 mM Histidine and 140 mM Niacinamide	194.2
300	140 mM Meglumine and 140 mM Niacinamide	316.5
300	70 mM Lysine·HCl and 140 mM Niacinamide	159.4
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	140 mM Arginine and 140 mM Niacin	24.7
200	140 mM Histidine and 140 mM Niacin	29.4
200	140 mM Meglumine and 140 mM Niacin	28.5
200	140 mM Lysine and 140 mM Niacin	22.5
200	70 mM Arginine·HCl and 140 mM Niacinamide	18.5
200	140 mM Histidine and 140 mM Niacinamide	19.2
200	140 mM Meglumine and 140 mM Niacinamide	33.3
200	70 mM Lysine·HCl and 140 mM Niacinamide	23.6
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	140 mM Arginine and 140 mM Niacin	2.7
100	140 mM Histidine and 140 mM Niacin	2.4
100	140 mM Meglumine and 140 mM Niacin	2.5
100	140 mM Lysine and 140 mM Niacin	2.4
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.6
100	140 mM Histidine and 140 mM Niacinamide	2.1
100	140 mM Meglumine and 140 mM Niacinamide	2.2
100	70 mM Lysine·HCl and 140 mM Niacinamide	1.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Table 27 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 50 mM Citrate buffer, at pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	355.3
300	300 mM Histidine and 300 mM Niacin	427.0
300	300 mM Meglumine and 300 mM Niacin	276.0
300	300 mM Lysine and 300 mM Niacin	295.4
300	140 mM Arginine·HCl and 300 mM Niacinamide	112.8
300	300 mM Histidine and 300 mM Niacinamide	185.0
300	300 mM Meglumine and 300 mM Niacinamide	301.9
300	140 mM Lysine·HCl and 300 mM Niacinamide	150.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	300 mM Arginine and 300 mM Niacin	23.4
200	300 mM Histidine and 300 mM Niacin	28.5
200	300 mM Meglumine and 300 mM Niacin	27.4
200	300 mM Lysine and 300 mM Niacin	21.4
200	140 mM Arginine·HCl and 300 mM Niacinamide	17.4
200	300 mM Histidine and 300 mM Niacinamide	17.9
200	300 mM Meglumine and 300 mM Niacinamide	31.7
200	140 mM Lysine·HCl and 300 mM Niacinamide	22.6
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	300 mM Arginine and 300 mM Niacin	2.5
100	300 mM Histidine and 300 mM Niacin	2.3
100	300 mM Meglumine and 300 mM Niacin	2.5
100	300 mM Lysine and 300 mM Niacin	2.3
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.8
100	300 mM Histidine and 300 mM Niacinamide	2.2
100	300 mM Meglumine and 300 mM Niacinamide	2.3
100	140 mM Lysine·HCl and 300 mM Niacinamide	2.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Table 28 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 5 mM Phosphate buffer, pH 6.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	431.5
300	30 mM Histidine and 30 mM Niacin	528.5
300	30 mM Meglumine and 30 mM Niacin	334.6
300	30 mM Lysine and 30 mM Niacin	369.2
300	30 mM Arginine·HCl and 30 mM Niacinamide	137.3
300	30 mM Histidine and 30 mM Niacinamide	224.0
300	30 mM Meglumine and 30 mM Niacinamide	374.7
300	30 mM Lysine·HCl and 30 mM Niacinamide	184.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	30 mM Arginine and 30 mM Niacin	28.5
200	30 mM Histidine and 30 mM Niacin	33.8
200	30 mM Meglumine and 30 mM Niacin	32.8
200	30 mM Lysine and 30 mM Niacin	26.5
200	30 mM Arginine·HCl and 30 mM Niacinamide	21.3
200	30 mM Histidine and 30 mM Niacinamide	22.6
200	30 mM Meglumine and 30 mM Niacinamide	38.2
200	30 mM Lysine·HCl and 30 mM Niacinamide	27.4
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	30 mM Arginine and 30 mM Niacin	3.1
100	30 mM Histidine and 30 mM Niacin	2.9
100	30 mM Meglumine and 30 mM Niacin	3.0
100	30 mM Lysine and 30 mM Niacin	2.8
100	30 mM Arginine·HCl and 30 mM Niacinamide	1.9
100	30 mM Histidine and 30 mM Niacinamide	2.5
100	30 mM Meglumine and 30 mM Niacinamide	2.6
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.3
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Table 29 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 20 mM Phosphate buffer, at pH 7.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	399.3
300	140 mM Histidine and 140 mM Niacin	478.9
300	140 mM Meglumine and 140 mM Niacin	311.5
300	140 mM Lysine and 140 mM Niacin	342.8
300	70 mM Arginine·HCl and 140 mM Niacinamide	127.1
300	140 mM Histidine and 140 mM Niacinamide	209.5
300	140 mM Meglumine and 140 mM Niacinamide	339.0
300	70 mM Lysine·HCl and 140 mM Niacinamide	171.2
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	140 mM Arginine and 140 mM Niacin	26.5
200	140 mM Histidine and 140 mM Niacin	31.5
200	140 mM Meglumine and 140 mM Niacin	30.9
200	140 mM Lysine and 140 mM Niacin	24.4
200	70 mM Arginine·HCl and 140 mM Niacinamide	19.9
200	140 mM Histidine and 140 mM Niacinamide	21.1
200	140 mM Meglumine and 140 mM Niacinamide	35.6
200	70 mM Lysine·HCl and 140 mM Niacinamide	25.4
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	140 mM Arginine and 140 mM Niacin	2.9
100	140 mM Histidine and 140 mM Niacin	2.7
100	140 mM Meglumine and 140 mM Niacin	2.8
100	140 mM Lysine and 140 mM Niacin	2.6
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.8
100	140 mM Histidine and 140 mM Niacinamide	2.4
100	140 mM Meglumine and 140 mM Niacinamide	2.5
100	70 mM Lysine·HCl and 140 mM Niacinamide	2.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Table 30 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 50 mM Phosphate buffer, at pH 7.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	384.0
300	300 mM Histidine and 300 mM Niacin	462.0
300	300 mM Meglumine and 300 mM Niacin	300.5
300	300 mM Lysine and 300 mM Niacin	322.0
300	140 mM Arginine·HCl and 300 mM Niacinamide	123.0
300	300 mM Histidine and 300 mM Niacinamide	200.0
300	300 mM Meglumine and 300 mM Niacinamide	326.8
300	140 mM Lysine·HCl and 300 mM Niacinamide	165.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	300 mM Arginine and 300 mM Niacin	25.6
200	300 mM Histidine and 300 mM Niacin	31.5
200	300 mM Meglumine and 300 mM Niacin	29.7
200	300 mM Lysine and 300 mM Niacin	23.3
200	140 mM Arginine·HCl and 300 mM Niacinamide	19.0
200	300 mM Histidine and 300 mM Niacinamide	20.0
200	300 mM Meglumine and 300 mM Niacinamide	35.1
200	140 mM Lysine·HCl and 300 mM Niacinamide	24.5
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	300 mM Arginine and 300 mM Niacin	3.0
100	300 mM Histidine and 300 mM Niacin	2.7
100	300 mM Meglumine and 300 mM Niacin	2.8
100	300 mM Lysine and 300 mM Niacin	2.6
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.8
100	300 mM Histidine and 300 mM Niacinamide	2.4
100	300 mM Meglumine and 300 mM Niacinamide	2.5
100	140 mM Lysine·HCl and 300 mM Niacinamide	2.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Table 31 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 5 mM Tris buffer, at pH 6.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	440.0
300	30 mM Histidine and 30 mM Niacin	540.0
300	30 mM Meglumine and 30 mM Niacin	338.0
300	30 mM Lysine and 30 mM Niacin	372.5
300	30 mM Arginine·HCl and 30 mM Niacinamide	139.0
300	30 mM Histidine and 30 mM Niacinamide	230.5
300	30 mM Meglumine and 30 mM Niacinamide	380.0
300	30 mM Lysine·HCl and 30 mM Niacinamide	186.0
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	30 mM Arginine and 30 mM Niacin	29.0
200	30 mM Histidine and 30 mM Niacin	34.5
200	30 mM Meglumine and 30 mM Niacin	33.5
200	30 mM Lysine and 30 mM Niacin	27.0
200	30 mM Arginine·HCl and 30 mM Niacinamide	22.0
200	30 mM Histidine and 30 mM Niacinamide	23.0
200	30 mM Meglumine and 30 mM Niacinamide	39.0
200	30 mM Lysine·HCl and 30 mM Niacinamide	28.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	30 mM Arginine and 30 mM Niacin	3.1
100	30 mM Histidine and 30 mM Niacin	3.0
100	30 mM Meglumine and 30 mM Niacin	3.0
100	30 mM Lysine and 30 mM Niacin	2.9
100	30 mM Arginine·HCl and 30 mM Niacinamide	2.1
100	30 mM Histidine and 30 mM Niacinamide	2.6
100	30 mM Meglumine and 30 mM Niacinamide	2.7
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Table 32 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 20 mM Tris buffer, pH 7.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	410.0
300	140 mM Histidine and 140 mM Niacin	490.4
300	140 mM Meglumine and 140 mM Niacin	320.3
300	140 mM Lysine and 140 mM Niacin	343.8
300	70 mM Arginine·HCl and 140 mM Niacinamide	130.7
300	140 mM Histidine and 140 mM Niacinamide	214.0
300	140 mM Meglumine and 140 mM Niacinamide	348.2
300	70 mM Lysine·HCl and 140 mM Niacinamide	175.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	140 mM Arginine and 140 mM Niacin	26.9
200	140 mM Histidine and 140 mM Niacin	32.4
200	140 mM Meglumine and 140 mM Niacin	31.4
200	140 mM Lysine and 140 mM Niacin	24.8
200	70 mM Arginine·HCl and 140 mM Niacinamide	20.4
200	140 mM Histidine and 140 mM Niacinamide	21.4
200	140 mM Meglumine and 140 mM Niacinamide	36.8
200	70 mM Lysine·HCl and 140 mM Niacinamide	25.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	140 mM Arginine and 140 mM Niacin	2.9
100	140 mM Histidine and 140 mM Niacin	2.6
100	140 mM Meglumine and 140 mM Niacin	2.7
100	140 mM Lysine and 140 mM Niacin	2.5
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.8
100	140 mM Histidine and 140 mM Niacinamide	2.3
100	140 mM Meglumine and 140 mM Niacinamide	2.4
100	70 mM Lysine·HCl and 140 mM Niacinamide	2.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Table 33 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 50 mM Tris buffer, at pH 7.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	393.9
300	300 mM Histidine and 300 mM Niacin	479.5
300	300 mM Meglumine and 300 mM Niacin	302.4
300	300 mM Lysine and 300 mM Niacin	332.0
300	140 mM Arginine·HCl and 300 mM Niacinamide	124.9
300	300 mM Histidine and 300 mM Niacinamide	205.0
300	300 mM Meglumine and 300 mM Niacinamide	336.6
300	140 mM Lysine·HCl and 300 mM Niacinamide	169.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	300 mM Arginine and 300 mM Niacin	26.4
200	300 mM Histidine and 300 mM Niacin	32.0
200	300 mM Meglumine and 300 mM Niacin	30.5
200	300 mM Lysine and 300 mM Niacin	23.7
200	140 mM Arginine·HCl and 300 mM Niacinamide	19.5
200	300 mM Histidine and 300 mM Niacinamide	20.5
200	300 mM Meglumine and 300 mM Niacinamide	36.3
200	140 mM Lysine·HCl and 300 mM Niacinamide	24.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	300 mM Arginine and 300 mM Niacin	3.1
100	300 mM Histidine and 300 mM Niacin	2.8
100	300 mM Meglumine and 300 mM Niacin	2.9
100	300 mM Lysine and 300 mM Niacin	2.7
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.9
100	300 mM Histidine and 300 mM Niacinamide	2.5
100	300 mM Meglumine and 300 mM Niacinamide	2.6
100	140 mM Lysine·HCl and 300 mM Niacinamide	2.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Table 34 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 5 mM Succinate buffer, pH 4.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	420.0
300	30 mM Histidine and 30 mM Niacin	504.0
300	30 mM Meglumine and 30 mM Niacin	328.5
300	30 mM Lysine and 30 mM Niacin	351.1
300	30 mM Arginine·HCl and 30 mM Niacinamide	134.1
300	30 mM Histidine and 30 mM Niacinamide	219.5
300	30 mM Meglumine and 30 mM Niacinamide	357.2
300	30 mM Lysine·HCl and 30 mM Niacinamide	179.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	30 mM Arginine and 30 mM Niacin	27.9
200	30 mM Histidine and 30 mM Niacin	32.5
200	30 mM Meglumine and 30 mM Niacin	31.9
200	30 mM Lysine and 30 mM Niacin	25.4
200	30 mM Arginine·HCl and 30 mM Niacinamide	20.9
200	30 mM Histidine and 30 mM Niacinamide	21.7
200	30 mM Meglumine and 30 mM Niacinamide	37.6
200	30 mM Lysine·HCl and 30 mM Niacinamide	26.6
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	30 mM Arginine and 30 mM Niacin	3.0
100	30 mM Histidine and 30 mM Niacin	2.8
100	30 mM Meglumine and 30 mM Niacin	2.9
100	30 mM Lysine and 30 mM Niacin	2.7
100	30 mM Arginine·HCl and 30 mM Niacinamide	1.8
100	30 mM Histidine and 30 mM Niacinamide	2.5
100	30 mM Meglumine and 30 mM Niacinamide	2.6
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Table 35 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 20 mM Succinate buffer, at pH 5.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	387.0
300	140 mM Histidine and 140 mM Niacin	462.0
300	140 mM Meglumine and 140 mM Niacin	301.3
300	140 mM Lysine and 140 mM Niacin	323.0
300	70 mM Arginine·HCl and 140 mM Niacinamide	123.1
300	140 mM Histidine and 140 mM Niacinamide	202.5
300	140 mM Meglumine and 140 mM Niacinamide	329.5
300	70 mM Lysine·HCl and 140 mM Niacinamide	165.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	140 mM Arginine and 140 mM Niacin	25.7
200	140 mM Histidine and 140 mM Niacin	30.6
200	140 mM Meglumine and 140 mM Niacin	29.5
200	140 mM Lysine and 140 mM Niacin	23.3
200	70 mM Arginine·HCl and 140 mM Niacinamide	19.3
200	140 mM Histidine and 140 mM Niacinamide	20.0
200	140 mM Meglumine and 140 mM Niacinamide	34.7
200	70 mM Lysine·HCl and 140 mM Niacinamide	24.7
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	140 mM Arginine and 140 mM Niacin	2.9
100	140 mM Histidine and 140 mM Niacin	2.6
100	140 mM Meglumine and 140 mM Niacin	2.7
100	140 mM Lysine and 140 mM Niacin	2.5
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.7
100	140 mM Histidine and 140 mM Niacinamide	2.3
100	140 mM Meglumine and 140 mM Niacinamide	2.4
100	70 mM Lysine·HCl and 140 mM Niacinamide	2.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Table 36 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Adalimumab in 50 mM Succinate buffer, at pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	369.2
300	300 mM Histidine and 300 mM Niacin	442.0
300	300 mM Meglumine and 300 mM Niacin	291.0
300	300 mM Lysine and 300 mM Niacin	311.0
300	140 mM Arginine·HCl and 300 mM Niacinamide	119.5
300	300 mM Histidine and 300 mM Niacinamide	193.0
300	300 mM Meglumine and 300 mM Niacinamide	314.5
300	140 mM Lysine·HCl and 300 mM Niacinamide	159.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	946.3
300	Water (Blank)	1443.0
200	300 mM Arginine and 300 mM Niacin	24.5
200	300 mM Histidine and 300 mM Niacin	29.5
200	300 mM Meglumine and 300 mM Niacin	28.5
200	300 mM Lysine and 300 mM Niacin	21.4
200	140 mM Arginine·HCl and 300 mM Niacinamide	18.0
200	300 mM Histidine and 300 mM Niacinamide	19.4
200	300 mM Meglumine and 300 mM Niacinamide	32.4
200	140 mM Lysine·HCl and 300 mM Niacinamide	23.5
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	46.6
200	Water (blank)	56.7
100	300 mM Arginine and 300 mM Niacin	2.9
100	300 mM Histidine and 300 mM Niacin	2.7
100	300 mM Meglumine and 300 mM Niacin	2.7
100	300 mM Lysine and 300 mM Niacin	2.6
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.7
100	300 mM Histidine and 300 mM Niacinamide	2.3
100	300 mM Meglumine and 300 mM Niacinamide	2.4
100	140 mM Lysine·HCl and 300 mM Niacinamide	2.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	3.3
100	Water (blank)	4.6

Example 3: Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab solutions in various buffers at 20°C.

[0077] This example describes the viscosity reducing effect of viscosity-reducing and stabilizing formulations of the present application on Trastuzumab solutions.

5 [0078] **Materials and Methods**

[0079] Trastuzumab (Herceptin®) is a commercially available mAb. In this example, it was produced by WuXi Biologics based on its sequence was sourced from Drug Bank (DB00072). The recombinant cell culture fermentation was harvested by centrifugation, and the resulting filtrate pool was loaded onto a Protein A column. The target protein was eluted at pH 3.8 and subsequently
10 neutralized to pH 5.5 using 1 M Tris base. The eluate then underwent depth filtration and was passed through a 0.2 µm filter. The intermediate filtration pool was loaded onto an AEX (Anion Exchange) column in flow-through mode. Following this step, the AEX flow-through pool was further processed on a CEX (Cation Exchange) column, and the target protein was eluted using a linear gradient elution. The CEX eluate was subsequently concentrated to a concentration of 40
15 g/L and diafiltrated over six dia-volumes to exchange the buffer to a final composition of a buffer concentration within 5-50 mM using histidine, acetate, citrate, phosphate, tris or succinate buffer system at a pH between 4.5 and 7.5, respectively. Through formulation exchange, Trastuzumab was transferred into test groups, encompassing with the component concentration varied from 30 mM to 300 mM, incorporating one of the viscosity-reducing and stabilizing formulations, shown
20 in Tables 37-54. Furthermore, there was a control group (i.e., positive control) comprising 25 mM phosphate buffer at pH 6.0, with 81.2 mM Nicotinic acid and 29.4 mM Tryptophan (matching the lead formulation 25 mM phosphate buffer at pH 6.0 along with 10 mg/mL Nicotinic acid (acid form) and 6 mg/mL Tryptophan from Examples 14, 16, 17, 18, 19, 20 and 21 in WO2018211517). An additional control group solely consisted of MilliQ water and the protein as blank control. The
25 formulation containing Trastuzumab was subsequently concentrated to 100-300 mg/mL (e.g., 100, 200, or 300 mg/mL) using an Eppendorf centrifuge with a concentration variation of 3%. To ascertain Trastuzumab's concentration in the groups, absorbance at 280 nm combined with SE-UPLC was gauged against corresponding buffers containing a viscosity-reducing and stabilizing agent for excipient-containing samples, and absorbance at 280 nm was measured for the protein
30 solution without a viscosity-reducing and stabilizing formulation. For Trastuzumab without

excipients, the buffer alone (i.e., devoid of excipients) served as a blank for protein concentration calculation. The extinction coefficient was measured at $1.48 \text{ (mg/mL)}^{-1} \cdot \text{cm}^{-1}$.

[0080] The viscosity of samples was measured by VROC® initium one plus viscometer (Rheosense) at 20°C. For samples with a viscosity exceeding 1000 cP, viscosity was measured
5 using a TA rheometer.

[0081] As shown in Tables 37-54, the data in demonstrated the viscosity reducing effect of the viscosity-reducing and stabilizing formulations of the present application on Trastuzumab in different buffers: histidine (pH 5.0 to 7.0), acetate (pH 4.5 to 6.0), citrate (pH 4.5 to 6.0), phosphate (pH 6.5 to 7.5), Tris (pH 6.5 to 7.5), and succinate (pH 4.5 to 6.0) Buffer. As for Trastuzumab at
10 a concentration from 100 to 300 mg/mL, the tested viscosity-reducing and stabilizing formulations exhibited superior viscosity reduction when compared with the reference lead formulation of WO2018211517 and excipient-free samples.

Table 37 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 5 mM Histidine buffer, at pH 5.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	522.7
300	30 mM Histidine and 30 mM Niacin	368.1
300	30 mM Meglumine and 30 mM Niacin	508.9
300	30 mM Lysine and 30 mM Niacin	497.8
300	30 mM Arginine·HCl and 30 mM Niacinamide	387.4
300	30 mM Histidine and 30 mM Niacinamide	585.2
300	30 mM Meglumine and 30 mM Niacinamide	395.6
300	30 mM Lysine·HCl and 30 mM Niacinamide	423.9
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	30 mM Arginine and 30 mM Niacin	25.1
200	30 mM Histidine and 30 mM Niacin	26.4
200	30 mM Meglumine and 30 mM Niacin	25.1
200	30 mM Lysine and 30 mM Niacin	23.2
200	30 mM Arginine·HCl and 30 mM Niacinamide	20.2
200	30 mM Histidine and 30 mM Niacinamide	24.0
200	30 mM Meglumine and 30 mM Niacinamide	23.7
200	30 mM Lysine·HCl and 30 mM Niacinamide	24.6
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	30 mM Arginine and 30 mM Niacin	2.3
100	30 mM Histidine and 30 mM Niacin	2.2
100	30 mM Meglumine and 30 mM Niacin	2.3
100	30 mM Lysine and 30 mM Niacin	2.3
100	30 mM Arginine·HCl and 30 mM Niacinamide	2.1
100	30 mM Histidine and 30 mM Niacinamide	2.3
100	30 mM Meglumine and 30 mM Niacinamide	2.3
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Table 38 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 20 mM Histidine buffer, pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	426.4
300	140 mM Histidine and 140 mM Niacin	359.1
300	140 mM Meglumine and 140 mM Niacin	439.1
300	140 mM Lysine and 140 mM Niacin	408.1
300	70 mM Arginine·HCl and 140 mM Niacinamide	319.9
300	140 mM Histidine and 140 mM Niacinamide	475.8
300	140 mM Meglumine and 140 mM Niacinamide	348.1
300	70 mM Lysine·HCl and 140 mM Niacinamide	385.9
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	140 mM Arginine and 140 mM Niacin	22.7
200	140 mM Histidine and 140 mM Niacin	21.2
200	140 mM Meglumine and 140 mM Niacin	24.3
200	140 mM Lysine and 140 mM Niacin	22.1
200	70 mM Arginine·HCl and 140 mM Niacinamide	19.6
200	140 mM Histidine and 140 mM Niacinamide	23.3
200	140 mM Meglumine and 140 mM Niacinamide	20.9
200	70 mM Lysine·HCl and 140 mM Niacinamide	23.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	140 mM Arginine and 140 mM Niacin	2.3
100	140 mM Histidine and 140 mM Niacin	2.2
100	140 mM Meglumine and 140 mM Niacin	2.2
100	140 mM Lysine and 140 mM Niacin	2.0
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.9
100	140 mM Histidine and 140 mM Niacinamide	2.1
100	140 mM Meglumine and 140 mM Niacinamide	2.3
100	70 mM Lysine·HCl and 140 mM Niacinamide	2.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Table 39 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 50 mM Histidine buffer, at pH 7.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	365.9
300	300 mM Histidine and 300 mM Niacin	296.2
300	300 mM Meglumine and 300 mM Niacin	343.4
300	300 mM Lysine and 300 mM Niacin	315.6
300	140 mM Arginine·HCl and 300 mM Niacinamide	205.1
300	300 mM Histidine and 300 mM Niacinamide	401.7
300	300 mM Meglumine and 300 mM Niacinamide	292.9
300	140 mM Lysine·HCl and 300 mM Niacinamide	308.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	300 mM Arginine and 300 mM Niacin	20.5
200	300 mM Histidine and 300 mM Niacin	19.8
200	300 mM Meglumine and 300 mM Niacin	22.8
200	300 mM Lysine and 300 mM Niacin	20.5
200	140 mM Arginine·HCl and 300 mM Niacinamide	17.7
200	300 mM Histidine and 300 mM Niacinamide	22.2
200	300 mM Meglumine and 300 mM Niacinamide	19.8
200	140 mM Lysine·HCl and 300 mM Niacinamide	22.5
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	300 mM Arginine and 300 mM Niacin	2.1
100	300 mM Histidine and 300 mM Niacin	2.2
100	300 mM Meglumine and 300 mM Niacin	2.0
100	300 mM Lysine and 300 mM Niacin	1.8
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.7
100	300 mM Histidine and 300 mM Niacinamide	1.9
100	300 mM Meglumine and 300 mM Niacinamide	2.2
100	140 mM Lysine·HCl and 300 mM Niacinamide	1.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Table 40 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 5 mM Acetate buffer, pH 4.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	510.2
300	30 mM Histidine and 30 mM Niacin	442.6
300	30 mM Meglumine and 30 mM Niacin	505.4
300	30 mM Lysine and 30 mM Niacin	485.1
300	30 mM Arginine·HCl and 30 mM Niacinamide	398.8
300	30 mM Histidine and 30 mM Niacinamide	514.3
300	30 mM Meglumine and 30 mM Niacinamide	461.9
300	30 mM Lysine·HCl and 30 mM Niacinamide	479.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	30 mM Arginine and 30 mM Niacin	26.1
200	30 mM Histidine and 30 mM Niacin	25.8
200	30 mM Meglumine and 30 mM Niacin	26.0
200	30 mM Lysine and 30 mM Niacin	24.0
200	30 mM Arginine·HCl and 30 mM Niacinamide	21.9
200	30 mM Histidine and 30 mM Niacinamide	24.5
200	30 mM Meglumine and 30 mM Niacinamide	24.2
200	30 mM Lysine·HCl and 30 mM Niacinamide	25.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	30 mM Arginine and 30 mM Niacin	2.3
100	30 mM Histidine and 30 mM Niacin	2.2
100	30 mM Meglumine and 30 mM Niacin	2.1
100	30 mM Lysine and 30 mM Niacin	2.1
100	30 mM Arginine·HCl and 30 mM Niacinamide	2.2
100	30 mM Histidine and 30 mM Niacinamide	2.3
100	30 mM Meglumine and 30 mM Niacinamide	2.3
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Table 41 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 20 mM Acetate buffer, at pH 5.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	452.7
300	140 mM Histidine and 140 mM Niacin	401.5
300	140 mM Meglumine and 140 mM Niacin	446.8
300	140 mM Lysine and 140 mM Niacin	415.2
300	70 mM Arginine·HCl and 140 mM Niacinamide	339.7
300	140 mM Histidine and 140 mM Niacinamide	413.1
300	140 mM Meglumine and 140 mM Niacinamide	389.8
300	70 mM Lysine·HCl and 140 mM Niacinamide	407.2
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	140 mM Arginine and 140 mM Niacin	24.5
200	140 mM Histidine and 140 mM Niacin	24.2
200	140 mM Meglumine and 140 mM Niacin	25.0
200	140 mM Lysine and 140 mM Niacin	22.8
200	70 mM Arginine·HCl and 140 mM Niacinamide	21.1
200	140 mM Histidine and 140 mM Niacinamide	23.9
200	140 mM Meglumine and 140 mM Niacinamide	23.6
200	70 mM Lysine·HCl and 140 mM Niacinamide	24.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	140 mM Arginine and 140 mM Niacin	2.3
100	140 mM Histidine and 140 mM Niacin	2.1
100	140 mM Meglumine and 140 mM Niacin	2.0
100	140 mM Lysine and 140 mM Niacin	2.0
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.8
100	140 mM Histidine and 140 mM Niacinamide	2.0
100	140 mM Meglumine and 140 mM Niacinamide	2.0
100	70 mM Lysine·HCl and 140 mM Niacinamide	2.3
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Table 42 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 50 mM Acetate buffer, at pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	425.3
300	300 mM Histidine and 300 mM Niacin	353.7
300	300 mM Meglumine and 300 mM Niacin	408.2
300	300 mM Lysine and 300 mM Niacin	416.4
300	140 mM Arginine·HCl and 300 mM Niacinamide	300.8
300	300 mM Histidine and 300 mM Niacinamide	325.2
300	300 mM Meglumine and 300 mM Niacinamide	349.4
300	140 mM Lysine·HCl and 300 mM Niacinamide	358.6
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	300 mM Arginine and 300 mM Niacin	23.8
200	300 mM Histidine and 300 mM Niacin	23.5
200	300 mM Meglumine and 300 mM Niacin	24.2
200	300 mM Lysine and 300 mM Niacin	22.1
200	140 mM Arginine·HCl and 300 mM Niacinamide	20.6
200	300 mM Histidine and 300 mM Niacinamide	23.4
200	300 mM Meglumine and 300 mM Niacinamide	23.1
200	140 mM Lysine·HCl and 300 mM Niacinamide	23.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	300 mM Arginine and 300 mM Niacin	1.9
100	300 mM Histidine and 300 mM Niacin	2.0
100	300 mM Meglumine and 300 mM Niacin	1.9
100	300 mM Lysine and 300 mM Niacin	1.8
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.7
100	300 mM Histidine and 300 mM Niacinamide	1.9
100	300 mM Meglumine and 300 mM Niacinamide	1.9
100	140 mM Lysine·HCl and 300 mM Niacinamide	2.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Table 43 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 5 mM Citrate buffer, at pH 4.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	427.1
300	30 mM Histidine and 30 mM Niacin	485.5
300	30 mM Meglumine and 30 mM Niacin	548.2
300	30 mM Lysine and 30 mM Niacin	425.6
300	30 mM Arginine·HCl and 30 mM Niacinamide	402.4
300	30 mM Histidine and 30 mM Niacinamide	528.9
300	30 mM Meglumine and 30 mM Niacinamide	578.2
300	30 mM Lysine·HCl and 30 mM Niacinamide	464.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	30 mM Arginine and 30 mM Niacin	23.5
200	30 mM Histidine and 30 mM Niacin	25.7
200	30 mM Meglumine and 30 mM Niacin	26.1
200	30 mM Lysine and 30 mM Niacin	23.3
200	30 mM Arginine·HCl and 30 mM Niacinamide	22.5
200	30 mM Histidine and 30 mM Niacinamide	25.7
200	30 mM Meglumine and 30 mM Niacinamide	26.2
200	30 mM Lysine·HCl and 30 mM Niacinamide	23.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	30 mM Arginine and 30 mM Niacin	2.1
100	30 mM Histidine and 30 mM Niacin	2.3
100	30 mM Meglumine and 30 mM Niacin	2.3
100	30 mM Lysine and 30 mM Niacin	2.2
100	30 mM Arginine·HCl and 30 mM Niacinamide	1.9
100	30 mM Histidine and 30 mM Niacinamide	2.2
100	30 mM Meglumine and 30 mM Niacinamide	2.3
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Table 44 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 20 mM Citrate buffer, pH 5.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	328.4
300	140 mM Histidine and 140 mM Niacin	345.8
300	140 mM Meglumine and 140 mM Niacin	398.1
300	140 mM Lysine and 140 mM Niacin	361.8
300	70 mM Arginine·HCl and 140 mM Niacinamide	299.0
300	140 mM Histidine and 140 mM Niacinamide	448.2
300	140 mM Meglumine and 140 mM Niacinamide	455.7
300	70 mM Lysine·HCl and 140 mM Niacinamide	357.4
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	140 mM Arginine and 140 mM Niacin	17.5
200	140 mM Histidine and 140 mM Niacin	20.1
200	140 mM Meglumine and 140 mM Niacin	23.2
200	140 mM Lysine and 140 mM Niacin	19.0
200	70 mM Arginine·HCl and 140 mM Niacinamide	16.2
200	140 mM Histidine and 140 mM Niacinamide	19.2
200	140 mM Meglumine and 140 mM Niacinamide	23.8
200	70 mM Lysine·HCl and 140 mM Niacinamide	18.5
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	140 mM Arginine and 140 mM Niacin	1.9
100	140 mM Histidine and 140 mM Niacin	2.0
100	140 mM Meglumine and 140 mM Niacin	2.1
100	140 mM Lysine and 140 mM Niacin	1.9
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.7
100	140 mM Histidine and 140 mM Niacinamide	1.8
100	140 mM Meglumine and 140 mM Niacinamide	2.1
100	70 mM Lysine·HCl and 140 mM Niacinamide	1.8
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Table 45 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 50 mM Citrate buffer, at pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	301.2
300	300 mM Histidine and 300 mM Niacin	331.4
300	300 mM Meglumine and 300 mM Niacin	346.8
300	300 mM Lysine and 300 mM Niacin	321.6
300	140 mM Arginine·HCl and 300 mM Niacinamide	247.5
300	300 mM Histidine and 300 mM Niacinamide	358.1
300	300 mM Meglumine and 300 mM Niacinamide	375.0
300	140 mM Lysine·HCl and 300 mM Niacinamide	277.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	300 mM Arginine and 300 mM Niacin	17.5
200	300 mM Histidine and 300 mM Niacin	20.1
200	300 mM Meglumine and 300 mM Niacin	23.2
200	300 mM Lysine and 300 mM Niacin	19.0
200	140 mM Arginine·HCl and 300 mM Niacinamide	11.2
200	300 mM Histidine and 300 mM Niacinamide	19.2
200	300 mM Meglumine and 300 mM Niacinamide	23.8
200	140 mM Lysine·HCl and 300 mM Niacinamide	12.5
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	300 mM Arginine and 300 mM Niacin	1.5
100	300 mM Histidine and 300 mM Niacin	1.8
100	300 mM Meglumine and 300 mM Niacin	1.9
100	300 mM Lysine and 300 mM Niacin	1.6
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.4
100	300 mM Histidine and 300 mM Niacinamide	1.7
100	300 mM Meglumine and 300 mM Niacinamide	1.8
100	140 mM Lysine·HCl and 300 mM Niacinamide	1.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Table 46 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 5 mM Phosphate buffer, pH 6.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	449.2
300	30 mM Histidine and 30 mM Niacin	486.6
300	30 mM Meglumine and 30 mM Niacin	515.7
300	30 mM Lysine and 30 mM Niacin	441.9
300	30 mM Arginine·HCl and 30 mM Niacinamide	431.6
300	30 mM Histidine and 30 mM Niacinamide	598.1
300	30 mM Meglumine and 30 mM Niacinamide	574.6
300	30 mM Lysine·HCl and 30 mM Niacinamide	461.7
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	30 mM Arginine and 30 mM Niacin	24.1
200	30 mM Histidine and 30 mM Niacin	25.5
200	30 mM Meglumine and 30 mM Niacin	25.8
200	30 mM Lysine and 30 mM Niacin	24.5
200	30 mM Arginine·HCl and 30 mM Niacinamide	23.1
200	30 mM Histidine and 30 mM Niacinamide	26.4
200	30 mM Meglumine and 30 mM Niacinamide	25.1
200	30 mM Lysine·HCl and 30 mM Niacinamide	22.5
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	30 mM Arginine and 30 mM Niacin	2.2
100	30 mM Histidine and 30 mM Niacin	2.3
100	30 mM Meglumine and 30 mM Niacin	2.3
100	30 mM Lysine and 30 mM Niacin	2.1
100	30 mM Arginine·HCl and 30 mM Niacinamide	2.0
100	30 mM Histidine and 30 mM Niacinamide	2.2
100	30 mM Meglumine and 30 mM Niacinamide	2.3
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Table 47 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 20 mM Phosphate buffer, at pH 7.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	384.1
300	140 mM Histidine and 140 mM Niacin	401.7
300	140 mM Meglumine and 140 mM Niacin	452.9
300	140 mM Lysine and 140 mM Niacin	367.1
300	70 mM Arginine·HCl and 140 mM Niacinamide	331.7
300	140 mM Histidine and 140 mM Niacinamide	466.1
300	140 mM Meglumine and 140 mM Niacinamide	415.7
300	70 mM Lysine·HCl and 140 mM Niacinamide	361.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	140 mM Arginine and 140 mM Niacin	19.5
200	140 mM Histidine and 140 mM Niacin	24.4
200	140 mM Meglumine and 140 mM Niacin	24.7
200	140 mM Lysine and 140 mM Niacin	23.6
200	70 mM Arginine·HCl and 140 mM Niacinamide	13.1
200	140 mM Histidine and 140 mM Niacinamide	19.4
200	140 mM Meglumine and 140 mM Niacinamide	21.1
200	70 mM Lysine·HCl and 140 mM Niacinamide	18.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	140 mM Arginine and 140 mM Niacin	1.8
100	140 mM Histidine and 140 mM Niacin	2.0
100	140 mM Meglumine and 140 mM Niacin	2.2
100	140 mM Lysine and 140 mM Niacin	1.9
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.6
100	140 mM Histidine and 140 mM Niacinamide	2.2
100	140 mM Meglumine and 140 mM Niacinamide	2.2
100	70 mM Lysine·HCl and 140 mM Niacinamide	1.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Table 48 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 50 mM Phosphate buffer, at pH 7.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	306.2
300	300 mM Histidine and 300 mM Niacin	371.8
300	300 mM Meglumine and 300 mM Niacin	355.2
300	300 mM Lysine and 300 mM Niacin	305.2
300	140 mM Arginine·HCl and 300 mM Niacinamide	261.6
300	300 mM Histidine and 300 mM Niacinamide	351.6
300	300 mM Meglumine and 300 mM Niacinamide	567.1
300	140 mM Lysine·HCl and 300 mM Niacinamide	300.4
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	300 mM Arginine and 300 mM Niacin	16.2
200	300 mM Histidine and 300 mM Niacin	19.7
200	300 mM Meglumine and 300 mM Niacin	21.2
200	300 mM Lysine and 300 mM Niacin	18.4
200	140 mM Arginine·HCl and 300 mM Niacinamide	9.8
200	300 mM Histidine and 300 mM Niacinamide	15.4
200	300 mM Meglumine and 300 mM Niacinamide	22.5
200	140 mM Lysine·HCl and 300 mM Niacinamide	16.2
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	300 mM Arginine and 300 mM Niacin	1.5
100	300 mM Histidine and 300 mM Niacin	1.9
100	300 mM Meglumine and 300 mM Niacin	2.0
100	300 mM Lysine and 300 mM Niacin	1.7
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.4
100	300 mM Histidine and 300 mM Niacinamide	2.0
100	300 mM Meglumine and 300 mM Niacinamide	2.3
100	140 mM Lysine·HCl and 300 mM Niacinamide	1.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Table 49 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 5 mM Tris buffer, at pH 6.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	453.8
300	30 mM Histidine and 30 mM Niacin	492.3
300	30 mM Meglumine and 30 mM Niacin	522.1
300	30 mM Lysine and 30 mM Niacin	448.5
300	30 mM Arginine·HCl and 30 mM Niacinamide	438.9
300	30 mM Histidine and 30 mM Niacinamide	605.7
300	30 mM Meglumine and 30 mM Niacinamide	581.2
300	30 mM Lysine·HCl and 30 mM Niacinamide	468.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	30 mM Arginine and 30 mM Niacin	24.8
200	30 mM Histidine and 30 mM Niacin	26.1
200	30 mM Meglumine and 30 mM Niacin	26.3
200	30 mM Lysine and 30 mM Niacin	25.1
200	30 mM Arginine·HCl and 30 mM Niacinamide	23.7
200	30 mM Histidine and 30 mM Niacinamide	26.0
200	30 mM Meglumine and 30 mM Niacinamide	25.7
200	30 mM Lysine·HCl and 30 mM Niacinamide	23.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	30 mM Arginine and 30 mM Niacin	2.3
100	30 mM Histidine and 30 mM Niacin	2.2
100	30 mM Meglumine and 30 mM Niacin	2.3
100	30 mM Lysine and 30 mM Niacin	2.2
100	30 mM Arginine·HCl and 30 mM Niacinamide	2.1
100	30 mM Histidine and 30 mM Niacinamide	2.2
100	30 mM Meglumine and 30 mM Niacinamide	2.3
100	30 mM Lysine·HCl and 30 mM Niacinamide	1.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Table 50 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 20 mM Tris buffer, pH 7.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	389.3
300	140 mM Histidine and 140 mM Niacin	406.5
300	140 mM Meglumine and 140 mM Niacin	459.2
300	140 mM Lysine and 140 mM Niacin	372.4
300	70 mM Arginine·HCl and 140 mM Niacinamide	336.2
300	140 mM Histidine and 140 mM Niacinamide	471.8
300	140 mM Meglumine and 140 mM Niacinamide	421.3
300	70 mM Lysine·HCl and 140 mM Niacinamide	366.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	140 mM Arginine and 140 mM Niacin	20.2
200	140 mM Histidine and 140 mM Niacin	24.9
200	140 mM Meglumine and 140 mM Niacin	25.2
200	140 mM Lysine and 140 mM Niacin	24.1
200	70 mM Arginine·HCl and 140 mM Niacinamide	13.6
200	140 mM Histidine and 140 mM Niacinamide	19.9
200	140 mM Meglumine and 140 mM Niacinamide	21.6
200	70 mM Lysine·HCl and 140 mM Niacinamide	19.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	140 mM Arginine and 140 mM Niacin	1.9
100	140 mM Histidine and 140 mM Niacin	2.1
100	140 mM Meglumine and 140 mM Niacin	2.3
100	140 mM Lysine and 140 mM Niacin	2.0
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.7
100	140 mM Histidine and 140 mM Niacinamide	2.3
100	140 mM Meglumine and 140 mM Niacinamide	2.3
100	70 mM Lysine·HCl and 140 mM Niacinamide	2.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Table 51 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 50 mM Tris buffer, at pH 7.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	310.7
300	300 mM Histidine and 300 mM Niacin	376.5
300	300 mM Meglumine and 300 mM Niacin	359.8
300	300 mM Lysine and 300 mM Niacin	310.3
300	140 mM Arginine·HCl and 300 mM Niacinamide	266.1
300	300 mM Histidine and 300 mM Niacinamide	357.2
300	300 mM Meglumine and 300 mM Niacinamide	573.8
300	140 mM Lysine·HCl and 300 mM Niacinamide	305.9
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	300 mM Arginine and 300 mM Niacin	16.8
200	300 mM Histidine and 300 mM Niacin	20.2
200	300 mM Meglumine and 300 mM Niacin	21.7
200	300 mM Lysine and 300 mM Niacin	18.9
200	140 mM Arginine·HCl and 300 mM Niacinamide	10.3
200	300 mM Histidine and 300 mM Niacinamide	15.9
200	300 mM Meglumine and 300 mM Niacinamide	23.0
200	140 mM Lysine·HCl and 300 mM Niacinamide	16.7
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	300 mM Arginine and 300 mM Niacin	1.6
100	300 mM Histidine and 300 mM Niacin	2.0
100	300 mM Meglumine and 300 mM Niacin	2.1
100	300 mM Lysine and 300 mM Niacin	1.8
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.5
100	300 mM Histidine and 300 mM Niacinamide	2.1
100	300 mM Meglumine and 300 mM Niacinamide	2.3
100	140 mM Lysine·HCl and 300 mM Niacinamide	1.7
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Table 52 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 5 mM Succinate buffer, pH 4.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	432.3
300	30 mM Histidine and 30 mM Niacin	491.2
300	30 mM Meglumine and 30 mM Niacin	554.7
300	30 mM Lysine and 30 mM Niacin	430.9
300	30 mM Arginine·HCl and 30 mM Niacinamide	408.8
300	30 mM Histidine and 30 mM Niacinamide	535.4
300	30 mM Meglumine and 30 mM Niacinamide	584.9
300	30 mM Lysine·HCl and 30 mM Niacinamide	470.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	30 mM Arginine and 30 mM Niacin	24.0
200	30 mM Histidine and 30 mM Niacin	26.2
200	30 mM Meglumine and 30 mM Niacin	26.2
200	30 mM Lysine and 30 mM Niacin	23.8
200	30 mM Arginine·HCl and 30 mM Niacinamide	23.0
200	30 mM Histidine and 30 mM Niacinamide	26.2
200	30 mM Meglumine and 30 mM Niacinamide	26.3
200	30 mM Lysine·HCl and 30 mM Niacinamide	23.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	30 mM Arginine and 30 mM Niacin	2.2
100	30 mM Histidine and 30 mM Niacin	2.3
100	30 mM Meglumine and 30 mM Niacin	2.3
100	30 mM Lysine and 30 mM Niacin	2.3
100	30 mM Arginine·HCl and 30 mM Niacinamide	2.0
100	30 mM Histidine and 30 mM Niacinamide	2.3
100	30 mM Meglumine and 30 mM Niacinamide	2.2
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Table 53 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 20 mM Succinate buffer, at pH 5.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	333.1
300	140 mM Histidine and 140 mM Niacin	351.4
300	140 mM Meglumine and 140 mM Niacin	404.3
300	140 mM Lysine and 140 mM Niacin	367.2
300	70 mM Arginine·HCl and 140 mM Niacinamide	304.7
300	140 mM Histidine and 140 mM Niacinamide	454.1
300	140 mM Meglumine and 140 mM Niacinamide	461.8
300	70 mM Lysine·HCl and 140 mM Niacinamide	362.9
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	140 mM Arginine and 140 mM Niacin	18.0
200	140 mM Histidine and 140 mM Niacin	20.6
200	140 mM Meglumine and 140 mM Niacin	23.7
200	140 mM Lysine and 140 mM Niacin	19.5
200	70 mM Arginine·HCl and 140 mM Niacinamide	16.7
200	140 mM Histidine and 140 mM Niacinamide	19.7
200	140 mM Meglumine and 140 mM Niacinamide	24.3
200	70 mM Lysine·HCl and 140 mM Niacinamide	19.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	140 mM Arginine and 140 mM Niacin	2.0
100	140 mM Histidine and 140 mM Niacin	2.1
100	140 mM Meglumine and 140 mM Niacin	2.2
100	140 mM Lysine and 140 mM Niacin	2.0
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.8
100	140 mM Histidine and 140 mM Niacinamide	1.9
100	140 mM Meglumine and 140 mM Niacinamide	2.2
100	70 mM Lysine·HCl and 140 mM Niacinamide	1.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Table 54 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab in 50 mM Succinate buffer, at pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	306.5
300	300 mM Histidine and 300 mM Niacin	336.2
300	300 mM Meglumine and 300 mM Niacin	352.1
300	300 mM Lysine and 300 mM Niacin	326.4
300	140 mM Arginine·HCl and 300 mM Niacinamide	253.0
300	300 mM Histidine and 300 mM Niacinamide	364.5
300	300 mM Meglumine and 300 mM Niacinamide	380.9
300	140 mM Lysine·HCl and 300 mM Niacinamide	282.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	626.7
300	Water (Blank)	910.1
200	300 mM Arginine and 300 mM Niacin	18.0
200	300 mM Histidine and 300 mM Niacin	20.6
200	300 mM Meglumine and 300 mM Niacin	23.7
200	300 mM Lysine and 300 mM Niacin	19.5
200	140 mM Arginine·HCl and 300 mM Niacinamide	11.8
200	300 mM Histidine and 300 mM Niacinamide	19.7
200	300 mM Meglumine and 300 mM Niacinamide	24.3
200	140 mM Lysine·HCl and 300 mM Niacinamide	13.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	26.5
200	Water (blank)	38.8
100	300 mM Arginine and 300 mM Niacin	1.6
100	300 mM Histidine and 300 mM Niacin	1.9
100	300 mM Meglumine and 300 mM Niacin	2.0
100	300 mM Lysine and 300 mM Niacin	1.7
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.5
100	300 mM Histidine and 300 mM Niacinamide	1.8
100	300 mM Meglumine and 300 mM Niacinamide	1.9
100	140 mM Lysine·HCl and 300 mM Niacinamide	1.7
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.4
100	Water (blank)	3.6

Example 4: Viscosity reducing effect of viscosity-reducing and stabilizing formulations on ADC (Trastuzumab-MMAE, DAR8 Cysteine conjugated) solutions in various buffers at 20°C.

[0082] This example tested the viscosity reducing effect of viscosity-reducing and stabilizing formulations of the present application on Trastuzumab-MMAE solutions.

[0083] Materials and Methods

[0084] Trastuzumab-MMAE is an ADC. Trastuzumab (Herceptin®) is a commercially available mAb. In this example, it was produced by WuXi Biologics based on its sequence was sourced from Drug Bank (DB00072). The recombinant cell culture fermentation was harvested by centrifugation, and the resulting filtrate pool was loaded onto a Protein A column. The target protein was eluted at pH 3.8 and subsequently neutralized to pH 5.5 using 1 M Tris base. The eluate then underwent depth filtration and was passed through a 0.2 µm filter. The intermediate filtration pool was loaded onto an AEX (Anion Exchange) column in flow-through mode. Following this step, the AEX flow-through pool was further processed on a CEX (Cation Exchange) column, and the target protein was eluted using a linear gradient elution. The CEX eluate was subsequently concentrated to a concentration of 40 g/L and diafiltrated over six dia-

10 volumes to exchange the buffer to a final composition of 20 mM histidine at pH 6.0. MC-VC-PAB-MMAE was purchased from WuXi STA. ADC material is prepared in a one-pot reaction: A 5 mM TCEP stock solution (TCEP/Trastuzumab mole ratio = 6.0) was added to the Trastuzumab solution, and the reaction mixture was incubated in a shaker at 200 rpm and 30°C for 2 hours.

20 Subsequently, a 10 mg/mL linker-drug stock solution (MC-VC-PAB-MMAE/Trastuzumab mole ratio = 11.0 in DMA) was added, and the reaction was continued under the same conditions (200 rpm, 30°C) for an additional 2 hours. The quench was conducted using 100 mM L-cysteine solution (L-cysteine/Trastuzumab mole ratio = 20) for 1 hour at 200 rpm, 30°C. The reaction

25 mixture was then purified using a Thermo Zeba™ Spin Desalting Column (40K, 0.5 mL), yielding the final product: Trastuzumab-MMAE conjugate (DAR 8). Through buffer exchange, Trastuzumab-MMAE conjugate was transferred into a final buffer composition with concentrations ranging from 5 to 50 mM, using histidine, acetate, citrate, phosphate, tris or succinate buffer system at a pH between 4.5 and 7.5, respectively, and into one of the viscosity-

30 reducing and stabilizing formulations with the component concentrations varying from 30 mM to

300 mM, as shown in Tables 55-72. Furthermore, there was a control group (i.e., positive control) comprising 25 mM phosphate buffer at pH 6.0, with 81.2 mM Nicotinic acid and 29.4 mM Tryptophan (matching the lead formulation 25 mM phosphate buffer at pH 6.0 along with 10 mg/mL Nicotinic acid (acid form) and 6 mg/mL Tryptophan from Examples 14, 16, 17, 18, 19, 20 and 21 in WO2018211517). An additional control group solely consisted of MilliQ water and the ADC product as blank control. The formulation containing Trastuzumab-MMAE was subsequently concentrated to 100-300 mg/mL (e.g., 100, 200, or 300 mg/mL) using an Eppendorf centrifuge with a concentration variation of 3%. To ascertain Trastuzumab-MMAE concentration in the groups, absorbance at 280 nm combined with SE-UPLC was gauged against corresponding buffers containing a viscosity-reducing and stabilizing agent for excipient-containing samples, and absorbance at 280 nm was measured for the Trastuzumab-MMAE solution without a viscosity-reducing and stabilizing formulation. For Trastuzumab-MMAE without excipients, the buffer alone (i.e., devoid of excipients) served as a blank for protein concentration calculation. The extinction coefficient was measured at $1.48 \text{ (mg/mL)}^{-1} \cdot \text{cm}^{-1}$.

[0085] The viscosity of samples was measured by VROC® initium one plus viscometer (Rheosense) at 20°C. For samples with a viscosity exceeding 1000 cP, viscosity was measured using a TA rheometer.

[0086] As shown in Tables 55-72, the data demonstrated the viscosity reducing effect of the viscosity-reducing and stabilizing formulations of the present application on Trastuzumab-MMAE in different buffers: histidine (pH 5.0 to 7.0), acetate (pH 4.5 to 6.0), citrate (pH 4.5 to 6.0), phosphate (pH 6.5 to 7.5), Tris (pH 6.5 to 7.5), and succinate (pH 4.5 to 6.0) Buffer. As for Trastuzumab-MMAE at a concentration from 100 to 300 mg/mL, the tested viscosity-reducing and stabilizing formulations exhibited superior viscosity reduction when compared to the reference lead formulation from WO2018211517 and excipient-free samples.

25

Table 55 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 5 mM Histidine buffer, at pH 5.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	528.1
300	30 mM Histidine and 30 mM Niacin	374.2
300	30 mM Meglumine and 30 mM Niacin	514.6
300	30 mM Lysine and 30 mM Niacin	505.3
300	30 mM Arginine·HCl and 30 mM Niacinamide	392.7
300	30 mM Histidine and 30 mM Niacinamide	594.8
300	30 mM Meglumine and 30 mM Niacinamide	400.5
300	30 mM Lysine·HCl and 30 mM Niacinamide	429.7
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	30 mM Arginine and 30 mM Niacin	25.7
200	30 mM Histidine and 30 mM Niacin	27.0
200	30 mM Meglumine and 30 mM Niacin	25.6
200	30 mM Lysine and 30 mM Niacin	23.6
200	30 mM Arginine·HCl and 30 mM Niacinamide	20.5
200	30 mM Histidine and 30 mM Niacinamide	24.3
200	30 mM Meglumine and 30 mM Niacinamide	24.1
200	30 mM Lysine·HCl and 30 mM Niacinamide	25.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	30 mM Arginine and 30 mM Niacin	2.5
100	30 mM Histidine and 30 mM Niacin	2.5
100	30 mM Meglumine and 30 mM Niacin	2.4
100	30 mM Lysine and 30 mM Niacin	2.4
100	30 mM Arginine·HCl and 30 mM Niacinamide	2.2
100	30 mM Histidine and 30 mM Niacinamide	2.4
100	30 mM Meglumine and 30 mM Niacinamide	2.5
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.5
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Table 56 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 20 mM Histidine buffer, pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	431.8
300	140 mM Histidine and 140 mM Niacin	364.5
300	140 mM Meglumine and 140 mM Niacin	445.2
300	140 mM Lysine and 140 mM Niacin	412.4
300	70 mM Arginine·HCl and 140 mM Niacinamide	324.1
300	140 mM Histidine and 140 mM Niacinamide	482.3
300	140 mM Meglumine and 140 mM Niacinamide	353.7
300	70 mM Lysine·HCl and 140 mM Niacinamide	391.2
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	140 mM Arginine and 140 mM Niacin	23.1
200	140 mM Histidine and 140 mM Niacin	21.5
200	140 mM Meglumine and 140 mM Niacin	24.6
200	140 mM Lysine and 140 mM Niacin	22.4
200	70 mM Arginine·HCl and 140 mM Niacinamide	19.9
200	140 mM Histidine and 140 mM Niacinamide	23.5
200	140 mM Meglumine and 140 mM Niacinamide	21.2
200	70 mM Lysine·HCl and 140 mM Niacinamide	24.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	140 mM Arginine and 140 mM Niacin	2.4
100	140 mM Histidine and 140 mM Niacin	2.3
100	140 mM Meglumine and 140 mM Niacin	2.3
100	140 mM Lysine and 140 mM Niacin	2.1
100	70 mM Arginine·HCl and 140 mM Niacinamide	2.0
100	140 mM Histidine and 140 mM Niacinamide	2.2
100	140 mM Meglumine and 140 mM Niacinamide	2.4
100	70 mM Lysine·HCl and 140 mM Niacinamide	2.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Table 57 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 50 mM Histidine buffer, at pH 7.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	370.2
300	300 mM Histidine and 300 mM Niacin	302.5
300	300 mM Meglumine and 300 mM Niacin	348.7
300	300 mM Lysine and 300 mM Niacin	321.0
300	140 mM Arginine·HCl and 300 mM Niacinamide	210.4
300	300 mM Histidine and 300 mM Niacinamide	410.5
300	300 mM Meglumine and 300 mM Niacinamide	298.3
300	140 mM Lysine·HCl and 300 mM Niacinamide	315.4
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	300 mM Arginine and 300 mM Niacin	21.0
200	300 mM Histidine and 300 mM Niacin	20.2
200	300 mM Meglumine and 300 mM Niacin	23.0
200	300 mM Lysine and 300 mM Niacin	21.0
200	140 mM Arginine·HCl and 300 mM Niacinamide	18.0
200	300 mM Histidine and 300 mM Niacinamide	22.5
200	300 mM Meglumine and 300 mM Niacinamide	20.1
200	140 mM Lysine·HCl and 300 mM Niacinamide	23.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	300 mM Arginine and 300 mM Niacin	2.2
100	300 mM Histidine and 300 mM Niacin	2.3
100	300 mM Meglumine and 300 mM Niacin	2.1
100	300 mM Lysine and 300 mM Niacin	1.9
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.8
100	300 mM Histidine and 300 mM Niacinamide	2.0
100	300 mM Meglumine and 300 mM Niacinamide	2.3
100	140 mM Lysine·HCl and 300 mM Niacinamide	2.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Table 58 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 5 mM Acetate buffer, pH 4.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	515.6
300	30 mM Histidine and 30 mM Niacin	448.3
300	30 mM Meglumine and 30 mM Niacin	510.1
300	30 mM Lysine and 30 mM Niacin	490.6
300	30 mM Arginine·HCl and 30 mM Niacinamide	404.2
300	30 mM Histidine and 30 mM Niacinamide	520.8
300	30 mM Meglumine and 30 mM Niacinamide	467.3
300	30 mM Lysine·HCl and 30 mM Niacinamide	485.2
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	30 mM Arginine and 30 mM Niacin	26.5
200	30 mM Histidine and 30 mM Niacin	26.2
200	30 mM Meglumine and 30 mM Niacin	26.4
200	30 mM Lysine and 30 mM Niacin	24.3
200	30 mM Arginine·HCl and 30 mM Niacinamide	22.2
200	30 mM Histidine and 30 mM Niacinamide	24.8
200	30 mM Meglumine and 30 mM Niacinamide	24.5
200	30 mM Lysine·HCl and 30 mM Niacinamide	25.2
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	30 mM Arginine and 30 mM Niacin	2.5
100	30 mM Histidine and 30 mM Niacin	2.3
100	30 mM Meglumine and 30 mM Niacin	2.2
100	30 mM Lysine and 30 mM Niacin	2.2
100	30 mM Arginine·HCl and 30 mM Niacinamide	2.3
100	30 mM Histidine and 30 mM Niacinamide	2.4
100	30 mM Meglumine and 30 mM Niacinamide	2.5
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.5
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Table 59 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 20 mM Acetate buffer, at pH 5.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	467.2
300	140 mM Histidine and 140 mM Niacin	418.9
300	140 mM Meglumine and 140 mM Niacin	461.4
300	140 mM Lysine and 140 mM Niacin	430.8
300	70 mM Arginine·HCl and 140 mM Niacinamide	355.3
300	140 mM Histidine and 140 mM Niacinamide	424.5
300	140 mM Meglumine and 140 mM Niacinamide	398.2
300	70 mM Lysine·HCl and 140 mM Niacinamide	420.9
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	140 mM Arginine and 140 mM Niacin	26.0
200	140 mM Histidine and 140 mM Niacin	25.2
200	140 mM Meglumine and 140 mM Niacin	26.1
200	140 mM Lysine and 140 mM Niacin	24.0
200	70 mM Arginine·HCl and 140 mM Niacinamide	22.3
200	140 mM Histidine and 140 mM Niacinamide	24.5
200	140 mM Meglumine and 140 mM Niacinamide	24.4
200	70 mM Lysine·HCl and 140 mM Niacinamide	25.2
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	140 mM Arginine and 140 mM Niacin	2.5
100	140 mM Histidine and 140 mM Niacin	2.3
100	140 mM Meglumine and 140 mM Niacin	2.4
100	140 mM Lysine and 140 mM Niacin	2.3
100	70 mM Arginine·HCl and 140 mM Niacinamide	2.1
100	140 mM Histidine and 140 mM Niacinamide	2.4
100	140 mM Meglumine and 140 mM Niacinamide	2.4
100	70 mM Lysine·HCl and 140 mM Niacinamide	2.5
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Table 60 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 50 mM Acetate buffer, at pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	430.6
300	300 mM Histidine and 300 mM Niacin	359.1
300	300 mM Meglumine and 300 mM Niacin	414.7
300	300 mM Lysine and 300 mM Niacin	420.1
300	140 mM Arginine·HCl and 300 mM Niacinamide	306.2
300	300 mM Histidine and 300 mM Niacinamide	330.4
300	300 mM Meglumine and 300 mM Niacinamide	355.8
300	140 mM Lysine·HCl and 300 mM Niacinamide	362.7
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	300 mM Arginine and 300 mM Niacin	24.2
200	300 mM Histidine and 300 mM Niacin	24.0
200	300 mM Meglumine and 300 mM Niacin	24.5
200	300 mM Lysine and 300 mM Niacin	22.5
200	140 mM Arginine·HCl and 300 mM Niacinamide	21.0
200	300 mM Histidine and 300 mM Niacinamide	23.7
200	300 mM Meglumine and 300 mM Niacinamide	23.4
200	140 mM Lysine·HCl and 300 mM Niacinamide	24.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	300 mM Arginine and 300 mM Niacin	2.0
100	300 mM Histidine and 300 mM Niacin	2.1
100	300 mM Meglumine and 300 mM Niacin	2.0
100	300 mM Lysine and 300 mM Niacin	1.9
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.8
100	300 mM Histidine and 300 mM Niacinamide	2.0
100	300 mM Meglumine and 300 mM Niacinamide	2.0
100	140 mM Lysine·HCl and 300 mM Niacinamide	2.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Table 61 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 5 mM Citrate buffer, at pH 4.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	432.4
300	30 mM Histidine and 30 mM Niacin	490.8
300	30 mM Meglumine and 30 mM Niacin	554.7
300	30 mM Lysine and 30 mM Niacin	430.2
300	30 mM Arginine·HCl and 30 mM Niacinamide	407.6
300	30 mM Histidine and 30 mM Niacinamide	536.1
300	30 mM Meglumine and 30 mM Niacinamide	584.3
300	30 mM Lysine·HCl and 30 mM Niacinamide	469.0
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	30 mM Arginine and 30 mM Niacin	24.0
200	30 mM Histidine and 30 mM Niacin	26.2
200	30 mM Meglumine and 30 mM Niacin	26.5
200	30 mM Lysine and 30 mM Niacin	23.7
200	30 mM Arginine·HCl and 30 mM Niacinamide	22.8
200	30 mM Histidine and 30 mM Niacinamide	26.0
200	30 mM Meglumine and 30 mM Niacinamide	26.5
200	30 mM Lysine·HCl and 30 mM Niacinamide	23.5
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	30 mM Arginine and 30 mM Niacin	2.2
100	30 mM Histidine and 30 mM Niacin	2.4
100	30 mM Meglumine and 30 mM Niacin	2.5
100	30 mM Lysine and 30 mM Niacin	2.3
100	30 mM Arginine·HCl and 30 mM Niacinamide	2.0
100	30 mM Histidine and 30 mM Niacinamide	2.3
100	30 mM Meglumine and 30 mM Niacinamide	2.4
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Table 62 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 20 mM Citrate buffer, pH 5.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	333.7
300	140 mM Histidine and 140 mM Niacin	351.2
300	140 mM Meglumine and 140 mM Niacin	403.8
300	140 mM Lysine and 140 mM Niacin	368.0
300	70 mM Arginine·HCl and 140 mM Niacinamide	305.1
300	140 mM Histidine and 140 mM Niacinamide	454.6
300	140 mM Meglumine and 140 mM Niacinamide	462.3
300	70 mM Lysine·HCl and 140 mM Niacinamide	362.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	140 mM Arginine and 140 mM Niacin	18.0
200	140 mM Histidine and 140 mM Niacin	20.5
200	140 mM Meglumine and 140 mM Niacin	23.6
200	140 mM Lysine and 140 mM Niacin	19.3
200	70 mM Arginine·HCl and 140 mM Niacinamide	16.5
200	140 mM Histidine and 140 mM Niacinamide	19.5
200	140 mM Meglumine and 140 mM Niacinamide	24.2
200	70 mM Lysine·HCl and 140 mM Niacinamide	18.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	140 mM Arginine and 140 mM Niacin	2.0
100	140 mM Histidine and 140 mM Niacin	2.1
100	140 mM Meglumine and 140 mM Niacin	2.2
100	140 mM Lysine and 140 mM Niacin	2.0
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.8
100	140 mM Histidine and 140 mM Niacinamide	1.9
100	140 mM Meglumine and 140 mM Niacinamide	2.2
100	70 mM Lysine·HCl and 140 mM Niacinamide	1.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Table 63 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 50 mM Citrate buffer, at pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	306.8
300	300 mM Histidine and 300 mM Niacin	336.2
300	300 mM Meglumine and 300 mM Niacin	352.5
300	300 mM Lysine and 300 mM Niacin	326.4
300	140 mM Arginine·HCl and 300 mM Niacinamide	252.8
300	300 mM Histidine and 300 mM Niacinamide	363.4
300	300 mM Meglumine and 300 mM Niacinamide	380.1
300	140 mM Lysine·HCl and 300 mM Niacinamide	282.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	300 mM Arginine and 300 mM Niacin	18.0
200	300 mM Histidine and 300 mM Niacin	20.6
200	300 mM Meglumine and 300 mM Niacin	23.5
200	300 mM Lysine and 300 mM Niacin	19.3
200	140 mM Arginine·HCl and 300 mM Niacinamide	12.0
200	300 mM Histidine and 300 mM Niacinamide	19.5
200	300 mM Meglumine and 300 mM Niacinamide	24.1
200	140 mM Lysine·HCl and 300 mM Niacinamide	13.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	300 mM Arginine and 300 mM Niacin	1.6
100	300 mM Histidine and 300 mM Niacin	1.9
100	300 mM Meglumine and 300 mM Niacin	2.0
100	300 mM Lysine and 300 mM Niacin	1.7
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.5
100	300 mM Histidine and 300 mM Niacinamide	1.8
100	300 mM Meglumine and 300 mM Niacinamide	1.9
100	140 mM Lysine·HCl and 300 mM Niacinamide	1.7
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Table 64 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 5 mM Phosphate buffer, pH 6.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	455.3
300	30 mM Histidine and 30 mM Niacin	493.1
300	30 mM Meglumine and 30 mM Niacin	521.8
300	30 mM Lysine and 30 mM Niacin	447.2
300	30 mM Arginine·HCl and 30 mM Niacinamide	437.4
300	30 mM Histidine and 30 mM Niacinamide	605.8
300	30 mM Meglumine and 30 mM Niacinamide	580.2
300	30 mM Lysine·HCl and 30 mM Niacinamide	468.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	30 mM Arginine and 30 mM Niacin	24.5
200	30 mM Histidine and 30 mM Niacin	26.0
200	30 mM Meglumine and 30 mM Niacin	26.3
200	30 mM Lysine and 30 mM Niacin	24.8
200	30 mM Arginine·HCl and 30 mM Niacinamide	23.4
200	30 mM Histidine and 30 mM Niacinamide	26.6
200	30 mM Meglumine and 30 mM Niacinamide	25.4
200	30 mM Lysine·HCl and 30 mM Niacinamide	23.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	30 mM Arginine and 30 mM Niacin	2.3
100	30 mM Histidine and 30 mM Niacin	2.4
100	30 mM Meglumine and 30 mM Niacin	2.4
100	30 mM Lysine and 30 mM Niacin	2.2
100	30 mM Arginine·HCl and 30 mM Niacinamide	2.1
100	30 mM Histidine and 30 mM Niacinamide	2.5
100	30 mM Meglumine and 30 mM Niacinamide	2.5
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Table 65 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 20 mM Phosphate buffer, at pH 7.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	389.3
300	140 mM Histidine and 140 mM Niacin	408.2
300	140 mM Meglumine and 140 mM Niacin	459.4
300	140 mM Lysine and 140 mM Niacin	372.8
300	70 mM Arginine·HCl and 140 mM Niacinamide	337.1
300	140 mM Histidine and 140 mM Niacinamide	472.3
300	140 mM Meglumine and 140 mM Niacinamide	420.5
300	70 mM Lysine·HCl and 140 mM Niacinamide	366.2
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	140 mM Arginine and 140 mM Niacin	20.0
200	140 mM Histidine and 140 mM Niacin	24.7
200	140 mM Meglumine and 140 mM Niacin	25.0
200	140 mM Lysine and 140 mM Niacin	24.1
200	70 mM Arginine·HCl and 140 mM Niacinamide	13.5
200	140 mM Histidine and 140 mM Niacinamide	19.8
200	140 mM Meglumine and 140 mM Niacinamide	21.4
200	70 mM Lysine·HCl and 140 mM Niacinamide	19.2
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	140 mM Arginine and 140 mM Niacin	1.9
100	140 mM Histidine and 140 mM Niacin	2.1
100	140 mM Meglumine and 140 mM Niacin	2.3
100	140 mM Lysine and 140 mM Niacin	2.0
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.7
100	140 mM Histidine and 140 mM Niacinamide	2.3
100	140 mM Meglumine and 140 mM Niacinamide	2.3
100	70 mM Lysine·HCl and 140 mM Niacinamide	2.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Table 66 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 50 mM Phosphate buffer, at pH 7.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	311.4
300	300 mM Histidine and 300 mM Niacin	376.5
300	300 mM Meglumine and 300 mM Niacin	360.8
300	300 mM Lysine and 300 mM Niacin	309.7
300	140 mM Arginine·HCl and 300 mM Niacinamide	266.4
300	300 mM Histidine and 300 mM Niacinamide	358.2
300	300 mM Meglumine and 300 mM Niacinamide	572.8
300	140 mM Lysine·HCl and 300 mM Niacinamide	305.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	300 mM Arginine and 300 mM Niacin	16.5
200	300 mM Histidine and 300 mM Niacin	20.1
200	300 mM Meglumine and 300 mM Niacin	21.5
200	300 mM Lysine and 300 mM Niacin	18.7
200	140 mM Arginine·HCl and 300 mM Niacinamide	10.2
200	300 mM Histidine and 300 mM Niacinamide	15.7
200	300 mM Meglumine and 300 mM Niacinamide	23.0
200	140 mM Lysine·HCl and 300 mM Niacinamide	16.5
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	300 mM Arginine and 300 mM Niacin	1.6
100	300 mM Histidine and 300 mM Niacin	2.0
100	300 mM Meglumine and 300 mM Niacin	2.1
100	300 mM Lysine and 300 mM Niacin	1.8
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.5
100	300 mM Histidine and 300 mM Niacinamide	2.1
100	300 mM Meglumine and 300 mM Niacinamide	2.5
100	140 mM Lysine·HCl and 300 mM Niacinamide	1.7
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Table 67 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 5 mM Tris buffer, at pH 6.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	458.9
300	30 mM Histidine and 30 mM Niacin	497.5
300	30 mM Meglumine and 30 mM Niacin	527.4
300	30 mM Lysine and 30 mM Niacin	453.0
300	30 mM Arginine·HCl and 30 mM Niacinamide	444.2
300	30 mM Histidine and 30 mM Niacinamide	612.1
300	30 mM Meglumine and 30 mM Niacinamide	586.8
300	30 mM Lysine·HCl and 30 mM Niacinamide	472.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	30 mM Arginine and 30 mM Niacin	25.1
200	30 mM Histidine and 30 mM Niacin	26.3
200	30 mM Meglumine and 30 mM Niacin	26.5
200	30 mM Lysine and 30 mM Niacin	25.4
200	30 mM Arginine·HCl and 30 mM Niacinamide	24.0
200	30 mM Histidine and 30 mM Niacinamide	26.2
200	30 mM Meglumine and 30 mM Niacinamide	26.0
200	30 mM Lysine·HCl and 30 mM Niacinamide	23.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	30 mM Arginine and 30 mM Niacin	2.4
100	30 mM Histidine and 30 mM Niacin	2.3
100	30 mM Meglumine and 30 mM Niacin	2.5
100	30 mM Lysine and 30 mM Niacin	2.3
100	30 mM Arginine·HCl and 30 mM Niacinamide	2.2
100	30 mM Histidine and 30 mM Niacinamide	2.5
100	30 mM Meglumine and 30 mM Niacinamide	2.5
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Table 68 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 20 mM Tris buffer, pH 7.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	394.8
300	140 mM Histidine and 140 mM Niacin	411.2
300	140 mM Meglumine and 140 mM Niacin	464.6
300	140 mM Lysine and 140 mM Niacin	377.0
300	70 mM Arginine·HCl and 140 mM Niacinamide	341.5
300	140 mM Histidine and 140 mM Niacinamide	478.2
300	140 mM Meglumine and 140 mM Niacinamide	426.0
300	70 mM Lysine·HCl and 140 mM Niacinamide	371.2
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	140 mM Arginine and 140 mM Niacin	20.5
200	140 mM Histidine and 140 mM Niacin	25.2
200	140 mM Meglumine and 140 mM Niacin	25.5
200	140 mM Lysine and 140 mM Niacin	24.4
200	70 mM Arginine·HCl and 140 mM Niacinamide	14.0
200	140 mM Histidine and 140 mM Niacinamide	20.1
200	140 mM Meglumine and 140 mM Niacinamide	21.8
200	70 mM Lysine·HCl and 140 mM Niacinamide	19.5
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	140 mM Arginine and 140 mM Niacin	2.0
100	140 mM Histidine and 140 mM Niacin	2.2
100	140 mM Meglumine and 140 mM Niacin	2.4
100	140 mM Lysine and 140 mM Niacin	2.1
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.8
100	140 mM Histidine and 140 mM Niacinamide	2.4
100	140 mM Meglumine and 140 mM Niacinamide	2.4
100	70 mM Lysine·HCl and 140 mM Niacinamide	2.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Table 69 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 50 mM Tris buffer, at pH 7.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	315.4
300	300 mM Histidine and 300 mM Niacin	381.0
300	300 mM Meglumine and 300 mM Niacin	365.2
300	300 mM Lysine and 300 mM Niacin	314.5
300	140 mM Arginine·HCl and 300 mM Niacinamide	270.8
300	300 mM Histidine and 300 mM Niacinamide	362.5
300	300 mM Meglumine and 300 mM Niacinamide	580.2
300	140 mM Lysine·HCl and 300 mM Niacinamide	309.7
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	300 mM Arginine and 300 mM Niacin	17.2
200	300 mM Histidine and 300 mM Niacin	20.5
200	300 mM Meglumine and 300 mM Niacin	22.0
200	300 mM Lysine and 300 mM Niacin	19.2
200	140 mM Arginine·HCl and 300 mM Niacinamide	10.7
200	300 mM Histidine and 300 mM Niacinamide	16.2
200	300 mM Meglumine and 300 mM Niacinamide	23.5
200	140 mM Lysine·HCl and 300 mM Niacinamide	17.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	300 mM Arginine and 300 mM Niacin	1.7
100	300 mM Histidine and 300 mM Niacin	2.1
100	300 mM Meglumine and 300 mM Niacin	2.2
100	300 mM Lysine and 300 mM Niacin	1.9
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.6
100	300 mM Histidine and 300 mM Niacinamide	2.2
100	300 mM Meglumine and 300 mM Niacinamide	2.4
100	140 mM Lysine·HCl and 300 mM Niacinamide	1.8
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Table 70 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 5 mM Succinate buffer, pH 4.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	437.8
300	30 mM Histidine and 30 mM Niacin	496.7
300	30 mM Meglumine and 30 mM Niacin	560.4
300	30 mM Lysine and 30 mM Niacin	435.3
300	30 mM Arginine·HCl and 30 mM Niacinamide	413.2
300	30 mM Histidine and 30 mM Niacinamide	541.1
300	30 mM Meglumine and 30 mM Niacinamide	589.2
300	30 mM Lysine·HCl and 30 mM Niacinamide	475.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	30 mM Arginine and 30 mM Niacin	24.3
200	30 mM Histidine and 30 mM Niacin	26.5
200	30 mM Meglumine and 30 mM Niacin	27.0
200	30 mM Lysine and 30 mM Niacin	24.1
200	30 mM Arginine·HCl and 30 mM Niacinamide	23.3
200	30 mM Histidine and 30 mM Niacinamide	26.5
200	30 mM Meglumine and 30 mM Niacinamide	26.8
200	30 mM Lysine·HCl and 30 mM Niacinamide	23.9
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	30 mM Arginine and 30 mM Niacin	2.3
100	30 mM Histidine and 30 mM Niacin	2.5
100	30 mM Meglumine and 30 mM Niacin	2.4
100	30 mM Lysine and 30 mM Niacin	2.4
100	30 mM Arginine·HCl and 30 mM Niacinamide	2.1
100	30 mM Histidine and 30 mM Niacinamide	2.4
100	30 mM Meglumine and 30 mM Niacinamide	2.5
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.3
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Table 71 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 20 mM Succinate buffer, at pH 5.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	338.5
300	140 mM Histidine and 140 mM Niacin	355.9
300	140 mM Meglumine and 140 mM Niacin	409.7
300	140 mM Lysine and 140 mM Niacin	371.0
300	70 mM Arginine·HCl and 140 mM Niacinamide	309.8
300	140 mM Histidine and 140 mM Niacinamide	460.2
300	140 mM Meglumine and 140 mM Niacinamide	467.3
300	70 mM Lysine·HCl and 140 mM Niacinamide	368.4
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	140 mM Arginine and 140 mM Niacin	18.3
200	140 mM Histidine and 140 mM Niacin	21.0
200	140 mM Meglumine and 140 mM Niacin	24.0
200	140 mM Lysine and 140 mM Niacin	19.8
200	70 mM Arginine·HCl and 140 mM Niacinamide	17.0
200	140 mM Histidine and 140 mM Niacinamide	20.0
200	140 mM Meglumine and 140 mM Niacinamide	24.6
200	70 mM Lysine·HCl and 140 mM Niacinamide	19.2
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	140 mM Arginine and 140 mM Niacin	2.1
100	140 mM Histidine and 140 mM Niacin	2.2
100	140 mM Meglumine and 140 mM Niacin	2.3
100	140 mM Lysine and 140 mM Niacin	2.1
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.9
100	140 mM Histidine and 140 mM Niacinamide	2.0
100	140 mM Meglumine and 140 mM Niacinamide	2.3
100	70 mM Lysine·HCl and 140 mM Niacinamide	2.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Table 72 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE in 50 mM Succinate buffer, at pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	311.7
300	300 mM Histidine and 300 mM Niacin	340.5
300	300 mM Meglumine and 300 mM Niacin	356.8
300	300 mM Lysine and 300 mM Niacin	331.2
300	140 mM Arginine·HCl and 300 mM Niacinamide	258.4
300	300 mM Histidine and 300 mM Niacinamide	369.1
300	300 mM Meglumine and 300 mM Niacinamide	386.2
300	140 mM Lysine·HCl and 300 mM Niacinamide	287.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	645.6
300	Water (Blank)	930.2
200	300 mM Arginine and 300 mM Niacin	18.5
200	300 mM Histidine and 300 mM Niacin	21.0
200	300 mM Meglumine and 300 mM Niacin	24.0
200	300 mM Lysine and 300 mM Niacin	19.8
200	140 mM Arginine·HCl and 300 mM Niacinamide	12.3
200	300 mM Histidine and 300 mM Niacinamide	20.1
200	300 mM Meglumine and 300 mM Niacinamide	24.6
200	140 mM Lysine·HCl and 300 mM Niacinamide	13.5
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	27.5
200	Water (blank)	40.2
100	300 mM Arginine and 300 mM Niacin	1.7
100	300 mM Histidine and 300 mM Niacin	2.0
100	300 mM Meglumine and 300 mM Niacin	2.1
100	300 mM Lysine and 300 mM Niacin	1.8
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.6
100	300 mM Histidine and 300 mM Niacinamide	1.9
100	300 mM Meglumine and 300 mM Niacinamide	2.0
100	140 mM Lysine·HCl and 300 mM Niacinamide	1.8
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.6
100	Water (blank)	3.8

Example 5: Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept solutions in various buffers at 20°C.

[0087] This example describes the viscosity reducing effect of viscosity-reducing and stabilizing formulations of the present application on Aflibercept solutions.

5 [0088] **Materials and Methods**

[0089] Aflibercept (Eylea®) is commercially available recombinant fusion protein. In this example, it was produced by WuXi Biologics based on its sequence was sourced from Drug Bank (DB08885). The recombinant cell culture fermentation was harvested by centrifugation, and the resulting filtrate pool was loaded onto a Protein A column. The target protein was eluted at pH 3.8
10 and subsequently neutralized to pH 5.5 using 1 M Tris base. The eluate then underwent depth filtration and was passed through a 0.2 µm filter. The intermediate filtration pool was loaded onto an AEX (Anion Exchange) column in flow-through mode. Following this step, the AEX flow-through pool was further processed on a CEX (Cation Exchange) column, and the target protein was eluted using a linear gradient elution. The CEX eluate was subsequently concentrated to a
15 concentration of 40 g/L and diafiltrated over six dia-volumes to exchange the buffer to a final composition of a buffer concentration within 5-50 mM using histidine, acetate, citrate, phosphate, tris or succinate buffer system at a pH between 4.5 and 7.5, respectively. Through formulation exchange, Aflibercept was transferred into test groups, encompassing with the component concentration varied from 30 mM to 300 mM, incorporating one of the viscosity-reducing and
20 stabilizing formulations, shown in Tables 73-90. Furthermore, there was a control group (i.e., positive control) comprising 25 mM phosphate buffer at pH 6.0, with 81.2 mM Nicotinic acid and 29.4 mM Tryptophan (matching the lead formulation 25 mM phosphate buffer at pH 6.0 along with 10 mg/mL Nicotinic acid (acid form) and 6 mg/mL Tryptophan from Examples 14, 16, 17, 18, 19, 20 and 21 in WO2018211517). An additional control group solely consisted of MilliQ
25 water and the protein as blank control. The formulation containing Aflibercept was subsequently concentrated to 100-300 mg/mL (e.g., 100, 200, or 300 mg/mL) using an Eppendorf centrifuge with a concentration variation of 3%. To ascertain Aflibercept concentration in the groups, absorbance at 280 nm combined with SE-UPLC was gauged against corresponding buffers containing a viscosity-reducing and stabilizing agent for excipient-containing samples, and
30 absorbance at 280 nm was measured for the protein solution without a viscosity-reducing and

stabilizing formulation. For Aflibercept without excipients, the buffer alone (i.e., devoid of excipients) served as a blank for protein concentration calculation. The extinction coefficient was measured at $1.15 \text{ (mg/mL)}^{-1} \cdot \text{cm}^{-1}$.

5 [0090] The viscosity of samples was measured by VROC® initium one plus viscometer (Rheosense) at 20°C. For samples with a viscosity exceeding 1000 cP, viscosity was measured using a TA rheometer.

10 [0091] As shown in Tables 73-90, the data in demonstrated the viscosity reducing effect of the viscosity-reducing and stabilizing formulations of the present application on Aflibercept in different buffers: histidine (pH 5.0 to 7.0), acetate (pH 4.5 to 6.0), citrate (pH 4.5 to 6.0), phosphate (pH 6.5 to 7.5), Tris (pH 6.5 to 7.5), and succinate (pH 4.5 to 6.0) Buffer. As for Aflibercept at a concentration from 100 to 300 mg/mL, the tested viscosity-reducing and stabilizing formulations exhibited superior viscosity reduction when compared with the reference lead formulation of WO2018211517 and excipient-free samples.

Table 73 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 5 mM Histidine buffer, at pH 5.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	32.1
300	30 mM Histidine and 30 mM Niacin	43.4
300	30 mM Meglumine and 30 mM Niacin	49.1
300	30 mM Lysine and 30 mM Niacin	45.7
300	30 mM Arginine·HCl and 30 mM Niacinamide	34.9
300	30 mM Histidine and 30 mM Niacinamide	43.1
300	30 mM Meglumine and 30 mM Niacinamide	50.1
300	30 mM Lysine·HCl and 30 mM Niacinamide	37.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	30 mM Arginine and 30 mM Niacin	11.3
200	30 mM Histidine and 30 mM Niacin	13.9
200	30 mM Meglumine and 30 mM Niacin	14.2
200	30 mM Lysine and 30 mM Niacin	11.6
200	30 mM Arginine·HCl and 30 mM Niacinamide	9.9
200	30 mM Histidine and 30 mM Niacinamide	12.9
200	30 mM Meglumine and 30 mM Niacinamide	11.8
200	30 mM Lysine·HCl and 30 mM Niacinamide	10.7
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	30 mM Arginine and 30 mM Niacin	2.4
100	30 mM Histidine and 30 mM Niacin	2.6
100	30 mM Meglumine and 30 mM Niacin	2.4
100	30 mM Lysine and 30 mM Niacin	2.5
100	30 mM Arginine·HCl and 30 mM Niacinamide	1.9
100	30 mM Histidine and 30 mM Niacinamide	2.3
100	30 mM Meglumine and 30 mM Niacinamide	2.6
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Table 74 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 20 mM Histidine buffer, pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	30.1
300	140 mM Histidine and 140 mM Niacin	49.3
300	140 mM Meglumine and 140 mM Niacin	47.9
300	140 mM Lysine and 140 mM Niacin	39.7
300	70 mM Arginine·HCl and 140 mM Niacinamide	22.8
300	140 mM Histidine and 140 mM Niacinamide	33.8
300	140 mM Meglumine and 140 mM Niacinamide	38.3
300	70 mM Lysine·HCl and 140 mM Niacinamide	27.2
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	140 mM Arginine and 140 mM Niacin	11.0
200	140 mM Histidine and 140 mM Niacin	13.4
200	140 mM Meglumine and 140 mM Niacin	14.0
200	140 mM Lysine and 140 mM Niacin	10.7
200	70 mM Arginine·HCl and 140 mM Niacinamide	9.3
200	140 mM Histidine and 140 mM Niacinamide	12.7
200	140 mM Meglumine and 140 mM Niacinamide	13.4
200	70 mM Lysine·HCl and 140 mM Niacinamide	10.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	140 mM Arginine and 140 mM Niacin	2.1
100	140 mM Histidine and 140 mM Niacin	2.5
100	140 mM Meglumine and 140 mM Niacin	2.4
100	140 mM Lysine and 140 mM Niacin	2.4
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.5
100	140 mM Histidine and 140 mM Niacinamide	2.5
100	140 mM Meglumine and 140 mM Niacinamide	2.5
100	70 mM Lysine·HCl and 140 mM Niacinamide	1.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Table 75 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 50 mM Histidine buffer, at pH 7.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	27.8
300	300 mM Histidine and 300 mM Niacin	45.5
300	300 mM Meglumine and 300 mM Niacin	50.4
300	300 mM Lysine and 300 mM Niacin	33.5
300	140 mM Arginine·HCl and 300 mM Niacinamide	21.4
300	300 mM Histidine and 300 mM Niacinamide	30.2
300	300 mM Meglumine and 300 mM Niacinamide	41.2
300	140 mM Lysine·HCl and 300 mM Niacinamide	23.4
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	300 mM Arginine and 300 mM Niacin	8.7
200	300 mM Histidine and 300 mM Niacin	11.5
200	300 mM Meglumine and 300 mM Niacin	14.0
200	300 mM Lysine and 300 mM Niacin	7.6
200	140 mM Arginine·HCl and 300 mM Niacinamide	7.9
200	300 mM Histidine and 300 mM Niacinamide	10.2
200	300 mM Meglumine and 300 mM Niacinamide	12.4
200	140 mM Lysine·HCl and 300 mM Niacinamide	9.7
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	300 mM Arginine and 300 mM Niacin	1.7
100	300 mM Histidine and 300 mM Niacin	1.8
100	300 mM Meglumine and 300 mM Niacin	1.6
100	300 mM Lysine and 300 mM Niacin	1.6
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.3
100	300 mM Histidine and 300 mM Niacinamide	1.9
100	300 mM Meglumine and 300 mM Niacinamide	1.7
100	140 mM Lysine·HCl and 300 mM Niacinamide	1.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Table 76 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 5 mM Acetate buffer, pH 4.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	39.2
300	30 mM Histidine and 30 mM Niacin	44.6
300	30 mM Meglumine and 30 mM Niacin	56.1
300	30 mM Lysine and 30 mM Niacin	41.5
300	30 mM Arginine·HCl and 30 mM Niacinamide	33.0
300	30 mM Histidine and 30 mM Niacinamide	47.8
300	30 mM Meglumine and 30 mM Niacinamide	48.7
300	30 mM Lysine·HCl and 30 mM Niacinamide	42.9
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	30 mM Arginine and 30 mM Niacin	12.3
200	30 mM Histidine and 30 mM Niacin	13.2
200	30 mM Meglumine and 30 mM Niacin	13.9
200	30 mM Lysine and 30 mM Niacin	11.1
200	30 mM Arginine·HCl and 30 mM Niacinamide	10.4
200	30 mM Histidine and 30 mM Niacinamide	12.1
200	30 mM Meglumine and 30 mM Niacinamide	11.9
200	30 mM Lysine·HCl and 30 mM Niacinamide	10.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	30 mM Arginine and 30 mM Niacin	2.1
100	30 mM Histidine and 30 mM Niacin	2.3
100	30 mM Meglumine and 30 mM Niacin	2.3
100	30 mM Lysine and 30 mM Niacin	1.9
100	30 mM Arginine·HCl and 30 mM Niacinamide	1.8
100	30 mM Histidine and 30 mM Niacinamide	2.4
100	30 mM Meglumine and 30 mM Niacinamide	2.6
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Table 77 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 20 mM Acetate buffer, at pH 5.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	35.2
300	140 mM Histidine and 140 mM Niacin	39.5
300	140 mM Meglumine and 140 mM Niacin	49.2
300	140 mM Lysine and 140 mM Niacin	35.9
300	70 mM Arginine·HCl and 140 mM Niacinamide	26.2
300	140 mM Histidine and 140 mM Niacinamide	31.4
300	140 mM Meglumine and 140 mM Niacinamide	32.9
300	70 mM Lysine·HCl and 140 mM Niacinamide	29.0
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	140 mM Arginine and 140 mM Niacin	11.2
200	140 mM Histidine and 140 mM Niacin	13.2
200	140 mM Meglumine and 140 mM Niacin	12.8
200	140 mM Lysine and 140 mM Niacin	11.2
200	70 mM Arginine·HCl and 140 mM Niacinamide	9.9
200	140 mM Histidine and 140 mM Niacinamide	9.7
200	140 mM Meglumine and 140 mM Niacinamide	14.0
200	70 mM Lysine·HCl and 140 mM Niacinamide	10.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	140 mM Arginine and 140 mM Niacin	2.0
100	140 mM Histidine and 140 mM Niacin	1.9
100	140 mM Meglumine and 140 mM Niacin	2.3
100	140 mM Lysine and 140 mM Niacin	2.6
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.8
100	140 mM Histidine and 140 mM Niacinamide	1.9
100	140 mM Meglumine and 140 mM Niacinamide	2.4
100	70 mM Lysine·HCl and 140 mM Niacinamide	1.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Table 78 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 50 mM Acetate buffer, at pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	32.4
300	300 mM Histidine and 300 mM Niacin	41.2
300	300 mM Meglumine and 300 mM Niacin	44.1
300	300 mM Lysine and 300 mM Niacin	39.1
300	140 mM Arginine·HCl and 300 mM Niacinamide	24.4
300	300 mM Histidine and 300 mM Niacinamide	35.7
300	300 mM Meglumine and 300 mM Niacinamide	30.2
300	140 mM Lysine·HCl and 300 mM Niacinamide	26.7
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	300 mM Arginine and 300 mM Niacin	11.2
200	300 mM Histidine and 300 mM Niacin	13.2
200	300 mM Meglumine and 300 mM Niacin	12.8
200	300 mM Lysine and 300 mM Niacin	11.2
200	140 mM Arginine·HCl and 300 mM Niacinamide	9.9
200	300 mM Histidine and 300 mM Niacinamide	9.7
200	300 mM Meglumine and 300 mM Niacinamide	14.0
200	140 mM Lysine·HCl and 300 mM Niacinamide	10.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	300 mM Arginine and 300 mM Niacin	1.7
100	300 mM Histidine and 300 mM Niacin	1.8
100	300 mM Meglumine and 300 mM Niacin	1.8
100	300 mM Lysine and 300 mM Niacin	2.4
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.4
100	300 mM Histidine and 300 mM Niacinamide	1.5
100	300 mM Meglumine and 300 mM Niacinamide	2.2
100	140 mM Lysine·HCl and 300 mM Niacinamide	1.5
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Table 79 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 5 mM Citrate buffer, at pH 4.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	45.4
300	30 mM Histidine and 30 mM Niacin	54.2
300	30 mM Meglumine and 30 mM Niacin	46.3
300	30 mM Lysine and 30 mM Niacin	49.5
300	30 mM Arginine·HCl and 30 mM Niacinamide	45.7
300	30 mM Histidine and 30 mM Niacinamide	38.2
300	30 mM Meglumine and 30 mM Niacinamide	42.5
300	30 mM Lysine·HCl and 30 mM Niacinamide	47.0
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	30 mM Arginine and 30 mM Niacin	14.0
200	30 mM Histidine and 30 mM Niacin	10.4
200	30 mM Meglumine and 30 mM Niacin	10.5
200	30 mM Lysine and 30 mM Niacin	12.9
200	30 mM Arginine·HCl and 30 mM Niacinamide	12.1
200	30 mM Histidine and 30 mM Niacinamide	11.5
200	30 mM Meglumine and 30 mM Niacinamide	9.9
200	30 mM Lysine·HCl and 30 mM Niacinamide	11.9
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	30 mM Arginine and 30 mM Niacin	2.4
100	30 mM Histidine and 30 mM Niacin	2.1
100	30 mM Meglumine and 30 mM Niacin	1.7
100	30 mM Lysine and 30 mM Niacin	2.5
100	30 mM Arginine·HCl and 30 mM Niacinamide	2.4
100	30 mM Histidine and 30 mM Niacinamide	1.8
100	30 mM Meglumine and 30 mM Niacinamide	1.5
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Table 80 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 20 mM Citrate buffer, pH 5.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	40.2
300	140 mM Histidine and 140 mM Niacin	49.5
300	140 mM Meglumine and 140 mM Niacin	30.7
300	140 mM Lysine and 140 mM Niacin	43.9
300	70 mM Arginine·HCl and 140 mM Niacinamide	45.7
300	140 mM Histidine and 140 mM Niacinamide	28.9
300	140 mM Meglumine and 140 mM Niacinamide	32.2
300	70 mM Lysine·HCl and 140 mM Niacinamide	39.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	140 mM Arginine and 140 mM Niacin	13.4
200	140 mM Histidine and 140 mM Niacin	9.2
200	140 mM Meglumine and 140 mM Niacin	9.8
200	140 mM Lysine and 140 mM Niacin	11.6
200	70 mM Arginine·HCl and 140 mM Niacinamide	11.5
200	140 mM Histidine and 140 mM Niacinamide	10.4
200	140 mM Meglumine and 140 mM Niacinamide	9.0
200	70 mM Lysine·HCl and 140 mM Niacinamide	10.7
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	140 mM Arginine and 140 mM Niacin	2.3
100	140 mM Histidine and 140 mM Niacin	2.2
100	140 mM Meglumine and 140 mM Niacin	1.6
100	140 mM Lysine and 140 mM Niacin	2.5
100	70 mM Arginine·HCl and 140 mM Niacinamide	2.2
100	140 mM Histidine and 140 mM Niacinamide	1.7
100	140 mM Meglumine and 140 mM Niacinamide	1.7
100	70 mM Lysine·HCl and 140 mM Niacinamide	2.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Table 81 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 50 mM Citrate buffer, at pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	44.5
300	300 mM Histidine and 300 mM Niacin	40.1
300	300 mM Meglumine and 300 mM Niacin	27.5
300	300 mM Lysine and 300 mM Niacin	46.6
300	140 mM Arginine·HCl and 300 mM Niacinamide	49.1
300	300 mM Histidine and 300 mM Niacinamide	24.9
300	300 mM Meglumine and 300 mM Niacinamide	29.2
300	140 mM Lysine·HCl and 300 mM Niacinamide	43.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	300 mM Arginine and 300 mM Niacin	12.6
200	300 mM Histidine and 300 mM Niacin	9.4
200	300 mM Meglumine and 300 mM Niacin	8.8
200	300 mM Lysine and 300 mM Niacin	12.1
200	140 mM Arginine·HCl and 300 mM Niacinamide	13.7
200	300 mM Histidine and 300 mM Niacinamide	9.8
200	300 mM Meglumine and 300 mM Niacinamide	8.4
200	140 mM Lysine·HCl and 300 mM Niacinamide	11.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	300 mM Arginine and 300 mM Niacin	2.2
100	300 mM Histidine and 300 mM Niacin	2.4
100	300 mM Meglumine and 300 mM Niacin	1.5
100	300 mM Lysine and 300 mM Niacin	2.3
100	140 mM Arginine·HCl and 300 mM Niacinamide	2.1
100	300 mM Histidine and 300 mM Niacinamide	1.6
100	300 mM Meglumine and 300 mM Niacinamide	1.7
100	140 mM Lysine·HCl and 300 mM Niacinamide	2.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Table 82 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 5 mM Phosphate buffer, pH 6.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	55.2
300	30 mM Histidine and 30 mM Niacin	50.4
300	30 mM Meglumine and 30 mM Niacin	49.2
300	30 mM Lysine and 30 mM Niacin	42.1
300	30 mM Arginine·HCl and 30 mM Niacinamide	45.1
300	30 mM Histidine and 30 mM Niacinamide	48.5
300	30 mM Meglumine and 30 mM Niacinamide	42.5
300	30 mM Lysine·HCl and 30 mM Niacinamide	47.6
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	30 mM Arginine and 30 mM Niacin	13.4
200	30 mM Histidine and 30 mM Niacin	12.5
200	30 mM Meglumine and 30 mM Niacin	12.3
200	30 mM Lysine and 30 mM Niacin	14.1
200	30 mM Arginine·HCl and 30 mM Niacinamide	13.0
200	30 mM Histidine and 30 mM Niacinamide	11.2
200	30 mM Meglumine and 30 mM Niacinamide	13.3
200	30 mM Lysine·HCl and 30 mM Niacinamide	13.4
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	30 mM Arginine and 30 mM Niacin	2.5
100	30 mM Histidine and 30 mM Niacin	2.3
100	30 mM Meglumine and 30 mM Niacin	2.2
100	30 mM Lysine and 30 mM Niacin	2.5
100	30 mM Arginine·HCl and 30 mM Niacinamide	2.5
100	30 mM Histidine and 30 mM Niacinamide	2.4
100	30 mM Meglumine and 30 mM Niacinamide	1.9
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.5
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Table 83 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 20 mM Phosphate buffer, at pH 7.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	51.4
300	140 mM Histidine and 140 mM Niacin	47.6
300	140 mM Meglumine and 140 mM Niacin	45.0
300	140 mM Lysine and 140 mM Niacin	46.2
300	70 mM Arginine·HCl and 140 mM Niacinamide	44.5
300	140 mM Histidine and 140 mM Niacinamide	45.2
300	140 mM Meglumine and 140 mM Niacinamide	35.6
300	70 mM Lysine·HCl and 140 mM Niacinamide	43.0
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	140 mM Arginine and 140 mM Niacin	12.4
200	140 mM Histidine and 140 mM Niacin	11.6
200	140 mM Meglumine and 140 mM Niacin	12.1
200	140 mM Lysine and 140 mM Niacin	13.7
200	70 mM Arginine·HCl and 140 mM Niacinamide	12.1
200	140 mM Histidine and 140 mM Niacinamide	7.3
200	140 mM Meglumine and 140 mM Niacinamide	9.3
200	70 mM Lysine·HCl and 140 mM Niacinamide	12.6
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	140 mM Arginine and 140 mM Niacin	1.9
100	140 mM Histidine and 140 mM Niacin	2.0
100	140 mM Meglumine and 140 mM Niacin	2.0
100	140 mM Lysine and 140 mM Niacin	2.3
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.9
100	140 mM Histidine and 140 mM Niacinamide	2.1
100	140 mM Meglumine and 140 mM Niacinamide	1.6
100	70 mM Lysine·HCl and 140 mM Niacinamide	1.8
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Table 84 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 50 mM Phosphate buffer, at pH 7.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	43.7
300	300 mM Histidine and 300 mM Niacin	44.8
300	300 mM Meglumine and 300 mM Niacin	38.2
300	300 mM Lysine and 300 mM Niacin	42.2
300	140 mM Arginine·HCl and 300 mM Niacinamide	37.5
300	300 mM Histidine and 300 mM Niacinamide	38.2
300	300 mM Meglumine and 300 mM Niacinamide	30.4
300	140 mM Lysine·HCl and 300 mM Niacinamide	42.0
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	300 mM Arginine and 300 mM Niacin	11.8
200	300 mM Histidine and 300 mM Niacin	12.2
200	300 mM Meglumine and 300 mM Niacin	11.5
200	300 mM Lysine and 300 mM Niacin	12.9
200	140 mM Arginine·HCl and 300 mM Niacinamide	10.2
200	300 mM Histidine and 300 mM Niacinamide	6.6
200	300 mM Meglumine and 300 mM Niacinamide	7.9
200	140 mM Lysine·HCl and 300 mM Niacinamide	11.2
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	300 mM Arginine and 300 mM Niacin	1.8
100	300 mM Histidine and 300 mM Niacin	1.7
100	300 mM Meglumine and 300 mM Niacin	1.6
100	300 mM Lysine and 300 mM Niacin	1.9
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.8
100	300 mM Histidine and 300 mM Niacinamide	1.6
100	300 mM Meglumine and 300 mM Niacinamide	1.5
100	140 mM Lysine·HCl and 300 mM Niacinamide	1.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Table 85 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 5 mM Tris buffer, at pH 6.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	55.8
300	30 mM Histidine and 30 mM Niacin	50.1
300	30 mM Meglumine and 30 mM Niacin	49.7
300	30 mM Lysine and 30 mM Niacin	42.3
300	30 mM Arginine·HCl and 30 mM Niacinamide	45.7
300	30 mM Histidine and 30 mM Niacinamide	48.9
300	30 mM Meglumine and 30 mM Niacinamide	42.8
300	30 mM Lysine·HCl and 30 mM Niacinamide	47.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	30 mM Arginine and 30 mM Niacin	13.6
200	30 mM Histidine and 30 mM Niacin	12.8
200	30 mM Meglumine and 30 mM Niacin	12.1
200	30 mM Lysine and 30 mM Niacin	14.1
200	30 mM Arginine·HCl and 30 mM Niacinamide	13.2
200	30 mM Histidine and 30 mM Niacinamide	11.6
200	30 mM Meglumine and 30 mM Niacinamide	13.5
200	30 mM Lysine·HCl and 30 mM Niacinamide	13.2
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	30 mM Arginine and 30 mM Niacin	2.6
100	30 mM Histidine and 30 mM Niacin	2.4
100	30 mM Meglumine and 30 mM Niacin	2.1
100	30 mM Lysine and 30 mM Niacin	2.6
100	30 mM Arginine·HCl and 30 mM Niacinamide	2.5
100	30 mM Histidine and 30 mM Niacinamide	2.5
100	30 mM Meglumine and 30 mM Niacinamide	1.8
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Table 86 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 20 mM Tris buffer, pH 7.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	50.5
300	140 mM Histidine and 140 mM Niacin	44.5
300	140 mM Meglumine and 140 mM Niacin	41.9
300	140 mM Lysine and 140 mM Niacin	40.7
300	70 mM Arginine·HCl and 140 mM Niacinamide	43.9
300	140 mM Histidine and 140 mM Niacinamide	38.7
300	140 mM Meglumine and 140 mM Niacinamide	40.9
300	70 mM Lysine·HCl and 140 mM Niacinamide	45.4
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	140 mM Arginine and 140 mM Niacin	12.7
200	140 mM Histidine and 140 mM Niacin	12.0
200	140 mM Meglumine and 140 mM Niacin	11.0
200	140 mM Lysine and 140 mM Niacin	13.4
200	70 mM Arginine·HCl and 140 mM Niacinamide	12.3
200	140 mM Histidine and 140 mM Niacinamide	10.7
200	140 mM Meglumine and 140 mM Niacinamide	11.5
200	70 mM Lysine·HCl and 140 mM Niacinamide	12.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	140 mM Arginine and 140 mM Niacin	2.2
100	140 mM Histidine and 140 mM Niacin	2.0
100	140 mM Meglumine and 140 mM Niacin	1.9
100	140 mM Lysine and 140 mM Niacin	2.2
100	70 mM Arginine·HCl and 140 mM Niacinamide	2.4
100	140 mM Histidine and 140 mM Niacinamide	2.1
100	140 mM Meglumine and 140 mM Niacinamide	1.6
100	70 mM Lysine·HCl and 140 mM Niacinamide	2.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Table 87 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 50 mM Tris buffer, at pH 7.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	52.6
300	300 mM Histidine and 300 mM Niacin	43.7
300	300 mM Meglumine and 300 mM Niacin	39.9
300	300 mM Lysine and 300 mM Niacin	32.9
300	140 mM Arginine·HCl and 300 mM Niacinamide	44.8
300	300 mM Histidine and 300 mM Niacinamide	36.9
300	300 mM Meglumine and 300 mM Niacinamide	32.8
300	140 mM Lysine·HCl and 300 mM Niacinamide	44.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	300 mM Arginine and 300 mM Niacin	12.2
200	300 mM Histidine and 300 mM Niacin	11.1
200	300 mM Meglumine and 300 mM Niacin	10.2
200	300 mM Lysine and 300 mM Niacin	12.7
200	140 mM Arginine·HCl and 300 mM Niacinamide	11.4
200	300 mM Histidine and 300 mM Niacinamide	10.1
200	300 mM Meglumine and 300 mM Niacinamide	9.6
200	140 mM Lysine·HCl and 300 mM Niacinamide	11.2
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	300 mM Arginine and 300 mM Niacin	2.1
100	300 mM Histidine and 300 mM Niacin	1.8
100	300 mM Meglumine and 300 mM Niacin	1.7
100	300 mM Lysine and 300 mM Niacin	2.1
100	140 mM Arginine·HCl and 300 mM Niacinamide	2.2
100	300 mM Histidine and 300 mM Niacinamide	2.0
100	300 mM Meglumine and 300 mM Niacinamide	1.5
100	140 mM Lysine·HCl and 300 mM Niacinamide	2.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Table 88 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 5 mM Succinate buffer, pH 4.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	30 mM Arginine and 30 mM Niacin	44.8
300	30 mM Histidine and 30 mM Niacin	53.5
300	30 mM Meglumine and 30 mM Niacin	45.7
300	30 mM Lysine and 30 mM Niacin	48.9
300	30 mM Arginine·HCl and 30 mM Niacinamide	44.9
300	30 mM Histidine and 30 mM Niacinamide	37.6
300	30 mM Meglumine and 30 mM Niacinamide	41.8
300	30 mM Lysine·HCl and 30 mM Niacinamide	46.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	30 mM Arginine and 30 mM Niacin	14.1
200	30 mM Histidine and 30 mM Niacin	10
200	30 mM Meglumine and 30 mM Niacin	10.1
200	30 mM Lysine and 30 mM Niacin	12.5
200	30 mM Arginine·HCl and 30 mM Niacinamide	11.7
200	30 mM Histidine and 30 mM Niacinamide	11.1
200	30 mM Meglumine and 30 mM Niacinamide	9.5
200	30 mM Lysine·HCl and 30 mM Niacinamide	11.4
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	30 mM Arginine and 30 mM Niacin	2.3
100	30 mM Histidine and 30 mM Niacin	2.0
100	30 mM Meglumine and 30 mM Niacin	1.6
100	30 mM Lysine and 30 mM Niacin	2.4
100	30 mM Arginine·HCl and 30 mM Niacinamide	2.3
100	30 mM Histidine and 30 mM Niacinamide	1.7
100	30 mM Meglumine and 30 mM Niacinamide	1.4
100	30 mM Lysine·HCl and 30 mM Niacinamide	2.3
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Table 89 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 20 mM Succinate buffer, at pH 5.5 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	140 mM Arginine and 140 mM Niacin	32.5
300	140 mM Histidine and 140 mM Niacin	39.3
300	140 mM Meglumine and 140 mM Niacin	33.1
300	140 mM Lysine and 140 mM Niacin	35.7
300	70 mM Arginine·HCl and 140 mM Niacinamide	32.0
300	140 mM Histidine and 140 mM Niacinamide	35.2
300	140 mM Meglumine and 140 mM Niacinamide	39.1
300	70 mM Lysine·HCl and 140 mM Niacinamide	33.2
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	140 mM Arginine and 140 mM Niacin	13.1
200	140 mM Histidine and 140 mM Niacin	9.2
200	140 mM Meglumine and 140 mM Niacin	9.1
200	140 mM Lysine and 140 mM Niacin	11.5
200	70 mM Arginine·HCl and 140 mM Niacinamide	10.7
200	140 mM Histidine and 140 mM Niacinamide	10.2
200	140 mM Meglumine and 140 mM Niacinamide	8.8
200	70 mM Lysine·HCl and 140 mM Niacinamide	10.5
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	140 mM Arginine and 140 mM Niacin	2.2
100	140 mM Histidine and 140 mM Niacin	1.7
100	140 mM Meglumine and 140 mM Niacin	1.6
100	140 mM Lysine and 140 mM Niacin	2.3
100	70 mM Arginine·HCl and 140 mM Niacinamide	1.9
100	140 mM Histidine and 140 mM Niacinamide	1.6
100	140 mM Meglumine and 140 mM Niacinamide	1.6
100	70 mM Lysine·HCl and 140 mM Niacinamide	1.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Table 90 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Aflibercept in 50 mM Succinate buffer, at pH 6.0 at 20°C. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
300	300 mM Arginine and 300 mM Niacin	30.8
300	300 mM Histidine and 300 mM Niacin	31.4
300	300 mM Meglumine and 300 mM Niacin	32.5
300	300 mM Lysine and 300 mM Niacin	32.9
300	140 mM Arginine·HCl and 300 mM Niacinamide	28.2
300	300 mM Histidine and 300 mM Niacinamide	27.5
300	300 mM Meglumine and 300 mM Niacinamide	32.2
300	140 mM Lysine·HCl and 300 mM Niacinamide	30.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	58.6
300	Water (Blank)	117.7
200	300 mM Arginine and 300 mM Niacin	12.7
200	300 mM Histidine and 300 mM Niacin	8.9
200	300 mM Meglumine and 300 mM Niacin	8.7
200	300 mM Lysine and 300 mM Niacin	11
200	140 mM Arginine·HCl and 300 mM Niacinamide	10.2
200	300 mM Histidine and 300 mM Niacinamide	9.8
200	300 mM Meglumine and 300 mM Niacinamide	8.4
200	140 mM Lysine·HCl and 300 mM Niacinamide	10
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	14.3
200	Water (blank)	17.0
100	300 mM Arginine and 300 mM Niacin	2.1
100	300 mM Histidine and 300 mM Niacin	1.6
100	300 mM Meglumine and 300 mM Niacin	1.5
100	300 mM Lysine and 300 mM Niacin	2.1
100	140 mM Arginine·HCl and 300 mM Niacinamide	1.8
100	300 mM Histidine and 300 mM Niacinamide	1.6
100	300 mM Meglumine and 300 mM Niacinamide	1.6
100	140 mM Lysine·HCl and 300 mM Niacinamide	1.7
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	2.7
100	Water (blank)	2.7

Example 6: Viscosity reducing effect of viscosity-reducing and stabilizing formulations on Rituximab solutions in 20 mM histidine buffer, pH 6.0 at 20°C.

[0092] This example tested the viscosity reducing effect of viscosity-reducing and stabilizing formulations of the present application on Rituximab solutions.

5 [0093] **Materials and Methods**

[0094] Rituximab is commercially available. In this example, it was produced by WuXi Biologics based on its sequence sourced from Drug Bank (DB00073). The recombinant cell culture fermentation was harvested by centrifugation, and the resulting filtrate pool was loaded onto a Protein A column. The target protein was eluted at pH 3.8 and subsequently neutralized to pH 5.5
10 using 1 M Tris base. The eluate then underwent depth filtration and was passed through a 0.2 µm filter. The intermediate filtration pool was loaded onto an AEX (Anion Exchange) column in flow-through mode. Following this step, the AEX flow-through pool was further processed on a CEX (Cation Exchange) column, and the target protein was eluted using a linear gradient elution. The CEX eluate was subsequently concentrated to a concentration of 40 g/L and diafiltrated over six
15 dia-volumes to exchange the buffer to a final composition of 20 mM histidine at pH 6.0. Through buffer exchange, Rituximab was transferred into ten test groups, encompassing eight with a 20 mM histidine pH 6.0 buffer, incorporating one of the viscosity-reducing and stabilizing formulations, shown in Table 91. Furthermore, there was a formulation comprising 25 mM phosphate buffer at pH 6.0, with 81.2 mM Nicotinic acid and 29.4 mM Tryptophan (matching the
20 lead formulation 25 mM phosphate buffer at pH 6.0 along with 10 mg/mL Nicotinic acid (acid form) and 6 mg/mL Tryptophan from Examples 14, 16, 17, 18, 19, 20 and 21 in WO2018211517) as a control group. An additional control group solely consisted of a 20 mM histidine buffer pH 6.0 and the protein as blank control. The formulation containing Rituximab was subsequently concentrated to around 200 mg/mL (200 ± 5 mg/mL) using an Eppendorf centrifuge. To ascertain
25 Rituximab's concentration in the groups, absorbance at 280 nm combine with SE-UPLC was gauged against corresponding buffers containing a viscosity-reducing and stabilizing agent for excipient-containing samples. For Rituximab without excipients, the buffer alone (i.e., devoid of excipients) served as a blank for protein concentration calculation. The extinction coefficient was measured at $1.65 \text{ (mg/mL)}^{-1} \cdot \text{cm}^{-1}$.

[0095] The viscosity of samples was measured by VROC® initium one plus viscometer (Rheosense) at 20°C. For samples with a viscosity exceeding 1000 cP, viscosity was measured using a TA rheometer.

[0096] As shown in Table 91, the data demonstrated the viscosity-reducing efficacy of viscosity-reducing and stabilizing formulations of the present application on Rituximab within histidine buffer. As for Rituximab at a concentration of 200 ± 5 mg/mL, the tested viscosity-reducing and stabilizing formulations exhibited significant viscosity reduction, better than the efficacy of the reference lead formulation from WO2018211517.

Table 91 Viscosity reducing effect of viscosity-reducing and stabilizing formulations on 200 ± 5 mg/mL Rituximab in histidine buffer, pH 6.0 at 20°C.

Protein Concentration (mg/mL)	Viscosity-reducing and stabilizing formulation	Viscosity (cP) @ 20°C
200	140 mM Arginine and 140 mM Niacin	28.1
200	140 mM Histidine and 140 mM Niacin	28.3
200	140 mM Meglumine and 140 mM Niacin	45.0
200	140 mM Lysine + 140 mM Niacinamide	40.1
200	70 mM Arginine-HCl and 140 mM Niacinamide	35.6
200	140 mM Histidine and 140 mM Niacinamide	44.8
200	140 mM Meglumine and 140 mM Niacinamide	44.7
200	70 mM Lysine HCl and 140 mM Niacinamide	44.6
200	Lead formulation from WO2018211517 25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form) and 29.4 mM Tryptophan, pH 6.0	53.4
200	20 mM histidine buffer, pH 6.0	61.4

Example 7: Effect of viscosity-reducing and stabilizing formulations on Pembrolizumab stability at various temperatures.

[0097] This example tested the effect of viscosity-reducing and stabilizing formulations of the present application on Pembrolizumab stability and compared it with the lead formulation (25 mM Phosphate, 81.2 mM of Nicotinic acid and 29.4 mM Tryptophan) in WO2018211517.

[0098] Materials and Methods

[0099] The Pembrolizumab (Keytruda®) samples were produced by WuXi Biologics, as described in Example 1, and formulated as shown in Tables 92-109. The prepared samples were

aseptically filtered with 0.22 μm PVDF membrane filters before filling. After filtration, samples were filled with a pipette to 2 mL vials, and the fill volume was 1.0 mL. Then the vials were stoppered and sealed and subjected to 5°C, 25°C and 40°C chambers to start the stability assessment. Furthermore, there was a formulation comprising 25 mM phosphate buffer at pH 6.0, with 81.2 mM Nicotinic acid and 29.4 mM Tryptophan (matching the lead formulation 25 mM phosphate buffer at pH 6.0 along with 10 mg/mL Nicotinic acid (acid form) and 6 mg/mL Tryptophan from Examples 14 and 16-21 in WO2018211517) as control group. After preparing the control group samples, the pH was adjusted to the target value using hydrochloric acid and sodium hydroxide. An additional group, consisting solely of MilliQ water and the protein, was prepared as a blank. The pH of the blank group was also adjusted to match the target pH using the same method. To ascertain Pembrolizumab's concentration in the groups, absorbance at 280 nm combined with SE-UPLC was gauged against corresponding buffers containing a viscosity-reducing and stabilizing agent for excipient-containing samples, and absorbance at 280 nm was measured for the protein solution without a viscosity-reducing and stabilizing formulation. For Pembrolizumab without excipients, the buffer alone (i.e., devoid of excipients) served as a blank for protein concentration calculation. The extinction coefficient was measured at 1.42 (mg/mL)⁻¹·cm⁻¹.

[00100] The test for protein stability was carried out over a 4-week period by SE-UPLC. Samples were prepared as described above. As shown in Tables 92-109, after 4 weeks, the monomer content of Pembrolizumab at a concentration from 100 to 300 mg/mL formulated with the tested viscosity-reducing and stabilizing formulations was higher than or close to 90% even at 40°C, comparable or better than the lead formulation in WO2018211517, regardless of the used buffers, indicating good stabilization effect of the tested viscosity-reducing and stabilizing formulations.

Table 92 SE-UPLC results of formulated Pembrolizumab in 5 mM Histidine buffer, pH 5.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	95.7	95.7	95.3	92.5	4.3	4.3	4.7	7.3
300	30 mM Histidine and 30 mM Niacin	95.6	95.5	95.1	92.4	4.4	4.5	4.9	7.4
300	30 mM Meglumine and 30 mM Niacin	95.7	95.7	95.3	92.5	4.3	4.3	4.7	7.3
300	30 mM Lysine and 30 mM Niacin	95.8	95.7	95.3	92.6	4.2	4.3	4.7	7.2
300	30 mM Arginine-HCl and 30 mM Niacinamide	95.6	95.6	95.3	92.8	4.4	4.4	4.7	7.0
300	30 mM Histidine and 30 mM Niacinamide	95.6	95.5	95.1	92.6	4.4	4.5	4.9	7.2
300	30 mM Meglumine and 30 mM Niacinamide	95.8	95.8	95.4	92.8	4.2	4.2	4.6	7.0
300	30 mM Lysine-HCl and 30 mM Niacinamide	95.7	95.6	95.3	92.7	4.3	4.4	4.7	7.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	95.5	95.5	92.9	89.0	4.5	4.5	7.1	10.7
300	Water (Blank), pH 5.0	95.0	94.9	92.1	88.1	5.0	5.1	7.9	11.7
200	30 mM Arginine and 30 mM Niacin	96.6	96.6	96.5	93.5	3.3	3.4	3.5	6.3
200	30 mM Histidine and 30 mM Niacin	96.6	96.6	96.5	94.3	3.3	3.4	3.5	5.5
200	30 mM Meglumine and 30 mM Niacin	96.6	96.6	96.3	93	3.3	3.4	3.7	6.8
200	30 mM Lysine and 30 mM Niacin	96.7	96.7	96.4	93.1	3.3	3.3	3.6	6.7
200	30 mM Arginine-HCl and 30 mM Niacinamide	96.5	96.5	95.9	95.3	3.8	3.5	4.1	4.5
200	30 mM Histidine and 30 mM Niacinamide	96.5	96.5	96.7	94.1	3.2	3.5	3.3	5.7
200	30 mM Meglumine and 30 mM Niacinamide	96.7	96.7	96.4	93.9	3.3	3.3	3.6	5.9
200	30 mM Lysine-HCl and 30 mM Niacinamide	96.6	96.6	96.2	93.7	3.4	3.4	3.8	6.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	96.4	96.3	94.1	92.0	3.6	3.7	4.9	7.0
200	Water (blank), pH 5.0	95.7	95.6	92.8	90.0	4.3	4.4	7.2	9.8
100	30 mM Arginine and 30 mM Niacin	96.7	96.7	96.2	93.9	3.3	3.3	3.8	5.9
100	30 mM Histidine and 30 mM Niacin	96.7	96.7	96.1	94.7	3.3	3.3	3.9	5.1
100	30 mM Meglumine and 30 mM Niacin	96.7	96.7	96.2	93.4	3.3	3.3	3.8	6.4
100	30 mM Lysine and 30 mM Niacin	96.8	96.8	96.3	93.5	3.2	3.2	3.7	6.3
100	30 mM Arginine-HCl and 30 mM Niacinamide	96.6	96.6	96.1	95.7	3.4	3.4	3.9	4.1
100	30 mM Histidine and 30 mM Niacinamide	96.6	96.6	96.1	94.5	3.4	3.4	3.9	5.3
100	30 mM Meglumine and 30 mM Niacinamide	96.8	96.8	96.3	94.3	3.2	3.2	3.7	5.5
100	30 mM Lysine-HCl and 30 mM Niacinamide	96.7	96.7	96.2	94.1	3.3	3.3	3.8	5.7
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	96.5	96.5	96.0	93.0	3.5	3.5	4.0	7.0
100	Water (blank), pH 5.0	95.9	95.9	95.7	92.6	4.1	4.1	4.3	7.3

Table 93 SE-UPLC results of formulated Pembrolizumab in 20 mM Histidine buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	95.8	95.7	95.4	93.0	4.2	4.3	4.6	6.8
300	140 mM Histidine and 140 mM Niacin	95.6	95.5	95.2	92.9	4.4	4.5	4.8	6.9
300	140 mM Meglumine and 140 mM Niacin	95.5	95.4	95.1	93.1	4.5	4.6	4.9	6.7
300	140 mM Lysine and 140 mM Niacin	95.4	95.3	95.2	93.2	4.6	4.7	4.8	6.6
300	70 mM Arginine·HCl and 140 mM Niacinamide	95.3	95.2	95.0	93.0	4.7	4.8	5.0	6.8
300	140 mM Histidine and 140 mM Niacinamide	95.2	95.1	95.0	92.8	4.8	4.9	5.0	7.0
300	140 mM Meglumine and 140 mM Niacinamide	95.1	95.0	94.9	92.7	4.9	5.0	5.1	7.1
300	70 mM Lysine·HCl and 140 mM Niacinamide	95.0	94.9	94.8	92.5	5.0	5.1	5.2	7.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	95.6	95.5	94.9	92.0	4.4	4.5	5.1	7.7
300	Water (blank), pH 6.0	95.0	94.9	94.1	91.0	4.9	5.0	5.9	8.9
200	140 mM Arginine and 140 mM Niacin	96.7	96.7	96.5	94.0	3.3	3.3	3.5	5.7
200	140 mM Histidine and 140 mM Niacin	96.7	96.7	96.5	94.8	3.3	3.3	3.5	4.9
200	140 mM Meglumine and 140 mM Niacin	96.7	96.7	96.3	93.5	3.3	3.3	3.7	6.3
200	140 mM Lysine and 140 mM Niacin	96.7	96.7	96.5	93.8	3.3	3.3	3.5	6.0
200	70 mM Arginine·HCl and 140 mM Niacinamide	96.2	96.2	95.9	95.8	3.8	3.8	4.1	3.9
200	140 mM Histidine and 140 mM Niacinamide	96.8	96.8	96.7	94.6	3.2	3.2	3.3	5.1
200	140 mM Meglumine and 140 mM Niacinamide	96.7	96.7	96.4	94.4	3.3	3.3	3.6	5.3
200	70 mM Lysine·HCl and 140 mM Niacinamide	96.6	96.6	96.3	94.0	3.4	3.4	3.7	5.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.4	96.3	95.1	92.8	3.6	3.7	4.9	7.0
200	Water (blank), pH 6.0	95.7	95.6	94.3	92.0	4.3	4.4	5.7	7.9
100	140 mM Arginine and 140 mM Niacin	96.8	96.8	96.3	94.5	3.2	3.2	3.7	5.3
100	140 mM Histidine and 140 mM Niacin	96.7	96.7	96.2	94.4	3.3	3.3	3.8	5.4
100	140 mM Meglumine and 140 mM Niacin	96.6	96.6	96.1	94.2	3.4	3.4	3.9	5.6
100	140 mM Lysine and 140 mM Niacin	96.5	96.5	96.0	93.9	3.5	3.5	4.0	5.9
100	70 mM Arginine·HCl and 140 mM Niacinamide	96.4	96.4	95.9	93.8	3.6	3.6	4.1	6.0
100	140 mM Histidine and 140 mM Niacinamide	96.5	96.5	96.0	94.1	3.5	3.5	4.0	5.7
100	140 mM Meglumine and 140 mM Niacinamide	96.6	96.6	96.2	93.5	3.4	3.4	3.8	6.3
100	70 mM Lysine·HCl and 140 mM Niacinamide	96.7	96.7	96.1	93.7	3.3	3.3	3.9	6.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.5	96.5	96.0	94.0	3.5	3.5	4.0	6.0
100	Water (blank), pH 6.0	96.0	96.0	95.7	93.7	4.0	4.0	4.3	6.3

Table 94 SE-UPLC results of formulated Pembrolizumab in 50 mM Histidine buffer, pH 7.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	95.6	95.6	95.2	93.8	4.4	4.4	4.8	6.0
300	300 mM Histidine and 300 mM Niacin	95.7	95.7	95.3	93.7	4.3	4.3	4.7	6.1
300	300 mM Meglumine and 300 mM Niacin	95.7	95.7	95.3	93.9	4.3	4.3	4.7	5.9
300	300 mM Lysine and 300 mM Niacin	95.4	95.4	95.0	94.0	4.6	4.6	5.0	5.8
300	140 mM Arginine·HCl and 300 mM Niacinamide	95.4	95.4	95.0	93.8	4.6	4.6	5.0	6.0
300	300 mM Histidine and 300 mM Niacinamide	95.0	95.0	94.6	93.6	5.0	5.0	5.4	6.2
300	300 mM Meglumine and 300 mM Niacinamide	95.0	95.0	94.6	93.5	5.0	5.0	5.4	6.3
300	140 mM Lysine·HCl and 300 mM Niacinamide	95.0	95.0	94.6	93.3	5.0	5.0	5.4	6.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	94.9	94.7	94.0	92.0	5.1	5.3	6.0	7.8
300	Water (Blank), pH 7.0	94.7	94.5	93.5	91.5	5.3	5.5	6.5	8.3
200	300 mM Arginine and 300 mM Niacin	96.7	96.7	96.3	94.0	3.3	3.3	3.7	5.8
200	300 mM Histidine and 300 mM Niacin	96.7	96.7	96.0	94.9	3.3	3.3	4.0	4.9
200	300 mM Meglumine and 300 mM Niacin	96.7	96.7	96.0	93.4	3.3	3.3	4.0	6.4
200	300 mM Lysine and 300 mM Niacin	96.7	96.7	96.2	94.0	3.3	3.3	3.8	5.8
200	140 mM Arginine·HCl and 300 mM Niacinamide	96.2	96.2	95.4	95.6	3.8	3.8	4.6	4.2
200	300 mM Histidine and 300 mM Niacinamide	96.8	96.8	96.3	94.7	3.2	3.2	3.7	5.1
200	300 mM Meglumine and 300 mM Niacinamide	96.7	96.7	96.3	94.5	3.3	3.3	3.7	5.3
200	140 mM Lysine·HCl and 300 mM Niacinamide	96.6	96.6	96.0	94.0	3.4	3.4	4.0	5.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	96.3	96.1	94.8	92.8	3.7	3.9	5.2	7.0
200	Water (blank), pH 7.0	95.7	95.6	94.0	91.8	4.3	4.4	5.9	8.1
100	300 mM Arginine and 300 mM Niacin	96.7	96.7	96.0	94.3	3.2	3.2	3.6	5.5
100	300 mM Histidine and 300 mM Niacin	96.7	96.7	95.9	95.2	3.3	3.3	3.8	4.6
100	300 mM Meglumine and 300 mM Niacin	96.7	96.7	95.9	93.7	3.4	3.4	3.9	6.1
100	300 mM Lysine and 300 mM Niacin	96.7	96.7	95.8	94.3	3.5	3.5	3.9	5.5
100	140 mM Arginine·HCl and 300 mM Niacinamide	96.2	96.2	96.1	95.7	3.6	3.6	4.0	4.1
100	300 mM Histidine and 300 mM Niacinamide	96.8	96.8	96.1	94.9	3.5	3.5	3.7	4.9
100	300 mM Meglumine and 300 mM Niacinamide	96.7	96.7	95.9	94.7	3.4	3.4	3.7	5.1
100	140 mM Lysine·HCl and 300 mM Niacinamide	96.6	96.6	96.2	94.2	3.3	3.3	3.9	5.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	96.5	96.5	95.8	93.7	3.5	3.5	4.2	6.3
100	Water (blank), pH 7.0	95.9	95.9	95.4	93.4	4.1	4.1	4.6	6.6

Table 95 SE-UPLC results of formulated Pembrolizumab in 5 mM Acetate buffer, pH 4.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	95.7	95.6	93.2	88.1	4.3	4.4	6.8	7.9
300	30 mM Histidine and 30 mM Niacin	95.6	95.3	92.9	88.9	4.4	4.7	7.1	7.1
300	30 mM Meglumine and 30 mM Niacin	95.7	95.5	93.0	89.0	4.3	4.5	7.0	7
300	30 mM Lysine and 30 mM Niacin	95.8	95.5	93.0	88.5	4.2	4.5	7.0	7.5
300	30 mM Arginine-HCl and 30 mM Niacinamide	95.6	95.5	93.0	88.3	4.4	4.5	7.0	7.7
300	30 mM Histidine and 30 mM Niacinamide	95.6	95.4	92.7	87.5	4.4	4.6	7.3	8.5
300	30 mM Meglumine and 30 mM Niacinamide	95.8	95.5	93.2	88.0	4.2	4.5	6.8	8
300	30 mM Lysine-HCl and 30 mM Niacinamide	95.7	95.4	92.8	89.0	4.3	4.6	7.2	7
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	95.5	95.0	91.5	79.5	4.5	5.0	8.5	12.5
300	Water (Blank), pH 4.5	95.0	94.0	90.1	76.1	5.0	6.0	9.9	15.9
200	30 mM Arginine and 30 mM Niacin	96.8	96.6	94.1	89.6	3.2	3.4	5.9	7.4
200	30 mM Histidine and 30 mM Niacin	96.7	96.4	93.7	89.9	3.3	3.6	6.3	7.1
200	30 mM Meglumine and 30 mM Niacin	96.8	96.5	94.2	89.8	3.2	3.5	5.8	7.2
200	30 mM Lysine and 30 mM Niacin	96.5	96.4	93.8	90.0	3.5	3.6	6.2	7
200	30 mM Arginine-HCl and 30 mM Niacinamide	96.5	96.2	93.6	90.0	3.5	3.8	6.4	7
200	30 mM Histidine and 30 mM Niacinamide	96.7	96.5	94.1	89.9	3.3	3.5	5.9	7.1
200	30 mM Meglumine and 30 mM Niacinamide	96.9	96.8	94.1	90.9	3.1	3.2	5.9	6.1
200	30 mM Lysine-HCl and 30 mM Niacinamide	96.6	96.5	94.1	90.1	3.4	3.5	5.9	6.9
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	96.4	96.0	92.1	81.0	3.6	4.0	7.9	12.0
200	Water (blank), pH 4.5	95.7	95.2	88.8	79.0	4.3	4.8	11.2	14.8
100	30 mM Arginine and 30 mM Niacin	96.8	96.6	93.9	90.9	3.2	3.4	6.1	6.1
100	30 mM Histidine and 30 mM Niacin	96.7	96.4	93.8	89.7	3.3	3.6	6.2	7.3
100	30 mM Meglumine and 30 mM Niacin	96.8	96.7	94.2	90.1	3.2	3.3	5.8	6.9
100	30 mM Lysine and 30 mM Niacin	96.5	96.3	93.5	89.8	3.5	3.7	6.5	7.2
100	30 mM Arginine-HCl and 30 mM Niacinamide	96.5	96.3	93.7	89.5	3.5	3.7	6.3	7.5
100	30 mM Histidine and 30 mM Niacinamide	96.7	96.6	93.9	90.7	3.3	3.4	6.1	6.3
100	30 mM Meglumine and 30 mM Niacinamide	96.9	96.7	94.1	89.9	3.1	3.3	5.9	7.1
100	30 mM Lysine-HCl and 30 mM Niacinamide	96.6	96.3	93.7	90.4	3.4	3.7	6.3	6.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	96.5	96.1	92.0	83.0	3.5	3.9	8.0	11.5
100	Water (blank), pH 4.5	95.7	95.0	87.7	82.6	4.3	5.0	12.3	12.3

Table 96 SE-UPLC results of formulated Pembrolizumab in 20 mM Acetate buffer, pH 5.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	95.6	95.6	95.2	92.6	4.3	4.3	4.8	7.2
300	140 mM Histidine and 140 mM Niacin	95.6	95.5	94.9	92.5	4.4	4.5	5.1	7.3
300	140 mM Meglumine and 140 mM Niacin	95.6	95.6	95.2	92.3	4.3	4.3	4.8	7.5
300	140 mM Lysine and 140 mM Niacin	95.6	95.6	95.2	92.8	4.2	4.3	4.8	7.0
300	70 mM Arginine·HCl and 140 mM Niacinamide	95.6	95.6	95	92.8	4.4	4.4	5.0	7.0
300	140 mM Histidine and 140 mM Niacinamide	95.6	95.5	94.9	92.4	4.4	4.5	5.1	7.4
300	140 mM Meglumine and 140 mM Niacinamide	95.6	95.5	95.2	92.8	4.2	4.2	4.8	7.0
300	70 mM Lysine·HCl and 140 mM Niacinamide	95.8	95.6	95.1	92.7	4.3	4.4	4.9	7.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	95.5	95.5	92.9	89.0	4.5	4.5	7.1	10.7
300	Water (Blank), pH 5.0	95.0	94.9	92.1	88.1	5.0	5.1	7.9	11.7
200	140 mM Arginine and 140 mM Niacin	96.8	96.8	95.7	93.9	3.2	3.2	4.3	5.9
200	140 mM Histidine and 140 mM Niacin	96.6	96.6	95.5	93.8	3.4	3.4	4.5	6.0
200	140 mM Meglumine and 140 mM Niacin	96.4	96.4	95.2	93.6	3.6	3.6	4.8	6.2
200	140 mM Lysine and 140 mM Niacin	96.7	96.7	95.7	94.1	3.3	3.3	4.3	5.7
200	70 mM Arginine·HCl and 140 mM Niacinamide	96.6	96.6	95.6	94	3.4	3.4	4.4	5.8
200	140 mM Histidine and 140 mM Niacinamide	96.4	96.4	95.3	93.4	3.6	3.6	4.7	6.4
200	140 mM Meglumine and 140 mM Niacinamide	96.5	96.5	95.5	94	3.5	3.5	4.5	5.8
200	70 mM Lysine·HCl and 140 mM Niacinamide	96.7	96.7	95.7	94	3.3	3.3	4.3	5.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	96.4	96.3	94.1	92.0	3.6	3.7	4.9	7.0
200	Water (blank), pH 5.0	95.7	95.6	92.8	90.0	4.3	4.4	7.2	9.8
100	140 mM Arginine and 140 mM Niacin	96.7	96.7	96.3	93.8	3.3	3.3	3.7	6.0
100	140 mM Histidine and 140 mM Niacin	96.7	96.7	95.9	93.8	3.3	3.3	4.1	6.0
100	140 mM Meglumine and 140 mM Niacin	96.7	96.7	95.6	93.4	3.3	3.3	4.4	6.4
100	140 mM Lysine and 140 mM Niacin	96.8	96.8	96.1	93.8	3.2	3.2	3.9	6.0
100	70 mM Arginine·HCl and 140 mM Niacinamide	96.6	96.6	96.0	93.7	3.4	3.4	4.0	6.1
100	140 mM Histidine and 140 mM Niacinamide	96.6	96.6	96.3	93.8	3.4	3.4	3.7	6.0
100	140 mM Meglumine and 140 mM Niacinamide	96.8	96.8	95.9	93.6	3.2	3.2	4.1	6.2
100	70 mM Lysine·HCl and 140 mM Niacinamide	96.7	96.7	96.2	93.9	3.3	3.3	3.8	5.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	96.5	96.5	96.0	93.0	3.5	3.5	4.0	7.0
100	Water (blank), pH 5.0	95.9	95.9	95.7	92.6	4.1	4.1	4.3	7.3

Table 97 SE-UPLC results of formulated Pembrolizumab in 50 mM Acetate buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing Formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	95.8	95.8	95.2	93.4	4.2	4.2	4.8	6.4
300	300 mM Histidine and 300 mM Niacin	95.6	95.6	95.3	93.0	4.4	4.4	4.7	6.8
300	300 mM Meglumine and 300 mM Niacin	95.5	95.5	95.1	92.9	4.5	4.5	4.9	6.9
300	300 mM Lysine and 300 mM Niacin	95.4	95.4	94.9	93.4	4.6	4.6	5.1	6.4
300	140 mM Arginine·HCl and 300 mM Niacinamide	95.3	95.3	94.9	92.8	4.7	4.7	5.1	7.0
300	300 mM Histidine and 300 mM Niacinamide	95.3	95.3	94.7	93.2	4.7	4.7	5.3	6.6
300	300 mM Meglumine and 300 mM Niacinamide	95.4	95.4	94.9	93.3	4.6	4.6	5.1	6.5
300	140 mM Lysine·HCl and 300 mM Niacinamide	95.3	95.3	95.0	92.7	4.7	4.7	5.0	7.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	95.6	95.5	94.9	92.0	4.4	4.5	5.1	7.7
300	Water (Blank), pH 6.0	95.0	94.9	94.1	91.0	4.9	5.0	5.9	8.9
200	300 mM Arginine and 300 mM Niacin	96.5	96.5	96	94.7	3.5	3.5	4.0	5.1
200	300 mM Histidine and 300 mM Niacin	96.6	96.6	95.7	94.2	3.4	3.4	4.3	5.6
200	300 mM Meglumine and 300 mM Niacin	96.5	96.5	95.9	94.5	3.5	3.5	4.1	5.3
200	300 mM Lysine and 300 mM Niacin	96.6	96.6	95.8	93.9	3.4	3.4	4.2	5.9
200	140 mM Arginine·HCl and 300 mM Niacinamide	96.5	96.5	95.6	94.3	3.5	3.5	4.4	5.5
200	300 mM Histidine and 300 mM Niacinamide	96.5	96.5	95.6	94.1	3.5	3.5	4.4	5.7
200	300 mM Meglumine and 300 mM Niacinamide	96.6	96.6	95.7	94.6	3.4	3.4	4.3	5.2
200	140 mM Lysine·HCl and 300 mM Niacinamide	96.6	96.6	95.9	94.2	3.4	3.4	4.1	5.6
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.4	96.3	95.1	92.8	3.6	3.7	4.9	7.0
200	Water (blank), pH 6.0	95.7	95.6	94.3	92.0	4.3	4.4	5.7	7.9
100	300 mM Arginine and 300 mM Niacin	96.7	96.7	96.4	95.1	3.3	3.3	3.6	4.7
100	300 mM Histidine and 300 mM Niacin	96.6	96.6	96.4	95.1	3.4	3.4	3.6	4.7
100	300 mM Meglumine and 300 mM Niacin	96.6	96.6	96.3	95	3.4	3.4	3.7	4.8
100	300 mM Lysine and 300 mM Niacin	96.5	96.5	96.3	95.2	3.5	3.5	3.7	4.6
100	140 mM Arginine·HCl and 300 mM Niacinamide	96.5	96.5	96.3	95.2	3.5	3.5	3.7	4.6
100	300 mM Histidine and 300 mM Niacinamide	96.5	96.5	96.4	95.1	3.5	3.5	3.6	4.7
100	300 mM Meglumine and 300 mM Niacinamide	96.6	96.6	96.5	95.1	3.4	3.4	3.5	4.7
100	140 mM Lysine·HCl and 300 mM Niacinamide	96.7	96.7	96.4	95.3	3.3	3.3	3.6	4.5
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.5	96.5	96.0	94.0	3.5	3.5	4.0	6.0
100	Water (blank), pH 6.0	96.0	96.0	95.7	93.7	4.0	4.0	4.3	6.3

Table 98 SE-UPLC results of formulated Pembrolizumab in 5 mM Citrate buffer, pH 4.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	95.7	95.7	93.3	88.3	4.3	4.3	6.7	7.7
300	30 mM Histidine and 30 mM Niacin	95.7	95.7	93.3	88.7	4.3	4.3	6.7	7.3
300	30 mM Meglumine and 30 mM Niacin	95.8	95.7	93.6	88.7	4.2	4.3	6.4	7.3
300	30 mM Lysine and 30 mM Niacin	95.7	95.7	93.5	88.2	4.3	4.3	6.5	7.8
300	30 mM Arginine-HCl and 30 mM Niacinamide	95.5	95.5	93.3	88.1	4.5	4.5	6.7	7.9
300	30 mM Histidine and 30 mM Niacinamide	95.7	95.6	93.5	87.4	4.3	4.4	6.5	8.6
300	30 mM Meglumine and 30 mM Niacinamide	95.7	95.6	93.3	87.4	4.3	4.4	6.7	8.6
300	30 mM Lysine-HCl and 30 mM Niacinamide	95.6	95.6	93.4	87.8	4.4	4.4	6.6	8.2
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	95.5	95.0	91.5	79.5	4.5	5.0	8.5	12.5
300	Water (Blank), pH 4.5	95.0	94.0	90.1	76.1	5.0	6.0	9.9	15.9
200	30 mM Arginine and 30 mM Niacin	96.7	96.6	94.4	89.3	3.3	3.4	5.6	7.7
200	30 mM Histidine and 30 mM Niacin	96.8	96.7	94.4	90.8	3.2	3.3	5.6	6.2
200	30 mM Meglumine and 30 mM Niacin	96.7	96.6	94.1	89.7	3.3	3.4	5.9	7.3
200	30 mM Lysine and 30 mM Niacin	96.6	96.6	94.3	90.5	3.4	3.4	5.7	6.5
200	30 mM Arginine-HCl and 30 mM Niacinamide	96.6	96.6	94.2	89.5	3.4	3.4	5.8	7.5
200	30 mM Histidine and 30 mM Niacinamide	96.6	96.6	94.1	90.1	3.4	3.4	5.9	6.9
200	30 mM Meglumine and 30 mM Niacinamide	96.8	96.7	94.6	90.4	3.2	3.3	5.4	6.6
200	30 mM Lysine-HCl and 30 mM Niacinamide	96.5	96.5	93.9	90.5	3.5	3.5	6.1	6.5
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	96.4	96.0	92.1	81.0	3.6	4.0	7.9	12.0
200	Water (blank), pH 4.5	95.7	95.2	88.8	79.0	4.3	4.8	11.2	14.8
100	30 mM Arginine and 30 mM Niacin	96.9	96.7	94.6	91.3	3.1	3.3	5.4	5.7
100	30 mM Histidine and 30 mM Niacin	96.8	96.7	94.3	91.2	3.2	3.3	5.7	5.8
100	30 mM Meglumine and 30 mM Niacin	96.8	96.7	94.5	91.2	3.2	3.3	5.5	5.8
100	30 mM Lysine and 30 mM Niacin	96.6	96.4	94.3	90.1	3.4	3.6	5.7	6.9
100	30 mM Arginine-HCl and 30 mM Niacinamide	96.6	96.5	94.2	90.1	3.4	3.5	5.8	6.9
100	30 mM Histidine and 30 mM Niacinamide	96.7	96.6	94.1	90.5	3.3	3.4	5.9	6.5
100	30 mM Meglumine and 30 mM Niacinamide	96.8	96.7	94.2	90.9	3.2	3.3	5.8	6.1
100	30 mM Lysine-HCl and 30 mM Niacinamide	96.6	96.6	94.3	90.1	3.4	3.4	5.7	6.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	96.5	96.1	92.0	83.0	3.5	3.9	8.0	11.5
100	Water (blank), pH 4.5	95.7	95.0	87.7	82.6	4.3	5.0	12.3	12.3

Table 99 SE-UPLC results of formulated Pembrolizumab in 20 mM Citrate buffer, pH 5.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	95.7	95.7	93.9	92.7	4.3	4.3	6.1	7.1
300	140 mM Histidine and 140 mM Niacin	95.7	95.7	93.8	92.8	4.3	4.3	6.2	7.0
300	140 mM Meglumine and 140 mM Niacin	95.7	95.7	93.9	92.6	4.3	4.3	6.1	7.2
300	140 mM Lysine and 140 mM Niacin	95.5	95.5	93.9	92.9	4.5	4.5	6.1	6.9
300	70 mM Arginine·HCl and 140 mM Niacinamide	95.5	95.5	94.0	92.5	4.5	4.5	6.0	7.3
300	140 mM Histidine and 140 mM Niacinamide	95.5	95.5	93.9	92.3	4.5	4.5	6.1	7.5
300	140 mM Meglumine and 140 mM Niacinamide	95.5	95.5	93.9	92.9	4.5	4.5	6.1	6.9
300	70 mM Lysine·HCl and 140 mM Niacinamide	95.9	95.9	94.2	92.5	4.1	4.1	5.8	7.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	95.5	95.5	93.1	90.0	4.5	4.5	6.9	9.8
300	Water (blank), pH 5.5	95.0	94.9	92.5	89.2	5.0	5.1	7.5	10.6
200	140 mM Arginine and 140 mM Niacin	96.7	96.7	95.1	93.9	3.3	3.3	4.9	5.9
200	140 mM Histidine and 140 mM Niacin	96.7	96.7	95.4	93.5	3.3	3.3	4.6	6.3
200	140 mM Meglumine and 140 mM Niacin	96.5	96.5	95.1	93.3	3.5	3.5	4.9	6.5
200	140 mM Lysine and 140 mM Niacin	96.7	96.7	95.1	93.6	3.3	3.3	4.9	6.2
200	70 mM Arginine·HCl and 140 mM Niacinamide	96.6	96.6	95.2	93.5	3.4	3.4	4.8	6.3
200	140 mM Histidine and 140 mM Niacinamide	96.5	96.5	95	93.3	3.5	3.5	5.0	6.5
200	140 mM Meglumine and 140 mM Niacinamide	96.5	96.5	94.9	93.5	3.5	3.5	5.1	6.3
200	70 mM Lysine·HCl and 140 mM Niacinamide	96.8	96.8	95.4	93.9	3.2	3.2	4.6	5.9
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	96.4	96.3	94.5	92.8	3.6	3.7	5.5	7.0
200	Water (blank), pH 5.5	95.7	95.6	93.2	90.8	4.3	4.4	6.8	9.0
100	140 mM Arginine and 140 mM Niacin	96.8	96.8	96.5	95.1	3.2	3.2	3.5	4.7
100	140 mM Histidine and 140 mM Niacin	96.7	96.7	96.4	95.2	3.3	3.3	3.6	4.6
100	140 mM Meglumine and 140 mM Niacin	96.8	96.8	96.6	95.1	3.2	3.2	3.4	4.7
100	140 mM Lysine and 140 mM Niacin	96.7	96.7	96.3	95.0	3.3	3.3	3.7	4.8
100	70 mM Arginine·HCl and 140 mM Niacinamide	96.6	96.6	96.3	94.9	3.4	3.4	3.7	4.9
100	140 mM Histidine and 140 mM Niacinamide	96.5	96.5	96.3	95.0	3.5	3.5	3.7	4.8
100	140 mM Meglumine and 140 mM Niacinamide	96.8	96.8	96.4	95.1	3.2	3.2	3.6	4.7
100	70 mM Lysine·HCl and 140 mM Niacinamide	96.8	96.8	96.5	95.3	3.2	3.2	3.5	4.5
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	96.5	96.5	96.1	93.3	3.5	3.5	3.9	6.5
100	Water (blank), pH 5.5	95.9	95.9	95.9	93.1	4.1	4.1	4.1	6.7

Table 100 SE-UPLC results of formulated Pembrolizumab in 50 mM Citrate buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing Formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	95.7	95.7	95.4	93.1	4.3	4.3	4.6	6.7
300	300 mM Histidine and 300 mM Niacin	95.7	95.7	95.4	92.9	4.3	4.3	4.6	6.9
300	300 mM Meglumine and 300 mM Niacin	95.6	95.6	95.3	92.9	4.4	4.4	4.7	6.9
300	300 mM Lysine and 300 mM Niacin	95.7	95.7	95.3	93.4	4.3	4.3	4.7	6.4
300	140 mM Arginine·HCl and 300 mM Niacinamide	95.6	95.6	95.3	93.3	4.4	4.4	4.7	6.5
300	300 mM Histidine and 300 mM Niacinamide	95.4	95.4	95.2	93.0	4.6	4.6	4.8	6.8
300	300 mM Meglumine and 300 mM Niacinamide	95.4	95.4	94.9	92.7	4.6	4.6	5.1	7.1
300	140 mM Lysine·HCl and 300 mM Niacinamide	95.0	95.0	94.8	92.8	5.0	5.0	5.2	7.0
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	95.6	95.5	94.9	92.0	4.4	4.5	5.1	7.7
300	Water (Blank), pH 6.0	95.0	94.9	94.1	91.0	4.9	5.0	5.9	8.9
200	300 mM Arginine and 300 mM Niacin	96.6	96.6	96.0	94.1	3.4	3.4	4.0	5.7
200	300 mM Histidine and 300 mM Niacin	96.7	96.7	96.2	94.2	3.3	3.3	3.8	5.6
200	300 mM Meglumine and 300 mM Niacin	96.7	96.7	96.1	94.2	3.3	3.3	3.9	5.6
200	300 mM Lysine and 300 mM Niacin	96.6	96.6	96.1	94.1	3.4	3.4	3.9	5.7
200	140 mM Arginine·HCl and 300 mM Niacinamide	96.4	96.4	95.6	94.0	3.6	3.6	4.4	5.8
200	300 mM Histidine and 300 mM Niacinamide	96.6	96.6	96.0	94.3	3.4	3.4	4.0	5.5
200	300 mM Meglumine and 300 mM Niacinamide	96.7	96.7	96.0	94.4	3.3	3.3	4.0	5.4
200	140 mM Lysine·HCl and 300 mM Niacinamide	96.6	96.6	95.8	94.3	3.4	3.4	4.2	5.5
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.4	96.3	95.1	92.8	3.6	3.7	4.9	7.0
200	Water (blank), pH 6.0	95.7	95.6	96.2	92.0	4.3	4.4	5.7	7.9
100	300 mM Arginine and 300 mM Niacin	96.7	96.7	96.4	95.2	3.3	3.3	3.6	4.6
100	300 mM Histidine and 300 mM Niacin	96.7	96.7	96.4	95.0	3.3	3.3	3.6	4.8
100	300 mM Meglumine and 300 mM Niacin	96.7	96.7	96.3	94.9	3.3	3.3	3.7	4.9
100	300 mM Lysine and 300 mM Niacin	96.6	96.6	96.4	94.8	3.4	3.4	3.6	5.0
100	140 mM Arginine·HCl and 300 mM Niacinamide	96.6	96.6	96.2	94.9	3.4	3.4	3.8	4.9
100	300 mM Histidine and 300 mM Niacinamide	96.5	96.5	96.1	95.0	3.5	3.5	3.9	4.8
100	300 mM Meglumine and 300 mM Niacinamide	96.6	96.6	96.3	94.8	3.4	3.4	3.7	5.0
100	140 mM Lysine·HCl and 300 mM Niacinamide	96.7	96.7	96.3	95.0	3.3	3.3	3.7	4.8
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.5	96.5	96.0	94.0	3.5	3.5	4.0	6.0
100	Water (blank), pH 6.0	96.0	96.0	95.7	93.7	4.0	4.0	4.3	6.3

Table 101 SE-UPLC results of formulated Pembrolizumab in 5 mM Phosphate buffer, pH 6.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	95.6	95.6	95.1	93.7	4.4	4.4	4.9	6.1
300	30 mM Histidine and 30 mM Niacin	95.7	95.5	95.1	93.9	4.3	4.5	4.9	5.9
300	30 mM Meglumine and 30 mM Niacin	95.5	95.4	95.0	93.5	4.5	4.6	5.0	6.3
300	30 mM Lysine and 30 mM Niacin	95.8	95.6	95.4	94.1	4.2	4.4	4.6	5.7
300	30 mM Arginine-HCl and 30 mM Niacinamide	95.5	95.5	95.3	93.9	4.5	4.5	4.7	5.9
300	30 mM Histidine and 30 mM Niacinamide	95.5	95.5	95.1	93.9	4.5	4.5	4.9	5.9
300	30 mM Meglumine and 30 mM Niacinamide	95.6	95.4	95.2	93.8	4.4	4.6	4.8	6.0
300	30 mM Lysine-HCl and 30 mM Niacinamide	95.5	95.4	95.2	93.7	4.5	4.6	4.8	6.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	95.7	95.6	95.0	92.5	4.3	4.4	5.0	7.3
300	Water (blank), pH 6.5	95.2	95.0	94.5	92	4.8	5.0	5.5	7.8
200	30 mM Arginine and 30 mM Niacin	96.4	96.4	95.6	94.4	3.6	3.6	4.4	5.4
200	30 mM Histidine and 30 mM Niacin	96.5	96.5	95.6	94.5	3.5	3.5	4.4	5.3
200	30 mM Meglumine and 30 mM Niacin	96.5	96.5	95.6	94.5	3.5	3.5	4.4	5.3
200	30 mM Lysine and 30 mM Niacin	96.4	96.4	95.7	94.3	3.6	3.6	4.3	5.5
200	30 mM Arginine-HCl and 30 mM Niacinamide	96.5	96.5	95.4	94.5	3.5	3.5	4.6	5.3
200	30 mM Histidine and 30 mM Niacinamide	96.4	96.4	95.3	94.3	3.6	3.6	4.7	5.5
200	30 mM Meglumine and 30 mM Niacinamide	96.6	96.6	95.4	94.4	3.4	3.4	4.6	5.4
200	30 mM Lysine-HCl and 30 mM Niacinamide	96.3	96.3	95.4	94.5	3.7	3.7	4.6	5.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	96.4	96.4	95.2	93.0	3.6	3.6	4.8	6.8
200	Water (blank), pH 6.5	95.8	95.7	94.4	92.2	4.2	4.3	5.5	7.7
100	30 mM Arginine and 30 mM Niacin	96.6	96.6	96.4	94.8	3.4	3.4	3.6	5.0
100	30 mM Histidine and 30 mM Niacin	96.5	96.5	96.3	94.5	3.5	3.5	3.7	5.3
100	30 mM Meglumine and 30 mM Niacin	96.5	96.5	96.3	94.8	3.5	3.5	3.7	5.0
100	30 mM Lysine and 30 mM Niacin	96.5	96.5	96.3	94.4	3.5	3.5	3.7	5.4
100	30 mM Arginine-HCl and 30 mM Niacinamide	96.5	96.5	96.3	94.5	3.5	3.5	3.7	5.3
100	30 mM Histidine and 30 mM Niacinamide	96.5	96.5	96.2	94.7	3.5	3.5	3.8	5.1
100	30 mM Meglumine and 30 mM Niacinamide	96.6	96.6	96.3	94.6	3.4	3.4	3.7	5.2
100	30 mM Lysine-HCl and 30 mM Niacinamide	96.6	96.5	96.2	94.7	3.4	3.5	3.8	5.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	96.5	96.5	96.1	94.2	3.5	3.5	3.9	5.8
100	Water (blank), pH 6.5	96.0	96.0	95.8	93.8	4.0	4.0	4.2	6.2

Table 102 SE-UPLC results of formulated Pembrolizumab in 20 mM Phosphate buffer, pH 7.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	95.7	95.5	95.1	93.5	4.3	4.5	4.9	6.3
300	140 mM Histidine and 140 mM Niacin	95.6	95.5	95.1	93.8	4.4	4.5	4.9	6.0
300	140 mM Meglumine and 140 mM Niacin	95.5	95.4	95.0	93.3	4.5	4.6	5.0	6.5
300	140 mM Lysine and 140 mM Niacin	95.7	95.6	95.4	93.9	4.3	4.4	4.6	5.9
300	70 mM Arginine·HCl and 140 mM Niacinamide	95.6	95.5	95.3	93.7	4.4	4.5	4.7	6.1
300	140 mM Histidine and 140 mM Niacinamide	95.6	95.5	95.1	93.7	4.4	4.5	4.9	6.1
300	140 mM Meglumine and 140 mM Niacinamide	95.5	95.4	94.9	93.3	4.5	4.6	5.1	6.5
300	70 mM Lysine·HCl and 140 mM Niacinamide	95.5	95.5	94.9	93.6	4.5	4.5	5.1	6.2
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	94.9	94.7	94.0	92.0	5.1	5.3	6.0	7.8
300	Water (Blank), pH 7.0	94.7	94.5	93.5	91.5	5.3	5.5	6.5	8.3
200	140 mM Arginine and 140 mM Niacin	96.4	96.3	95.5	94.5	3.6	3.7	4.5	5.3
200	140 mM Histidine and 140 mM Niacin	96.5	96.4	95.7	94.6	3.5	3.6	4.3	5.2
200	140 mM Meglumine and 140 mM Niacin	96.5	96.4	95.6	94.4	3.5	3.6	4.4	5.4
200	140 mM Lysine and 140 mM Niacin	96.4	96.3	95.5	94.2	3.6	3.7	4.5	5.6
200	70 mM Arginine·HCl and 140 mM Niacinamide	96.4	96.3	95.3	94.6	3.6	3.7	4.7	5.2
200	140 mM Histidine and 140 mM Niacinamide	96.4	96.3	95.2	94.4	3.6	3.7	4.8	5.4
200	140 mM Meglumine and 140 mM Niacinamide	96.5	96.4	95.5	94.4	3.5	3.6	4.5	5.4
200	70 mM Lysine·HCl and 140 mM Niacinamide	96.4	96.3	95.5	94.6	3.6	3.7	4.5	5.2
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	96.3	96.1	94.8	92.8	3.7	3.9	5.2	7.0
200	Water (blank), pH 7.0	95.7	95.6	94.0	91.8	4.3	4.4	5.9	8.1
100	140 mM Arginine and 140 mM Niacin	96.5	96.5	96.3	94.7	3.5	3.5	3.7	5.1
100	140 mM Histidine and 140 mM Niacin	96.6	96.6	96.5	94.4	3.4	3.4	3.5	5.4
100	140 mM Meglumine and 140 mM Niacin	96.6	96.6	96.4	94.7	3.4	3.4	3.6	5.1
100	140 mM Lysine and 140 mM Niacin	96.5	96.5	96.2	94.4	3.5	3.5	3.8	5.4
100	70 mM Arginine·HCl and 140 mM Niacinamide	96.5	96.5	96.2	94.5	3.5	3.5	3.8	5.3
100	140 mM Histidine and 140 mM Niacinamide	96.5	96.5	96.4	94.7	3.5	3.5	3.6	5.1
100	140 mM Meglumine and 140 mM Niacinamide	96.6	96.6	96.4	94.5	3.4	3.4	3.6	5.3
100	70 mM Lysine·HCl and 140 mM Niacinamide	96.5	96.5	96.4	94.7	3.5	3.5	3.6	5.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	96.5	96.5	95.8	93.7	3.5	3.5	4.2	6.3
100	Water (blank), pH 7.0	95.9	95.9	95.4	93.4	4.1	4.1	4.6	6.6

Table 103 SE-UPLC results of formulated Pembrolizumab in 50 mM Phosphate buffer, pH 7.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing Formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	95.1	94.9	93.9	92.1	4.9	5.1	6.1	7.7
300	300 mM Histidine and 300 mM Niacin	95.0	94.8	93.9	92.3	5.0	5.2	6.1	7.5
300	300 mM Meglumine and 300 mM Niacin	95.0	94.8	93.8	92.2	5.0	5.2	6.2	7.6
300	300 mM Lysine and 300 mM Niacin	95.1	94.8	93.8	92.3	4.9	5.2	6.2	7.5
300	140 mM Arginine-HCl and 300 mM Niacinamide	95.1	95	93.9	92.3	4.9	5.0	6.1	7.5
300	300 mM Histidine and 300 mM Niacinamide	95.1	95	93.9	92.4	4.9	5.0	6.1	7.4
300	300 mM Meglumine and 300 mM Niacinamide	95.0	94.9	93.7	92.3	5.0	5.1	6.3	7.5
300	140 mM Lysine-HCl and 300 mM Niacinamide	95.0	94.9	93.8	92.3	5.0	5.1	6.2	7.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	95.0	94.6	93.0	90.5	5.0	5.4	7.0	9.3
300	Water (Blank), pH 7.5	94.2	93.8	92.0	90.0	5.8	6.2	8.0	9.8
200	300 mM Arginine and 300 mM Niacin	95.7	95.7	95.0	92.7	4.3	4.3	5.0	7.1
200	300 mM Histidine and 300 mM Niacin	95.7	95.7	95.0	92.7	4.3	4.3	5.0	7.1
200	300 mM Meglumine and 300 mM Niacin	95.8	95.8	95.0	93.1	4.2	4.2	5.0	6.7
200	300 mM Lysine and 300 mM Niacin	95.7	95.7	95.1	92.7	4.3	4.3	4.9	7.1
200	140 mM Arginine-HCl and 300 mM Niacinamide	95.8	95.8	95.1	93.1	4.2	4.2	4.9	6.7
200	300 mM Histidine and 300 mM Niacinamide	95.7	95.7	95.0	92.6	4.3	4.3	5.0	7.2
200	300 mM Meglumine and 300 mM Niacinamide	95.7	95.7	95.1	92.8	4.3	4.3	4.9	7.0
200	140 mM Lysine-HCl and 300 mM Niacinamide	95.8	95.8	95.1	92.8	4.2	4.2	4.9	7.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	95.8	95.6	94.1	91.8	4.2	4.4	5.9	9.0
200	Water (blank), pH 7.5	95.0	94.7	93.2	90.5	5.0	5.3	6.8	9.3
100	300 mM Arginine and 300 mM Niacin	95.7	95.7	95.1	92.8	4.3	4.3	4.9	7.0
100	300 mM Histidine and 300 mM Niacin	95.7	95.7	95.1	92.8	4.3	4.3	4.9	7.0
100	300 mM Meglumine and 300 mM Niacin	95.8	95.8	95.1	92.9	4.2	4.2	4.9	6.9
100	300 mM Lysine and 300 mM Niacin	95.7	95.7	95.2	93.1	4.3	4.3	4.8	6.7
100	140 mM Arginine-HCl and 300 mM Niacinamide	95.8	95.8	95.2	93.0	4.2	4.2	4.8	6.8
100	300 mM Histidine and 300 mM Niacinamide	95.7	95.7	95.1	92.8	4.3	4.3	4.9	7.0
100	300 mM Meglumine and 300 mM Niacinamide	95.7	95.7	95.2	93.2	4.3	4.3	4.8	6.6
100	140 mM Lysine-HCl and 300 mM Niacinamide	95.8	95.8	95.2	92.9	4.2	4.2	4.8	6.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	95.8	95.6	94.1	91.9	4.2	4.4	5.9	9.0
100	Water (blank), pH 7.5	95.1	94.7	93.2	90.5	4.9	5.3	6.8	9.3

Table 104 SE-UPLC results of formulated Pembrolizumab in 5 mM Tris buffer, pH 6.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	95.5	95.5	95.1	93.3	4.5	4.5	4.9	6.5
300	30 mM Histidine and 30 mM Niacin	95.8	95.8	95.3	93.5	4.2	4.2	4.7	6.3
300	30 mM Meglumine and 30 mM Niacin	95.5	95.5	95.0	93.0	4.5	4.5	5.0	6.8
300	30 mM Lysine and 30 mM Niacin	95.9	95.9	95.4	93.2	4.1	4.1	4.6	6.6
300	30 mM Arginine-HCl and 30 mM Niacinamide	95.6	95.6	95.3	93.2	4.4	4.4	4.7	6.6
300	30 mM Histidine and 30 mM Niacinamide	95.5	95.5	95.0	93.5	4.5	4.5	5.0	6.3
300	30 mM Meglumine and 30 mM Niacinamide	95.6	95.6	95.1	93.2	4.4	4.4	4.9	6.6
300	30 mM Lysine-HCl and 30 mM Niacinamide	95.6	95.6	95.1	92.9	4.4	4.4	4.9	6.9
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	95.7	95.6	95.0	92.5	4.3	4.4	5.0	7.3
300	Water (Blank), pH 6.5	95.2	95.0	94.5	92	4.8	5.0	5.5	7.8
200	30 mM Arginine and 30 mM Niacin	96.4	96.3	95.6	94.1	3.6	3.7	4.4	5.7
200	30 mM Histidine and 30 mM Niacin	96.5	96.5	95.6	94.1	3.5	3.5	4.4	5.7
200	30 mM Meglumine and 30 mM Niacin	96.5	96.5	95.6	93.9	3.5	3.5	4.4	5.9
200	30 mM Lysine and 30 mM Niacin	96.4	96.4	95.5	93.8	3.6	3.6	4.5	6.0
200	30 mM Arginine-HCl and 30 mM Niacinamide	96.5	96.5	95.7	94.2	3.5	3.5	4.3	5.6
200	30 mM Histidine and 30 mM Niacinamide	96.4	96.3	95.7	94.3	3.6	3.7	4.3	5.5
200	30 mM Meglumine and 30 mM Niacinamide	96.6	96.6	95.8	94.5	3.4	3.4	4.2	5.3
200	30 mM Lysine-HCl and 30 mM Niacinamide	96.3	96.3	95.4	94.1	3.7	3.7	4.6	5.7
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	96.4	96.4	95.2	93.0	3.6	3.6	4.8	6.8
200	Water (Blank), pH 6.5	95.8	95.7	94.4	92.2	4.2	4.3	5.5	7.7
100	30 mM Arginine and 30 mM Niacin	96.5	96.4	96.2	94.9	3.5	3.6	3.8	4.9
100	30 mM Histidine and 30 mM Niacin	96.5	96.5	96.2	94.7	3.5	3.5	3.8	5.1
100	30 mM Meglumine and 30 mM Niacin	96.5	96.5	96.2	94.7	3.5	3.5	3.8	5.1
100	30 mM Lysine and 30 mM Niacin	96.5	96.5	96.2	94.6	3.5	3.5	3.8	5.2
100	30 mM Arginine-HCl and 30 mM Niacinamide	96.5	96.5	96.2	94.6	3.5	3.5	3.8	5.2
100	30 mM Histidine and 30 mM Niacinamide	96.5	96.5	96.2	94.5	3.5	3.5	3.8	5.3
100	30 mM Meglumine and 30 mM Niacinamide	96.6	96.6	96.3	94.7	3.4	3.4	3.7	5.1
100	30 mM Lysine-HCl and 30 mM Niacinamide	96.6	96.5	96.2	94.7	3.4	3.5	3.8	5.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	96.5	96.5	96.1	94.2	3.5	3.5	3.9	5.8
100	Water (Blank), pH 6.5	96.0	96.0	95.8	93.8	4.0	4.0	4.2	6.2

Table 105 SE-UPLC results of formulated Pembrolizumab in 20 mM Tris buffer, pH 7.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	95.7	95.6	95.2	93.7	4.3	4.4	4.8	6.1
300	140 mM Histidine and 140 mM Niacin	95.7	95.6	95.2	93.1	4.3	4.4	4.8	6.7
300	140 mM Meglumine and 140 mM Niacin	95.5	95.4	95.0	93.5	4.5	4.6	5.0	6.3
300	140 mM Lysine and 140 mM Niacin	95.7	95.6	95.4	93.4	4.3	4.4	4.6	6.4
300	70 mM Arginine·HCl and 140 mM Niacinamide	95.6	95.5	95.3	93.4	4.4	4.5	4.7	6.4
300	140 mM Histidine and 140 mM Niacinamide	95.6	95.5	95.2	93.5	4.4	4.5	4.8	6.3
300	140 mM Meglumine and 140 mM Niacinamide	95.6	95.5	94.9	93.4	4.4	4.5	5.1	6.4
300	70 mM Lysine·HCl and 140 mM Niacinamide	95.7	95.6	94.9	93.5	4.3	4.4	5.1	6.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	94.9	94.7	94.0	92.0	5.1	5.3	6.0	7.8
300	Water (Blank), pH 7.0	94.7	94.5	93.5	91.5	5.3	5.5	6.5	8.3
200	140 mM Arginine and 140 mM Niacin	96.4	96.4	95.7	94.1	3.6	3.6	4.3	5.7
200	140 mM Histidine and 140 mM Niacin	96.5	96.5	95.6	94.3	3.5	3.5	4.4	5.5
200	140 mM Meglumine and 140 mM Niacin	96.6	96.6	95.9	94.2	3.4	3.4	4.1	5.6
200	140 mM Lysine and 140 mM Niacin	96.4	96.4	95.5	93.9	3.6	3.6	4.5	5.9
200	70 mM Arginine·HCl and 140 mM Niacinamide	96.4	96.4	95.6	93.8	3.6	3.6	4.4	6.0
200	140 mM Histidine and 140 mM Niacinamide	96.5	96.5	95.5	94.2	3.5	3.5	4.5	5.6
200	140 mM Meglumine and 140 mM Niacinamide	96.5	96.5	95.8	94.4	3.5	3.5	4.2	5.4
200	70 mM Lysine·HCl and 140 mM Niacinamide	96.5	96.5	95.5	94.4	3.5	3.5	4.5	5.4
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	96.3	96.1	94.8	92.8	3.7	3.9	5.2	7.0
200	Water (blank), pH 7.0	95.7	95.6	94.0	91.8	4.3	4.4	5.9	8.1
100	140 mM Arginine and 140 mM Niacin	96.6	96.6	96.3	94.9	3.4	3.4	3.7	4.9
100	140 mM Histidine and 140 mM Niacin	96.6	96.6	96.4	94.6	3.4	3.4	3.6	5.2
100	140 mM Meglumine and 140 mM Niacin	96.6	96.6	96.3	94.9	3.4	3.4	3.7	4.9
100	140 mM Lysine and 140 mM Niacin	96.5	96.5	96.1	94.4	3.5	3.5	3.9	5.4
100	70 mM Arginine·HCl and 140 mM Niacinamide	96.5	96.5	96.2	94.8	3.5	3.5	3.8	5.0
100	140 mM Histidine and 140 mM Niacinamide	96.5	96.5	96.4	94.5	3.5	3.5	3.6	5.3
100	140 mM Meglumine and 140 mM Niacinamide	96.6	96.6	96.3	94.7	3.4	3.4	3.7	5.1
100	70 mM Lysine·HCl and 140 mM Niacinamide	96.5	96.5	96.4	94.8	3.5	3.5	3.6	5.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	96.5	96.5	95.8	93.7	3.5	3.5	4.2	6.3
100	Water (blank), pH 7.0	95.9	95.9	95.4	93.4	4.1	4.1	4.6	6.6

Table 106 SE-UPLC results of formulated Pembrolizumab in 50 mM Tris buffer, pH 7.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing Formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	95.1	95.0	94.1	92.0	4.9	5.0	5.9	7.8
300	300 mM Histidine and 300 mM Niacin	95.1	95.1	94.0	92.4	4.9	4.9	6.0	7.4
300	300 mM Meglumine and 300 mM Niacin	95.1	95.0	94.0	92.3	4.9	5.0	6.0	7.5
300	300 mM Lysine and 300 mM Niacin	95.0	94.9	93.9	92.2	5.0	5.1	6.1	7.6
300	140 mM Arginine-HCl and 300 mM Niacinamide	95.1	95.1	94.0	92.3	4.9	4.9	6.0	7.5
300	300 mM Histidine and 300 mM Niacinamide	95.0	94.9	94.1	92.4	5.0	5.1	5.9	7.4
300	300 mM Meglumine and 300 mM Niacinamide	95.0	94.9	93.8	92.3	5.0	5.1	6.2	7.5
300	140 mM Lysine-HCl and 300 mM Niacinamide	95.1	95.1	94.0	92.3	4.9	4.9	6.0	7.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	95.0	94.6	93.0	90.5	5.0	5.4	7.0	9.3
300	Water (Blank), pH 7.5	94.2	93.8	92.0	90.0	5.8	6.2	8.0	9.8
200	300 mM Arginine and 300 mM Niacin	95.8	95.7	95.1	93.5	4.2	4.3	4.9	6.3
200	300 mM Histidine and 300 mM Niacin	95.7	95.6	95.1	93.4	4.3	4.4	4.9	6.4
200	300 mM Meglumine and 300 mM Niacin	95.8	95.7	95.1	93.3	4.2	4.3	4.9	6.5
200	300 mM Lysine and 300 mM Niacin	95.7	95.7	95.2	93.3	4.3	4.3	4.8	6.5
200	140 mM Arginine-HCl and 300 mM Niacinamide	95.9	95.8	95.2	93.4	4.1	4.2	4.8	6.4
200	300 mM Histidine and 300 mM Niacinamide	95.6	95.5	95.1	93.7	4.4	4.5	4.9	6.1
200	300 mM Meglumine and 300 mM Niacinamide	95.7	95.6	95.2	93.2	4.3	4.4	4.8	6.6
200	140 mM Lysine-HCl and 300 mM Niacinamide	95.7	95.6	95.1	93.4	4.3	4.4	4.9	6.4
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	95.8	95.6	94.1	91.8	4.2	4.4	5.9	9.0
200	Water (blank), pH 7.5	95.0	94.7	93.2	90.5	5.0	5.3	6.8	9.3
100	300 mM Arginine and 300 mM Niacin	95.8	95.8	95.3	93.6	4.2	4.2	4.7	6.2
100	300 mM Histidine and 300 mM Niacin	95.8	95.8	95.3	93.6	4.2	4.2	4.7	6.2
100	300 mM Meglumine and 300 mM Niacin	95.7	95.7	95.1	93.5	4.3	4.3	4.9	6.3
100	300 mM Lysine and 300 mM Niacin	95.8	95.8	95.2	93.4	4.2	4.2	4.8	6.4
100	140 mM Arginine-HCl and 300 mM Niacinamide	95.7	95.7	95.2	93.5	4.3	4.3	4.8	6.3
100	300 mM Histidine and 300 mM Niacinamide	95.7	95.7	95.3	93.9	4.3	4.3	4.7	5.9
100	300 mM Meglumine and 300 mM Niacinamide	95.7	95.7	95.2	93.3	4.3	4.3	4.8	6.5
100	140 mM Lysine-HCl and 300 mM Niacinamide	95.7	95.7	95.1	93.6	4.3	4.3	4.9	6.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	95.8	95.6	94.1	91.9	4.2	4.4	5.9	9.0
100	Water (blank), pH 7.5	95.1	94.7	93.2	90.5	4.9	5.3	6.8	9.3

Table 107 SE-UPLC results of formulated Pembrolizumab in 5 mM Succinate buffer, pH 4.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	95.6	95.6	93.5	88.1	4.4	4.4	6.5	7.9
300	30 mM Histidine and 30 mM Niacin	95.8	95.8	93.4	88.5	4.2	4.2	6.6	7.5
300	30 mM Meglumine and 30 mM Niacin	95.7	95.6	93.4	88.2	4.3	4.4	6.6	7.8
300	30 mM Lysine and 30 mM Niacin	95.6	95.6	93.7	88	4.4	4.4	6.3	8.0
300	30 mM Arginine-HCl and 30 mM Niacinamide	95.8	95.7	93.2	88.3	4.2	4.3	6.8	7.7
300	30 mM Histidine and 30 mM Niacinamide	95.5	95.4	93.5	87.6	4.5	4.6	6.5	8.4
300	30 mM Meglumine and 30 mM Niacinamide	95.6	95.5	93.4	87.5	4.4	4.5	6.6	8.5
300	30 mM Lysine-HCl and 30 mM Niacinamide	95.7	95.7	93.6	87.9	4.3	4.3	6.4	8.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	95.5	95.0	91.5	79.5	4.5	5.0	8.5	12.5
300	Water (Blank), pH 4.5	95.0	94.0	90.1	76.1	5.0	6.0	9.9	15.9
200	30 mM Arginine and 30 mM Niacin	96.5	96.5	94.3	89.5	3.5	3.5	5.7	7.5
200	30 mM Histidine and 30 mM Niacin	96.9	96.8	94.5	90.2	3.1	3.2	5.5	6.8
200	30 mM Meglumine and 30 mM Niacin	96.6	96.5	94	89.8	3.4	3.5	6.0	7.2
200	30 mM Lysine and 30 mM Niacin	96.5	96.5	94.2	90.3	3.5	3.5	5.8	6.7
200	30 mM Arginine-HCl and 30 mM Niacinamide	96.7	96.7	94.4	89.6	3.3	3.3	5.6	7.4
200	30 mM Histidine and 30 mM Niacinamide	96.7	96.6	94.2	90	3.3	3.4	5.8	7.0
200	30 mM Meglumine and 30 mM Niacinamide	96.9	96.8	94.7	90.6	3.1	3.2	5.3	6.4
200	30 mM Lysine-HCl and 30 mM Niacinamide	96.5	96.5	93.8	90.4	3.5	3.5	6.2	6.6
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	96.4	96.0	92.1	81.0	3.6	4.0	7.9	12.0
200	Water (blank), pH 4.5	95.7	95.2	88.8	79.0	4.3	4.8	11.2	14.8
100	30 mM Arginine and 30 mM Niacin	96.8	96.6	94.5	91.1	3.2	3.4	5.5	5.9
100	30 mM Histidine and 30 mM Niacin	96.7	96.6	94.2	91.0	3.3	3.4	5.8	6.0
100	30 mM Meglumine and 30 mM Niacin	96.7	96.6	94.4	91.0	3.3	3.4	5.6	6.0
100	30 mM Lysine and 30 mM Niacin	96.5	96.3	94.2	90.2	3.5	3.7	5.8	6.8
100	30 mM Arginine-HCl and 30 mM Niacinamide	96.5	96.4	94.3	90.3	3.5	3.6	5.7	6.7
100	30 mM Histidine and 30 mM Niacinamide	96.6	96.5	94.0	90.4	3.4	3.5	6.0	6.6
100	30 mM Meglumine and 30 mM Niacinamide	96.8	96.6	94.3	90.8	3.2	3.4	5.7	6.2
100	30 mM Lysine-HCl and 30 mM Niacinamide	96.5	96.5	94.2	90.3	3.5	3.5	5.8	6.7
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	96.5	96.1	92.0	83.0	3.5	3.9	8.0	11.5
100	Water (blank), pH 4.5	95.7	95.0	87.7	82.6	4.3	5.0	12.3	12.3

Table 108 SE-UPLC results of formulated Pembrolizumab in 20 mM Succinate buffer, pH 5.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	95.6	95.6	93.8	92.8	4.4	4.4	6.2	7.0
300	140 mM Histidine and 140 mM Niacin	95.8	95.7	93.7	92.9	4.2	4.3	6.3	6.9
300	140 mM Meglumine and 140 mM Niacin	95.6	95.6	93.8	92.5	4.4	4.4	6.2	7.3
300	140 mM Lysine and 140 mM Niacin	95.6	95.5	93.8	92.6	4.4	4.5	6.2	7.2
300	70 mM Arginine·HCl and 140 mM Niacinamide	95.5	95.5	94.1	92.4	4.5	4.5	5.9	7.4
300	140 mM Histidine and 140 mM Niacinamide	95.6	95.6	93.7	92.2	4.4	4.4	6.3	7.6
300	140 mM Meglumine and 140 mM Niacinamide	95.5	95.5	93.8	92.7	4.5	4.5	6.2	7.1
300	70 mM Lysine·HCl and 140 mM Niacinamide	95.9	95.8	94.3	92.4	4.1	4.2	5.7	7.4
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	95.5	95.5	93.1	90.0	4.5	4.5	6.9	9.8
300	Water (Blank), pH 5.5	95.0	94.9	92.5	89.2	5.0	5.1	7.5	10.6
200	140 mM Arginine and 140 mM Niacin	96.6	96.6	95.2	93.8	3.4	3.4	4.8	6.0
200	140 mM Histidine and 140 mM Niacin	96.6	96.6	95.3	93.6	3.4	3.4	4.7	6.2
200	140 mM Meglumine and 140 mM Niacin	96.5	96.5	95.2	93.2	3.5	3.5	4.8	6.6
200	140 mM Lysine and 140 mM Niacin	96.7	96.7	95.2	93.5	3.3	3.3	4.8	6.3
200	70 mM Arginine·HCl and 140 mM Niacinamide	96.6	96.6	95.1	93.4	3.4	3.4	4.9	6.4
200	140 mM Histidine and 140 mM Niacinamide	96.6	96.6	95.1	93.2	3.4	3.4	4.9	6.6
200	140 mM Meglumine and 140 mM Niacinamide	96.6	96.6	95.1	93.4	3.4	3.4	4.9	6.4
200	70 mM Lysine·HCl and 140 mM Niacinamide	96.8	96.8	95.2	93.7	3.2	3.2	4.8	6.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	96.4	96.3	94.5	92.8	3.6	3.7	5.5	7.0
200	Water (Blank), pH 5.5	95.7	95.6	93.2	90.8	4.3	4.4	6.8	9.0
100	140 mM Arginine and 140 mM Niacin	96.6	96.6	96.4	95.2	3.4	3.4	3.6	4.6
100	140 mM Histidine and 140 mM Niacin	96.6	96.6	96.4	95.3	3.4	3.4	3.6	4.5
100	140 mM Meglumine and 140 mM Niacin	96.5	96.5	96.3	95.2	3.5	3.5	3.7	4.6
100	140 mM Lysine and 140 mM Niacin	96.7	96.7	96.4	95.1	3.3	3.3	3.6	4.7
100	70 mM Arginine·HCl and 140 mM Niacinamide	96.6	96.6	96.4	95.0	3.4	3.4	3.6	4.8
100	140 mM Histidine and 140 mM Niacinamide	96.6	96.6	96.4	95.1	3.4	3.4	3.6	4.7
100	140 mM Meglumine and 140 mM Niacinamide	96.6	96.6	96.4	95.2	3.4	3.4	3.6	4.6
100	70 mM Lysine·HCl and 140 mM Niacinamide	96.8	96.8	96.5	95.4	3.2	3.2	3.5	4.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	96.5	96.5	96.1	93.3	3.5	3.5	3.9	6.5
100	Water (Blank), pH 5.5	95.9	95.9	95.9	93.1	4.1	4.1	4.1	6.7

Table 109 SE-UPLC results of formulated Pembrolizumab in 50 mM Succinate buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing Formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	95.7	95.7	95.5	93.2	4.3	4.3	4.5	6.6
300	300 mM Histidine and 300 mM Niacin	95.7	95.7	95.3	93.1	4.3	4.3	4.7	6.7
300	300 mM Meglumine and 300 mM Niacin	95.7	95.7	95.2	92.8	4.3	4.3	4.8	7.0
300	300 mM Lysine and 300 mM Niacin	95.6	95.6	95.2	93.1	4.4	4.4	4.8	6.7
300	140 mM Arginine-HCl and 300 mM Niacinamide	95.5	95.5	95.3	93.4	4.5	4.5	4.7	6.4
300	300 mM Histidine and 300 mM Niacinamide	95.4	95.4	95.3	93.1	4.6	4.6	4.7	6.7
300	300 mM Meglumine and 300 mM Niacinamide	95.4	95.4	95.0	92.8	4.6	4.6	5.0	7.0
300	140 mM Lysine-HCl and 300 mM Niacinamide	95.2	95.2	94.9	92.9	4.8	4.8	5.1	6.9
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	95.6	95.5	94.9	92.0	4.4	4.5	5.1	7.7
300	Water (Blank), pH 6.0	95.0	94.9	94.1	91.0	4.9	5.0	5.9	8.9
200	300 mM Arginine and 300 mM Niacin	96.7	96.7	96.1	94.2	3.3	3.3	3.9	5.6
200	300 mM Histidine and 300 mM Niacin	96.7	96.7	96.1	94.1	3.3	3.3	3.9	5.7
200	300 mM Meglumine and 300 mM Niacin	96.7	96.7	96.0	94.1	3.3	3.3	4.0	5.7
200	300 mM Lysine and 300 mM Niacin	96.7	96.7	96.0	94.2	3.3	3.3	4.0	5.6
200	140 mM Arginine-HCl and 300 mM Niacinamide	96.5	96.5	95.8	94.1	3.5	3.5	4.2	5.7
200	300 mM Histidine and 300 mM Niacinamide	96.6	96.6	96.1	94.2	3.4	3.4	3.9	5.6
200	300 mM Meglumine and 300 mM Niacinamide	96.7	96.7	96.1	94.3	3.3	3.3	3.9	5.5
200	140 mM Lysine-HCl and 300 mM Niacinamide	96.7	96.7	95.9	94.2	3.3	3.3	4.1	5.6
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.4	96.3	95.1	92.8	3.6	3.7	4.9	7.0
200	Water (Blank), pH 6.0	95.7	95.6	94.3	92.0	4.3	4.4	5.7	7.9
100	300 mM Arginine and 300 mM Niacin	96.7	96.7	96.5	95.3	3.3	3.3	3.5	4.5
100	300 mM Histidine and 300 mM Niacin	96.7	96.7	96.5	95.1	3.3	3.3	3.5	4.7
100	300 mM Meglumine and 300 mM Niacin	96.7	96.7	96.4	94.9	3.3	3.3	3.6	4.9
100	300 mM Lysine and 300 mM Niacin	96.7	96.6	96.4	94.9	3.3	3.4	3.6	4.9
100	140 mM Arginine-HCl and 300 mM Niacinamide	96.7	96.7	96.5	94.9	3.3	3.3	3.5	4.9
100	300 mM Histidine and 300 mM Niacinamide	96.6	96.5	96.4	95.1	3.4	3.5	3.6	4.7
100	300 mM Meglumine and 300 mM Niacinamide	96.6	96.6	96.3	94.9	3.4	3.4	3.7	4.9
100	140 mM Lysine-HCl and 300 mM Niacinamide	96.7	96.6	96.3	95.1	3.3	3.4	3.7	4.7
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.5	96.5	96.0	94.0	3.5	3.5	4.0	6.0
100	Water (Blank), pH 6.0	96.0	96.0	95.7	93.7	4.0	4.0	4.3	6.3

Example 8: Effect of viscosity-reducing and stabilizing formulations on Adalimumab stability at various temperatures.

[00101] This example tested the effect of viscosity-reducing and stabilizing formulations of the present application on Adalimumab stability and compared it with the lead formulation (25 mM Phosphate, 81.2 mM of Nicotinic acid and 29.4 mM Tryptophan) in WO2018211517.

[00102] Materials and Methods

[00103] The Adalimumab (Humira®) samples were produced by WuXi Biologics, as described in Example 2, and formulated as shown in Tables 110-127. The prepared samples were aseptically filtered with 0.22 µm PVDF membrane filters before filling. After filtration, samples were filled with a pipette to 2 mL vials, and the fill volume was 1.0 mL. Then the vials were stoppered and sealed and subjected to 5°C, 25°C and 40°C chambers to start the stability assessment. Furthermore, there was a control group group comprising 25 mM phosphate buffer at pH 6.0, with 81.2 mM Nicotinic acid and 29.4 mM Tryptophan (matching the lead formulation 25 mM phosphate buffer at pH 6.0 along with 10 mg/mL Nicotinic acid (acid form) and 6 mg/mL Tryptophan from Examples 14 and 16-21 in WO2018211517). After preparing the control group samples, the pH was adjusted to the target value using hydrochloric acid and sodium hydroxide. An additional control group, consisting solely of MilliQ water and the protein, was prepared as a blank. The pH of the blank group was also adjusted to match the target pH using the same method. To ascertain Adalimumab's concentration in the groups, absorbance at 280 nm combined with SE-UPLC was gauged against corresponding buffers containing a viscosity-reducing and stabilizing agent for excipient-containing samples, and absorbance at 280 nm was measured for the protein solution without a viscosity-reducing and stabilizing formulation. For Adalimumab without excipients, the buffer alone (i.e., devoid of excipients) served as a blank for protein concentration calculation. The extinction coefficient was measured at $1.40 \text{ (mg/mL)}^{-1} \cdot \text{cm}^{-1}$.

[00104] The test for protein stability was carried out over a 4-week period by SE-UPLC. Samples were prepared as described above. As shown in Tables 110-127, after 4 weeks, the monomer content of Pembrolizumab at a concentration from 100 to 300 mg/mL formulated with the tested viscosity-reducing and stabilizing formulations was higher than 90% even at 40°C, comparable or better than the lead formulation in WO2018211517, regardless of the used buffers, indicating good stabilization effect of the tested viscosity-reducing and stabilizing formulations.

Table 110 SE-UPLC results of formulated Adalimumab in 5 mM Histidine buffer, pH 5.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	96.6	96.6	95.9	94.1	3.0	3.0	3.7	4.9
300	30 mM Histidine and 30 mM Niacin	96.6	96.6	96.0	94.0	3.0	3.0	3.6	5.0
300	30 mM Meglumine and 30 mM Niacin	96.7	96.7	96.1	94.2	2.9	2.9	3.5	4.8
300	30 mM Lysine and 30 mM Niacin	96.6	96.6	96.1	94.2	3.0	3.0	3.5	4.8
300	30 mM Arginine-HCl and 30 mM Niacinamide	96.7	96.7	96.1	94.4	2.9	2.9	3.5	4.6
300	30 mM Histidine and 30 mM Niacinamide	96.7	96.7	96.0	94.1	2.9	2.9	3.6	4.9
300	30 mM Meglumine and 30 mM Niacinamide	96.6	96.6	96.0	94.2	3.0	3.0	3.6	4.8
300	30 mM Lysine-HCl and 30 mM Niacinamide	96.6	96.6	96.2	94.4	3.0	3.0	3.4	4.6
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	96.6	96.5	95.7	92.3	3.0	3.1	3.9	6.7
300	Water (Blank), pH 5.0	96.0	95.8	94.8	90.1	3.6	3.8	4.8	8.9
200	30 mM Arginine and 30 mM Niacin	97.0	97.0	96.7	95.4	2.6	2.6	2.9	3.6
200	30 mM Histidine and 30 mM Niacin	97.1	97.1	96.9	95.4	2.5	2.5	2.7	3.6
200	30 mM Meglumine and 30 mM Niacin	97.0	97.0	96.8	95.5	2.6	2.6	2.8	3.5
200	30 mM Lysine and 30 mM Niacin	97.1	97.1	96.9	95.4	2.5	2.5	2.7	3.6
200	30 mM Arginine-HCl and 30 mM Niacinamide	97.1	97.1	96.9	95.5	2.5	2.5	2.7	3.5
200	30 mM Histidine and 30 mM Niacinamide	97.0	97.0	96.7	95.2	2.6	2.6	2.9	3.8
200	30 mM Meglumine and 30 mM Niacinamide	97.1	97.1	96.7	95.3	2.5	2.5	2.9	3.7
200	30 mM Lysine-HCl and 30 mM Niacinamide	97.0	97.0	96.7	95.4	2.6	2.6	2.9	3.6
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	97.0	97.0	96.3	93.6	2.6	2.6	3.3	5.4
200	Water (Blank), pH 5.0	96.6	96.5	95.6	92.6	3.0	3.1	4.0	6.4
100	30 mM Arginine and 30 mM Niacin	97.4	97.4	97.3	96.3	2.2	2.2	2.3	2.7
100	30 mM Histidine and 30 mM Niacin	97.5	97.5	97.3	96.6	2.1	2.1	2.3	2.4
100	30 mM Meglumine and 30 mM Niacin	97.5	97.5	97.3	96.6	2.1	2.1	2.3	2.4
100	30 mM Lysine and 30 mM Niacin	97.5	97.5	97.3	96.4	2.1	2.1	2.3	2.6
100	30 mM Arginine-HCl and 30 mM Niacinamide	97.5	97.5	97.3	96.4	2.1	2.1	2.3	2.6
100	30 mM Histidine and 30 mM Niacinamide	97.4	97.4	97.2	96.4	2.2	2.2	2.4	2.6
100	30 mM Meglumine and 30 mM Niacinamide	97.5	97.5	97.3	96.7	2.1	2.1	2.3	2.3
100	30 mM Lysine-HCl and 30 mM Niacinamide	97.5	97.5	97.3	96.6	2.1	2.1	2.3	2.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	97.4	97.3	97.1	95.4	2.2	2.3	2.5	3.6
100	Water (Blank), pH 5.0	97.1	97.1	96.9	94.5	2.5	2.5	2.7	4.5

Table 111 SE-UPLC results of formulated Adalimumab in 20 mM Histidine buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	96.9	96.9	96.5	95.4	2.7	2.7	3.1	3.6
300	140 mM Histidine and 140 mM Niacin	96.9	96.9	96.5	95.5	2.7	2.7	3.1	3.5
300	140 mM Meglumine and 140 mM Niacin	96.9	96.9	96.3	95.4	2.7	2.7	3.3	3.6
300	140 mM Lysine and 140 mM Niacin	96.9	96.9	96.5	95.3	2.7	2.7	3.1	3.7
300	70 mM Arginine·HCl and 140 mM Niacinamide	96.9	96.9	96.5	95.4	2.7	2.7	3.1	3.6
300	140 mM Histidine and 140 mM Niacinamide	96.9	96.9	96.3	95.4	2.7	2.7	3.3	3.6
300	140 mM Meglumine and 140 mM Niacinamide	96.9	96.9	96.4	95.3	2.7	2.7	3.2	3.7
300	70 mM Lysine·HCl and 140 mM Niacinamide	96.9	96.9	96.3	95.7	2.7	2.7	3.3	3.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.9	96.9	96.0	93.3	2.7	2.7	3.6	5.8
300	Water (Blank), pH 6.0	96.3	96.1	95.1	91.1	3.3	3.5	4.5	8.0
200	140 mM Arginine and 140 mM Niacin	97.2	97.2	97.0	95.7	2.4	2.4	2.6	3.3
200	140 mM Histidine and 140 mM Niacin	97.2	97.2	97.0	95.8	2.4	2.4	2.6	3.2
200	140 mM Meglumine and 140 mM Niacin	97.2	97.2	97.0	95.6	2.4	2.4	2.6	3.4
200	140 mM Lysine and 140 mM Niacin	97.2	97.2	97.0	95.7	2.4	2.4	2.6	3.3
200	70 mM Arginine·HCl and 140 mM Niacinamide	97.2	97.2	97.0	95.7	2.4	2.4	2.6	3.3
200	140 mM Histidine and 140 mM Niacinamide	97.2	97.2	97.0	95.7	2.4	2.4	2.6	3.3
200	140 mM Meglumine and 140 mM Niacinamide	97.2	97.2	97.0	96.0	2.4	2.4	2.6	3.0
200	70 mM Lysine·HCl and 140 mM Niacinamide	97.2	97.2	97.0	95.9	2.4	2.4	2.6	3.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.1	97.2	96.6	94.3	2.5	2.4	3.0	4.7
200	Water (Blank), pH 6.0	96.9	96.5	95.8	93.4	2.7	3.1	3.8	5.6
100	140 mM Arginine and 140 mM Niacin	97.4	97.3	97.3	96.6	2.2	2.3	2.3	2.4
100	140 mM Histidine and 140 mM Niacin	97.4	97.4	97.3	96.2	2.2	2.2	2.3	2.8
100	140 mM Meglumine and 140 mM Niacin	97.4	97.4	97.3	96.5	2.2	2.2	2.3	2.5
100	140 mM Lysine and 140 mM Niacin	97.4	97.3	97.2	96.5	2.2	2.3	2.4	2.5
100	70 mM Arginine·HCl and 140 mM Niacinamide	97.4	97.4	97.3	96.2	2.2	2.2	2.3	2.8
100	140 mM Histidine and 140 mM Niacinamide	97.4	97.3	97.2	96.3	2.2	2.3	2.4	2.7
100	140 mM Meglumine and 140 mM Niacinamide	97.4	97.4	97.3	96.4	2.2	2.2	2.3	2.6
100	70 mM Lysine·HCl and 140 mM Niacinamide	97.4	97.3	97.2	96.4	2.2	2.3	2.4	2.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.4	97.3	97.2	95.6	2.2	2.2	2.5	3.4
100	Water (Blank), pH 6.0	97.2	97.2	97.0	94.7	2.4	2.4	2.6	4.4

Table 112 SE-UPLC results of formulated Adalimumab in 50 mM Histidine buffer, pH 7.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing Formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	96.9	96.9	96.5	95.4	2.7	2.7	3.1	3.6
300	300 mM Histidine and 300 mM Niacin	96.9	96.9	96.4	95.4	2.7	2.7	3.2	3.6
300	300 mM Meglumine and 300 mM Niacin	96.9	96.9	96.4	94.5	2.7	2.7	3.2	4.5
300	300 mM Lysine and 300 mM Niacin	96.9	96.9	96.6	94.8	2.7	2.7	3.0	4.2
300	140 mM Arginine-HCl and 300 mM Niacinamide	96.9	96.9	96.6	94.8	2.7	2.7	3.0	4.2
300	300 mM Histidine and 300 mM Niacinamide	96.9	96.9	96.3	95.1	2.7	2.7	3.3	3.9
300	300 mM Meglumine and 300 mM Niacinamide	96.9	96.9	96.3	94.7	2.7	2.7	3.3	4.3
300	140 mM Lysine-HCl and 300 mM Niacinamide	96.9	96.9	96.4	94.6	2.7	2.7	3.2	4.4
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	96.8	96.8	95.8	93.0	2.8	2.8	3.8	6.1
300	Water (Blank), pH 7.0	96.2	96.0	94.9	90.8	3.4	3.6	4.7	8.3
200	300 mM Arginine and 300 mM Niacin	97.2	97.2	97.0	95.7	2.4	2.4	2.6	3.3
200	300 mM Histidine and 300 mM Niacin	97.1	97.1	96.9	95.6	2.5	2.5	2.7	3.4
200	300 mM Meglumine and 300 mM Niacin	97.2	97.2	97.0	96.1	2.4	2.4	2.6	2.9
200	300 mM Lysine and 300 mM Niacin	97.2	97.2	97.0	95.9	2.4	2.4	2.6	3.1
200	140 mM Arginine-HCl and 300 mM Niacinamide	97.1	97.1	96.9	96	2.5	2.5	2.7	3.0
200	300 mM Histidine and 300 mM Niacinamide	97.1	97.1	96.9	95.5	2.5	2.5	2.7	3.5
200	300 mM Meglumine and 300 mM Niacinamide	97.2	97.2	97.0	95.7	2.4	2.4	2.6	3.3
200	140 mM Lysine-HCl and 300 mM Niacinamide	97.2	97.2	97.0	95.6	2.4	2.4	2.6	3.4
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	97.1	97.1	96.5	94.1	2.5	2.5	3.1	4.9
200	Water (Blank), pH 7.0	96.8	96.4	95.6	93.2	2.8	3.2	4.0	5.8
100	300 mM Arginine and 300 mM Niacin	97.4	97.3	97.3	96.7	2.2	2.3	2.3	2.3
100	300 mM Histidine and 300 mM Niacin	97.4	97.4	97.3	96.2	2.2	2.2	2.3	2.8
100	300 mM Meglumine and 300 mM Niacin	97.4	97.4	97.3	96.6	2.2	2.2	2.3	2.4
100	300 mM Lysine and 300 mM Niacin	97.4	97.3	97.2	96.4	2.2	2.3	2.4	2.6
100	140 mM Arginine-HCl and 300 mM Niacinamide	97.4	97.4	97.3	96.6	2.2	2.2	2.3	2.4
100	300 mM Histidine and 300 mM Niacinamide	97.4	97.3	97.2	96.3	2.2	2.3	2.4	2.7
100	300 mM Meglumine and 300 mM Niacinamide	97.4	97.4	97.3	96.2	2.2	2.2	2.3	2.8
100	140 mM Lysine-HCl and 300 mM Niacinamide	97.4	97.3	97.2	96.2	2.2	2.3	2.4	2.8
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	97.3	97.3	97.1	95.4	2.3	2.3	2.6	3.6
100	Water (Blank), pH 7.0	97.1	97.1	97.0	94.5	2.5	2.5	2.6	4.6

Table 113 SE-UPLC results of formulated Adalimumab in 5 mM Acetate buffer, pH 4.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	96.6	96.5	95.7	93.3	3.0	3.1	3.9	5.7
300	30 mM Histidine and 30 mM Niacin	96.6	96.5	95.8	93.6	3.0	3.1	3.8	5.4
300	30 mM Meglumine and 30 mM Niacin	96.6	96.5	95.6	93.5	3.0	3.1	4.0	5.5
300	30 mM Lysine and 30 mM Niacin	96.6	96.5	95.9	93	3.0	3.1	3.7	6.0
300	30 mM Arginine-HCl and 30 mM Niacinamide	96.6	96.5	95.7	92.6	3.0	3.1	3.9	6.4
300	30 mM Histidine and 30 mM Niacinamide	96.6	96.5	95.7	93	3.0	3.1	3.9	6.0
300	30 mM Meglumine and 30 mM Niacinamide	96.6	96.5	95.8	93.6	3.0	3.1	3.8	5.4
300	30 mM Lysine-HCl and 30 mM Niacinamide	96.6	96.5	95.7	93.3	3.0	3.1	3.9	5.7
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	96.6	96.5	95.2	90.3	3.0	3.1	4.4	8.7
300	Water (Blank), pH 4.5	96.0	95.8	94.4	88.1	3.6	3.8	5.2	10.9
200	30 mM Arginine and 30 mM Niacin	97.1	97.1	96.5	94.3	2.5	2.5	3.1	4.7
200	30 mM Histidine and 30 mM Niacin	97.1	97.1	96.5	93.9	2.5	2.5	3.1	5.1
200	30 mM Meglumine and 30 mM Niacin	97.1	97.1	96.6	93.8	2.5	2.5	3.0	5.2
200	30 mM Lysine and 30 mM Niacin	97.1	97.1	96.6	94.2	2.5	2.5	3.0	4.8
200	30 mM Arginine-HCl and 30 mM Niacinamide	97.1	97.1	96.7	94.6	2.5	2.5	2.9	4.4
200	30 mM Histidine and 30 mM Niacinamide	97.1	97.1	96.7	94.4	2.5	2.5	2.9	4.6
200	30 mM Meglumine and 30 mM Niacinamide	97.1	97.1	96.6	93.8	2.5	2.5	3.0	5.2
200	30 mM Lysine-HCl and 30 mM Niacinamide	97.1	97.1	96.5	94	2.5	2.5	3.1	5.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	97.0	97.0	96.0	92.2	2.6	2.6	3.6	6.8
200	Water (Blank), pH 4.5	96.6	96.5	95.0	91.6	3.0	3.1	4.6	7.4
100	30 mM Arginine and 30 mM Niacin	97.4	97.3	96.8	95.9	2.2	2.3	2.8	3.1
100	30 mM Histidine and 30 mM Niacin	97.4	97.3	97.1	95.7	2.2	2.3	2.5	3.3
100	30 mM Meglumine and 30 mM Niacin	97.4	97.3	96.8	95.5	2.2	2.3	2.8	3.5
100	30 mM Lysine and 30 mM Niacin	97.4	97.3	96.8	95.6	2.2	2.3	2.8	3.4
100	30 mM Arginine-HCl and 30 mM Niacinamide	97.4	97.3	97.1	95.7	2.2	2.3	2.5	3.3
100	30 mM Histidine and 30 mM Niacinamide	97.4	97.3	96.9	95.5	2.2	2.3	2.7	3.5
100	30 mM Meglumine and 30 mM Niacinamide	97.4	97.3	96.8	95.7	2.2	2.3	2.8	3.3
100	30 mM Lysine-HCl and 30 mM Niacinamide	97.4	97.3	96.8	95.4	2.2	2.3	2.8	3.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	97.4	97.3	96.5	94.0	2.2	2.3	3.1	5.0
100	Water (Blank), pH 4.5	97.1	97.1	96.1	93.5	2.5	2.5	3.5	5.5

Table 114 SE-UPLC results of formulated Adalimumab in 20 mM Acetate buffer, pH 5.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	96.6	96.6	95.8	94.0	3.0	3.0	3.8	5.0
300	140 mM Histidine and 140 mM Niacin	96.7	96.7	96	93.8	2.9	2.9	3.6	5.2
300	140 mM Meglumine and 140 mM Niacin	96.7	96.7	96.2	93.9	2.9	2.9	3.4	5.1
300	140 mM Lysine and 140 mM Niacin	96.6	96.6	96.1	94.1	3.0	3.0	3.5	4.9
300	70 mM Arginine·HCl and 140 mM Niacinamide	96.7	96.7	96.2	94.1	2.9	2.9	3.4	4.9
300	140 mM Histidine and 140 mM Niacinamide	96.6	96.6	96.1	93.9	3.0	3.0	3.5	5.1
300	140 mM Meglumine and 140 mM Niacinamide	96.6	96.6	96.1	94.1	3.0	3.0	3.5	4.9
300	70 mM Lysine·HCl and 140 mM Niacinamide	96.6	96.6	96.1	94.2	3.0	3.0	3.5	4.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	96.6	96.5	95.7	92.3	3.0	3.1	3.9	6.7
300	Water (Blank), pH 5.0	96.0	95.8	94.8	90.1	3.6	3.8	4.8	8.9
200	140 mM Arginine and 140 mM Niacin	97.0	97.0	96.6	95.2	2.6	2.6	3.0	3.8
200	140 mM Histidine and 140 mM Niacin	97.0	97.0	97.0	95.1	2.6	2.6	2.6	3.9
200	140 mM Meglumine and 140 mM Niacin	97.0	97.0	96.7	95.2	2.6	2.6	2.9	3.8
200	140 mM Lysine and 140 mM Niacin	97.0	97.0	96.9	95.2	2.6	2.6	2.7	3.8
200	70 mM Arginine·HCl and 140 mM Niacinamide	97.0	97.0	97.0	95.2	2.6	2.6	2.6	3.8
200	140 mM Histidine and 140 mM Niacinamide	97.0	97.0	96.8	95.1	2.6	2.6	2.8	3.9
200	140 mM Meglumine and 140 mM Niacinamide	97.0	97.0	96.8	95.0	2.6	2.6	2.8	4.0
200	70 mM Lysine·HCl and 140 mM Niacinamide	97.0	97.0	96.6	95.2	2.6	2.6	3.0	3.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	97.0	97.0	96.3	93.6	2.6	2.6	3.3	5.4
200	Water (Blank), pH 5.0	96.6	96.5	95.6	92.6	3.0	3.1	4.0	6.4
100	140 mM Arginine and 140 mM Niacin	97.4	97.3	97.2	96.1	2.2	2.3	2.4	2.9
100	140 mM Histidine and 140 mM Niacin	97.4	97.3	97.2	96.5	2.2	2.3	2.4	2.5
100	140 mM Meglumine and 140 mM Niacin	97.4	97.3	97.2	96.3	2.2	2.3	2.4	2.7
100	140 mM Lysine and 140 mM Niacin	97.4	97.3	97.2	96.2	2.2	2.3	2.4	2.8
100	70 mM Arginine·HCl and 140 mM Niacinamide	97.4	97.3	97.2	96.1	2.2	2.3	2.4	2.9
100	140 mM Histidine and 140 mM Niacinamide	97.4	97.3	97.2	96.3	2.2	2.3	2.4	2.7
100	140 mM Meglumine and 140 mM Niacinamide	97.4	97.3	97.2	96.6	2.2	2.3	2.4	2.4
100	70 mM Lysine·HCl and 140 mM Niacinamide	97.4	97.3	97.2	96.4	2.2	2.3	2.4	2.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	97.4	97.3	97.1	95.4	2.2	2.3	2.5	3.6
100	Water (Blank), pH 5.0	97.1	97.1	96.9	94.5	2.5	2.5	2.7	4.5

Table 115 SE-UPLC results of formulated Adalimumab in 50 mM Acetate buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing Formulation	Monomer%				Aggregation%			
		T0	5°C	25°C C	40°C C	T0	5°C	25°C C	40°C C
300	300 mM Arginine and 300 mM Niacin	96.9	96.9	96.4	95.2	2.7	2.7	3.2	3.8
300	300 mM Histidine and 300 mM Niacin	96.9	96.9	96.4	95.3	2.7	2.7	3.2	3.7
300	300 mM Meglumine and 300 mM Niacin	96.9	96.9	96.4	95.2	2.7	2.7	3.2	3.8
300	300 mM Lysine and 300 mM Niacin	96.9	96.9	96.5	95.2	2.7	2.7	3.1	3.8
300	140 mM Arginine·HCl and 300 mM Niacinamide	96.9	96.9	96.5	95.3	2.7	2.7	3.1	3.7
300	300 mM Histidine and 300 mM Niacinamide	96.9	96.9	96.4	95.4	2.7	2.7	3.2	3.6
300	300 mM Meglumine and 300 mM Niacinamide	96.9	96.9	96.3	95.3	2.7	2.7	3.3	3.7
300	140 mM Lysine·HCl and 300 mM Niacinamide	96.9	96.9	96.3	95.4	2.7	2.7	3.3	3.6
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.9	96.9	96.0	93.3	2.7	2.7	3.6	5.8
300	Water (Blank), pH 6.0	96.3	96.1	95.1	91.1	3.3	3.5	4.5	8.0
200	300 mM Arginine and 300 mM Niacin	97.2	97.2	97.0	95.6	2.4	2.4	2.6	3.4
200	300 mM Histidine and 300 mM Niacin	97.2	97.2	97.1	95.5	2.4	2.4	2.5	3.5
200	300 mM Meglumine and 300 mM Niacin	97.2	97.2	97.1	95.3	2.4	2.4	2.5	3.7
200	300 mM Lysine and 300 mM Niacin	97.2	97.2	96.9	95.5	2.4	2.4	2.7	3.5
200	140 mM Arginine·HCl and 300 mM Niacinamide	97.2	97.2	97.0	95.4	2.4	2.4	2.6	3.6
200	300 mM Histidine and 300 mM Niacinamide	97.2	97.2	97.1	95.6	2.4	2.4	2.5	3.4
200	300 mM Meglumine and 300 mM Niacinamide	97.2	97.2	97.0	95.8	2.4	2.4	2.6	3.2
200	140 mM Lysine·HCl and 300 mM Niacinamide	97.2	97.2	97.1	95.6	2.4	2.4	2.5	3.4
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.1	97.2	96.6	94.3	2.5	2.4	3.0	4.7
200	Water (Blank), pH 6.0	96.9	96.5	95.8	93.4	2.7	3.1	3.8	5.6
100	300 mM Arginine and 300 mM Niacin	97.4	97.3	97.3	96.5	2.2	2.3	2.3	2.5
100	300 mM Histidine and 300 mM Niacin	97.4	97.3	97.2	95.9	2.2	2.3	2.4	3.1
100	300 mM Meglumine and 300 mM Niacin	97.4	97.4	97.3	96.4	2.2	2.2	2.3	2.6
100	300 mM Lysine and 300 mM Niacin	97.4	97.3	97.2	96.3	2.2	2.3	2.4	2.7
100	140 mM Arginine·HCl and 300 mM Niacinamide	97.4	97.3	97.2	96.1	2.2	2.3	2.4	2.9
100	300 mM Histidine and 300 mM Niacinamide	97.4	97.3	97.2	96.2	2.2	2.3	2.4	2.8
100	300 mM Meglumine and 300 mM Niacinamide	97.4	97.3	97.2	96.1	2.2	2.3	2.4	2.9
100	140 mM Lysine·HCl and 300 mM Niacinamide	97.4	97.3	97.2	96.2	2.2	2.3	2.4	2.8
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.4	97.3	97.2	95.6	2.2	2.2	2.5	3.4
100	Water (Blank), pH 6.0	97.2	97.2	97.0	94.7	2.4	2.4	2.6	4.4

Table 116 SE-UPLC results of formulated Adalimumab in 5 mM Citrate buffer, pH 4.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	96.6	96.5	95.6	93.3	3.0	3.1	4.0	5.7
300	30 mM Histidine and 30 mM Niacin	96.6	96.5	95.8	93.6	3.0	3.1	3.8	5.4
300	30 mM Meglumine and 30 mM Niacin	96.6	96.5	95.5	93.6	3.0	3.1	4.1	5.4
300	30 mM Lysine and 30 mM Niacin	96.6	96.5	95.9	92.9	3.0	3.1	3.7	6.1
300	30 mM Arginine-HCl and 30 mM Niacinamide	96.6	96.5	95.8	92.7	3.0	3.1	3.8	6.3
300	30 mM Histidine and 30 mM Niacinamide	96.6	96.5	95.8	93.1	3.0	3.1	3.8	5.9
300	30 mM Meglumine and 30 mM Niacinamide	96.6	96.5	95.7	93.5	3.0	3.1	3.9	5.5
300	30 mM Lysine-HCl and 30 mM Niacinamide	96.6	96.5	95.6	93.4	3.0	3.1	4.0	5.6
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	96.6	96.5	95.2	90.3	3.0	3.1	4.4	8.7
300	Water (Blank), pH 4.5	96.0	95.8	94.4	88.1	3.6	3.8	5.2	10.9
200	30 mM Arginine and 30 mM Niacin	97.0	97.0	96.4	94.3	2.6	2.6	3.2	4.7
200	30 mM Histidine and 30 mM Niacin	97.0	97.0	96.5	93.9	2.6	2.6	3.1	5.1
200	30 mM Meglumine and 30 mM Niacin	97.0	97.0	96.6	93.7	2.6	2.6	3.0	5.3
200	30 mM Lysine and 30 mM Niacin	97.0	97.0	96.6	94.1	2.6	2.6	3.0	4.9
200	30 mM Arginine-HCl and 30 mM Niacinamide	97.0	97.0	96.6	94.7	2.6	2.6	3.0	4.3
200	30 mM Histidine and 30 mM Niacinamide	97.0	97.0	96.6	94.3	2.6	2.6	3.0	4.7
200	30 mM Meglumine and 30 mM Niacinamide	97.0	97.0	96.7	93.8	2.6	2.6	2.9	5.2
200	30 mM Lysine-HCl and 30 mM Niacinamide	97.0	97.0	96.5	94.1	2.6	2.6	3.1	4.9
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	97.0	97.0	96.0	92.2	2.6	2.6	3.6	6.8
200	Water (blank), pH 4.5	96.6	96.5	95.0	91.6	3.0	3.1	4.6	7.4
100	30 mM Arginine and 30 mM Niacin	97.4	97.3	96.7	95.9	2.2	2.3	2.9	3.1
100	30 mM Histidine and 30 mM Niacin	97.4	97.3	97.0	95.6	2.2	2.3	2.6	3.4
100	30 mM Meglumine and 30 mM Niacin	97.4	97.3	96.7	95.5	2.2	2.3	2.9	3.5
100	30 mM Lysine and 30 mM Niacin	97.4	97.3	96.7	95.5	2.2	2.3	2.9	3.5
100	30 mM Arginine-HCl and 30 mM Niacinamide	97.4	97.3	97.2	95.5	2.2	2.3	2.4	3.5
100	30 mM Histidine and 30 mM Niacinamide	97.4	97.3	96.9	95.3	2.2	2.3	2.7	3.7
100	30 mM Meglumine and 30 mM Niacinamide	97.4	97.3	96.9	95.5	2.2	2.3	2.7	3.5
100	30 mM Lysine-HCl and 30 mM Niacinamide	97.4	97.3	96.8	95.4	2.2	2.3	2.8	3.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	97.4	97.3	96.5	94.0	2.2	2.3	3.1	5.0
100	Water (blank), pH 4.5	97.1	97.1	96.1	93.5	2.5	2.5	3.5	5.5

Table 117 SE-UPLC results of formulated Adalimumab in 20 mM Citrate buffer, pH 5.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	96.8	96.7	96.3	95.0	2.8	2.9	3.3	4.0
300	140 mM Histidine and 140 mM Niacin	96.8	96.7	96.4	95.0	2.8	2.9	3.2	4.0
300	140 mM Meglumine and 140 mM Niacin	96.8	96.7	96.3	95.0	2.8	2.9	3.3	4.0
300	140 mM Lysine and 140 mM Niacin	96.8	96.7	96.4	94.9	2.8	2.9	3.2	4.1
300	70 mM Arginine·HCl and 140 mM Niacinamide	96.8	96.7	96.5	95.0	2.8	2.9	3.1	4.0
300	140 mM Histidine and 140 mM Niacinamide	96.8	96.7	96.4	95.0	2.8	2.9	3.2	4.0
300	140 mM Meglumine and 140 mM Niacinamide	96.8	96.7	96.3	94.9	2.8	2.9	3.3	4.1
300	70 mM Lysine·HCl and 140 mM Niacinamide	96.8	96.7	96.3	95.2	2.8	2.9	3.3	3.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	96.8	96.7	96.0	92.8	2.8	2.9	3.6	6.2
300	Water (Blank), pH 5.5	96.2	96.0	94.9	90.5	3.4	3.6	4.7	8.5
200	140 mM Arginine and 140 mM Niacin	97.0	97.0	96.8	95.0	2.6	2.6	2.8	4.0
200	140 mM Histidine and 140 mM Niacin	97.0	97.0	96.7	95.1	2.6	2.6	2.9	3.9
200	140 mM Meglumine and 140 mM Niacin	97.0	97.0	96.8	95.0	2.6	2.6	2.8	4.0
200	140 mM Lysine and 140 mM Niacin	97.0	97.0	96.7	95.1	2.6	2.6	2.9	3.9
200	70 mM Arginine·HCl and 140 mM Niacinamide	97.0	97.0	96.7	95.1	2.6	2.6	2.9	3.9
200	140 mM Histidine and 140 mM Niacinamide	97.0	97.0	96.8	95.1	2.6	2.6	2.8	3.9
200	140 mM Meglumine and 140 mM Niacinamide	97.0	97.0	96.7	95.4	2.6	2.6	2.9	3.6
200	70 mM Lysine·HCl and 140 mM Niacinamide	97.0	97.0	96.8	95.3	2.6	2.6	2.8	3.7
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	97.0	97.0	96.3	93.6	2.6	2.6	3.3	5.4
200	Water (Blank), pH 5.5	96.6	96.5	95.6	92.6	3.0	3.1	4.0	6.4
100	140 mM Arginine and 140 mM Niacin	97.4	97.3	97.2	96.4	2.2	2.3	2.4	2.6
100	140 mM Histidine and 140 mM Niacin	97.4	97.4	97.3	96.0	2.2	2.2	2.3	3.0
100	140 mM Meglumine and 140 mM Niacin	97.4	97.4	97.3	96.3	2.2	2.2	2.3	2.7
100	140 mM Lysine and 140 mM Niacin	97.4	97.3	97.2	96.3	2.2	2.3	2.4	2.7
100	70 mM Arginine·HCl and 140 mM Niacinamide	97.4	97.4	97.3	96.1	2.2	2.2	2.3	2.9
100	140 mM Histidine and 140 mM Niacinamide	97.4	97.3	97.1	96.1	2.2	2.3	2.5	2.9
100	140 mM Meglumine and 140 mM Niacinamide	97.4	97.4	97.2	96.1	2.2	2.2	2.4	2.9
100	70 mM Lysine·HCl and 140 mM Niacinamide	97.4	97.3	97.2	96.2	2.2	2.3	2.4	2.8
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	97.4	97.3	97.1	95.4	2.2	2.3	2.5	3.6
100	Water (Blank), pH 5.5	97.1	97.1	96.9	94.5	2.5	2.5	2.7	4.5

Table 118 SE-UPLC results of formulated Adalimumab in 50 mM Citrate buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing Formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	96.9	96.9	96.3	95.0	2.7	2.7	3.3	4.0
300	300 mM Histidine and 300 mM Niacin	96.9	96.9	96.3	95.1	2.7	2.7	3.3	3.9
300	300 mM Meglumine and 300 mM Niacin	96.9	96.9	96.3	95.1	2.7	2.7	3.3	3.9
300	300 mM Lysine and 300 mM Niacin	96.9	96.9	96.4	95.1	2.7	2.7	3.2	3.9
300	140 mM Arginine-HCl and 300 mM Niacinamide	96.9	96.9	96.5	95.3	2.7	2.7	3.1	3.7
300	300 mM Histidine and 300 mM Niacinamide	96.9	96.9	96.4	95.4	2.7	2.7	3.2	3.6
300	300 mM Meglumine and 300 mM Niacinamide	96.9	96.9	96.3	95.2	2.7	2.7	3.3	3.8
300	140 mM Lysine-HCl and 300 mM Niacinamide	96.9	96.9	96.2	95.2	2.7	2.7	3.4	3.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.9	96.9	96.0	93.3	2.7	2.7	3.6	5.8
300	Water (Blank), pH 6.0	96.3	96.1	95.1	91.1	3.3	3.5	4.5	8.0
200	300 mM Arginine and 300 mM Niacin	97.2	97.2	96.9	95.5	2.4	2.4	2.7	3.5
200	300 mM Histidine and 300 mM Niacin	97.2	97.2	97.1	95.3	2.4	2.4	2.5	3.7
200	300 mM Meglumine and 300 mM Niacin	97.2	97.2	97.1	95.3	2.4	2.4	2.5	3.7
200	300 mM Lysine and 300 mM Niacin	97.2	97.2	96.9	95.4	2.4	2.4	2.7	3.6
200	140 mM Arginine-HCl and 300 mM Niacinamide	97.2	97.2	96.9	95.3	2.4	2.4	2.7	3.7
200	300 mM Histidine and 300 mM Niacinamide	97.2	97.2	97.0	95.6	2.4	2.4	2.6	3.4
200	300 mM Meglumine and 300 mM Niacinamide	97.2	97.2	96.9	95.7	2.4	2.4	2.7	3.3
200	140 mM Lysine-HCl and 300 mM Niacinamide	97.2	97.2	97.0	95.6	2.4	2.4	2.6	3.4
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.1	97.2	96.6	94.3	2.5	2.4	3.0	4.7
200	Water (Blank), pH 6.0	96.9	96.5	95.8	93.4	2.7	3.1	3.8	5.6
100	300 mM Arginine and 300 mM Niacin	97.4	97.3	97.2	96.5	2.2	2.3	2.4	2.5
100	300 mM Histidine and 300 mM Niacin	97.4	97.3	97.2	95.7	2.2	2.3	2.4	3.3
100	300 mM Meglumine and 300 mM Niacin	97.4	97.4	97.3	96.3	2.2	2.2	2.3	2.7
100	300 mM Lysine and 300 mM Niacin	97.4	97.3	97.2	96.2	2.2	2.3	2.4	2.8
100	140 mM Arginine-HCl and 300 mM Niacinamide	97.4	97.3	97.2	96.1	2.2	2.3	2.4	2.9
100	300 mM Histidine and 300 mM Niacinamide	97.4	97.3	97.2	96.0	2.2	2.3	2.4	3.0
100	300 mM Meglumine and 300 mM Niacinamide	97.4	97.3	97.2	95.9	2.2	2.3	2.4	3.1
100	140 mM Lysine-HCl and 300 mM Niacinamide	97.4	97.3	97.2	96.2	2.2	2.3	2.4	2.8
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.4	97.3	97.2	95.6	2.2	2.2	2.5	3.4
100	Water (Blank), pH 6.0	97.2	97.2	97.0	94.7	2.4	2.4	2.6	4.4

Table 119 SE-UPLC results of formulated Adalimumab in 5 mM Phosphate buffer, pH 6.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	96.9	96.9	96.3	95.0	2.7	2.7	3.3	4.0
300	30 mM Histidine and 30 mM Niacin	96.9	96.9	96.2	94.9	2.7	2.7	3.4	4.1
300	30 mM Meglumine and 30 mM Niacin	96.9	96.9	96.3	94.0	2.7	2.7	3.3	5.0
300	30 mM Lysine and 30 mM Niacin	96.9	96.9	96.5	94.3	2.7	2.7	3.1	4.7
300	30 mM Arginine-HCl and 30 mM Niacinamide	96.9	96.9	96.5	94.3	2.7	2.7	3.1	4.7
300	30 mM Histidine and 30 mM Niacinamide	96.9	96.9	96.1	94.6	2.7	2.7	3.5	4.4
300	30 mM Meglumine and 30 mM Niacinamide	96.9	96.9	96.2	94.2	2.7	2.7	3.4	4.8
300	30 mM Lysine-HCl and 30 mM Niacinamide	96.9	96.9	96.2	94.2	2.7	2.7	3.4	4.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	96.9	96.9	96.2	93.7	2.7	2.7	3.4	5.4
300	Water (Blank), pH 6.5	96.4	96.2	95.2	91.3	3.2	3.4	4.4	7.8
200	30 mM Arginine and 30 mM Niacin	97.2	97.1	96.8	95.2	2.4	2.5	2.8	3.8
200	30 mM Histidine and 30 mM Niacin	97.1	97.1	96.8	95.3	2.5	2.5	2.8	3.7
200	30 mM Meglumine and 30 mM Niacin	97.2	97.1	96.8	95.7	2.4	2.5	2.8	3.3
200	30 mM Lysine and 30 mM Niacin	97.2	97.1	96.8	95.5	2.4	2.5	2.8	3.5
200	30 mM Arginine-HCl and 30 mM Niacinamide	97.1	97.1	96.7	95.6	2.5	2.5	2.9	3.4
200	30 mM Histidine and 30 mM Niacinamide	97.1	97.1	96.8	95.1	2.5	2.5	2.8	3.9
200	30 mM Meglumine and 30 mM Niacinamide	97.2	97.1	96.8	95.4	2.4	2.5	2.8	3.6
200	30 mM Lysine-HCl and 30 mM Niacinamide	97.2	97.1	96.9	95.2	2.4	2.5	2.7	3.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	97.2	97.2	96.7	94.5	2.4	2.4	2.9	4.5
200	Water (Blank), pH 6.5	96.9	96.6	95.9	93.6	2.7	3.0	3.7	5.4
100	30 mM Arginine and 30 mM Niacin	97.4	97.3	97.2	96.5	2.2	2.8	2.3	2.4
100	30 mM Histidine and 30 mM Niacin	97.4	97.3	97.2	96.1	2.2	2.8	2.3	2.4
100	30 mM Meglumine and 30 mM Niacin	97.4	97.3	97.2	96.5	2.2	2.8	2.3	2.4
100	30 mM Lysine and 30 mM Niacin	97.4	97.3	97.2	96.3	2.2	2.8	2.3	2.4
100	30 mM Arginine-HCl and 30 mM Niacinamide	97.4	97.3	97.2	96.4	2.2	2.8	2.3	2.4
100	30 mM Histidine and 30 mM Niacinamide	97.4	97.3	97.2	96.1	2.2	2.8	2.3	2.4
100	30 mM Meglumine and 30 mM Niacinamide	97.4	97.3	97.2	96.1	2.2	2.8	2.3	2.4
100	30 mM Lysine-HCl and 30 mM Niacinamide	97.4	97.3	97.2	96.0	2.2	2.8	2.3	2.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	97.4	97.3	97.2	95.7	2.2	2.2	2.5	3.3
100	Water (Blank), pH 6.5	97.3	97.2	97.1	94.9	2.3	2.4	2.5	4.2

Table 120 SE-UPLC results of formulated Adalimumab in 20 mM Phosphate buffer, pH 7.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	96.9	96.9	96.4	95.0	2.7	2.7	3.2	4.0
300	140 mM Histidine and 140 mM Niacin	96.9	96.9	96.3	95.1	2.7	2.7	3.3	3.9
300	140 mM Meglumine and 140 mM Niacin	96.9	96.9	96.3	94.2	2.7	2.7	3.3	4.8
300	140 mM Lysine and 140 mM Niacin	96.9	96.9	96.5	94.3	2.7	2.7	3.1	4.7
300	70 mM Arginine·HCl and 140 mM Niacinamide	96.9	96.9	96.5	94.4	2.7	2.7	3.1	4.6
300	140 mM Histidine and 140 mM Niacinamide	96.9	96.9	96.2	94.6	2.7	2.7	3.4	4.4
300	140 mM Meglumine and 140 mM Niacinamide	96.9	96.9	96.2	94.4	2.7	2.7	3.4	4.6
300	70 mM Lysine·HCl and 140 mM Niacinamide	96.9	96.9	96.3	94.1	2.7	2.7	3.3	4.9
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	96.8	96.8	95.8	93.0	2.8	2.8	3.8	6.1
300	Water (Blank), pH 7.0	96.2	96.0	94.9	90.8	3.4	3.6	4.7	8.3
200	140 mM Arginine and 140 mM Niacin	97.2	97.1	96.8	95.4	2.4	2.5	2.8	3.6
200	140 mM Histidine and 140 mM Niacin	97.1	97.1	96.8	95.3	2.5	2.5	2.8	3.7
200	140 mM Meglumine and 140 mM Niacin	97.2	97.1	96.8	95.6	2.4	2.5	2.8	3.4
200	140 mM Lysine and 140 mM Niacin	97.2	97.1	96.9	95.6	2.4	2.5	2.7	3.4
200	70 mM Arginine·HCl and 140 mM Niacinamide	97.1	97.1	96.8	95.5	2.5	2.5	2.8	3.5
200	140 mM Histidine and 140 mM Niacinamide	97.1	97.1	96.7	95.0	2.5	2.5	2.9	4.0
200	140 mM Meglumine and 140 mM Niacinamide	97.2	97.1	96.8	95.2	2.4	2.5	2.8	3.8
200	70 mM Lysine·HCl and 140 mM Niacinamide	97.2	97.1	96.8	95.3	2.4	2.5	2.8	3.7
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	97.1	97.1	96.5	94.1	2.5	2.5	3.1	4.9
200	Water (Blank), pH 7.0	96.8	96.4	95.6	93.2	2.8	3.2	4.0	5.8
100	140 mM Arginine and 140 mM Niacin	97.4	97.3	97.2	96.3	2.2	2.3	2.4	2.7
100	140 mM Histidine and 140 mM Niacin	97.4	97.3	97.2	95.9	2.2	2.3	2.4	3.1
100	140 mM Meglumine and 140 mM Niacin	97.4	97.3	97.2	96.1	2.2	2.3	2.4	2.9
100	140 mM Lysine and 140 mM Niacin	97.4	97.3	97.2	96.1	2.2	2.3	2.4	2.9
100	70 mM Arginine·HCl and 140 mM Niacinamide	97.4	97.3	97.2	96.3	2.2	2.3	2.4	2.7
100	140 mM Histidine and 140 mM Niacinamide	97.4	97.3	97.2	95.9	2.2	2.3	2.4	3.1
100	140 mM Meglumine and 140 mM Niacinamide	97.4	97.3	97.2	95.9	2.2	2.3	2.4	3.1
100	70 mM Lysine·HCl and 140 mM Niacinamide	97.4	97.3	97.2	95.9	2.2	2.3	2.4	3.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	97.3	97.3	97.1	95.4	2.3	2.3	2.6	3.6
100	Water (Blank), pH 7.0	97.1	97.1	97.0	94.5	2.5	2.5	2.6	4.6

Table 121 SE-UPLC results of formulated Adalimumab in 50 mM Phosphate buffer, pH 7.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing Formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	96.9	96.9	96.2	94.5	2.7	2.7	3.4	4.5
300	300 mM Histidine and 300 mM Niacin	96.9	96.9	96.1	94.7	2.7	2.7	3.5	4.3
300	300 mM Meglumine and 300 mM Niacin	96.9	96.9	96.1	93.9	2.7	2.7	3.5	5.1
300	300 mM Lysine and 300 mM Niacin	96.9	96.9	96.3	93.8	2.7	2.7	3.3	5.2
300	140 mM Arginine-HCl and 300 mM Niacinamide	96.9	96.9	96.3	94.0	2.7	2.7	3.3	5.0
300	300 mM Histidine and 300 mM Niacinamide	96.9	96.9	96.0	94.2	2.7	2.7	3.6	4.8
300	300 mM Meglumine and 300 mM Niacinamide	96.9	96.9	96.0	93.9	2.7	2.7	3.6	5.1
300	140 mM Lysine-HCl and 300 mM Niacinamide	96.9	96.9	96.1	93.7	2.7	2.7	3.5	5.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	96.9	96.9	95.8	92.9	2.7	2.7	3.8	6.1
300	Water (Blank), pH 7.5	96.1	96.0	95.0	90.5	3.5	3.6	4.6	8.5
200	300 mM Arginine and 300 mM Niacin	97.2	97.1	96.6	94.9	2.4	2.5	3.0	4.1
200	300 mM Histidine and 300 mM Niacin	97.1	97.1	96.6	94.8	2.5	2.5	3.0	4.2
200	300 mM Meglumine and 300 mM Niacin	97.2	97.1	96.6	95.3	2.4	2.5	3.0	3.7
200	300 mM Lysine and 300 mM Niacin	97.2	97.1	96.7	95.1	2.4	2.5	2.9	3.9
200	140 mM Arginine-HCl and 300 mM Niacinamide	97.1	97.1	96.6	95.1	2.5	2.5	3.0	3.9
200	300 mM Histidine and 300 mM Niacinamide	97.1	97.1	96.5	94.5	2.5	2.5	3.1	4.5
200	300 mM Meglumine and 300 mM Niacinamide	97.2	97.1	96.6	94.9	2.4	2.5	3.0	4.1
200	140 mM Lysine-HCl and 300 mM Niacinamide	97.2	97.1	96.6	94.9	2.4	2.5	3.0	4.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	97.0	97.0	96.4	94.0	2.6	2.6	3.2	5.0
200	Water (Blank), pH 7.5	96.6	96.6	95.6	92.8	3.0	3.0	4.0	6.2
100	300 mM Arginine and 300 mM Niacin	97.4	97.3	97.2	95.8	2.2	2.3	2.4	3.2
100	300 mM Histidine and 300 mM Niacin	97.4	97.3	97.2	95.5	2.2	2.3	2.4	3.5
100	300 mM Meglumine and 300 mM Niacin	97.4	97.3	97.2	95.8	2.2	2.3	2.4	3.2
100	300 mM Lysine and 300 mM Niacin	97.4	97.3	97.2	95.6	2.2	2.3	2.4	3.4
100	140 mM Arginine-HCl and 300 mM Niacinamide	97.4	97.3	97.2	95.9	2.2	2.3	2.4	3.1
100	300 mM Histidine and 300 mM Niacinamide	97.4	97.3	97.2	95.5	2.2	2.3	2.4	3.5
100	300 mM Meglumine and 300 mM Niacinamide	97.4	97.3	97.2	95.6	2.2	2.3	2.4	3.4
100	140 mM Lysine-HCl and 300 mM Niacinamide	97.4	97.3	97.2	95.5	2.2	2.3	2.4	3.5
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	97.3	97.3	97.1	95.0	2.3	2.3	2.5	4.0
100	Water (Blank), pH 7.5	97.1	97.1	96.8	93.7	2.5	2.5	2.8	5.3

Table 122 SE-UPLC results of formulated Adalimumab in 5 mM Tris buffer, pH 6.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	96.9	96.9	96.2	94.7	2.7	2.7	3.4	4.3
300	30 mM Histidine and 30 mM Niacin	96.9	96.9	96.2	94.5	2.7	2.7	3.4	4.5
300	30 mM Meglumine and 30 mM Niacin	96.9	96.9	96.2	93.5	2.7	2.7	3.4	5.5
300	30 mM Lysine and 30 mM Niacin	96.9	96.9	96.4	93.8	2.7	2.7	3.2	5.2
300	30 mM Arginine·HCl and 30 mM Niacinamide	96.9	96.9	96.4	93.9	2.7	2.7	3.2	5.1
300	30 mM Histidine and 30 mM Niacinamide	96.9	96.9	96.1	94.3	2.7	2.7	3.5	4.7
300	30 mM Meglumine and 30 mM Niacinamide	96.9	96.9	96.2	93.8	2.7	2.7	3.4	5.2
300	30 mM Lysine·HCl and 30 mM Niacinamide	96.9	96.9	96.1	93.7	2.7	2.7	3.5	5.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	96.9	96.9	96.2	93.7	2.7	2.7	3.4	5.4
300	Water (Blank), pH 6.5	96.4	96.2	95.2	91.3	3.2	3.4	4.4	7.8
200	30 mM Arginine and 30 mM Niacin	97.2	97.1	96.7	94.9	2.4	2.5	2.9	4.1
200	30 mM Histidine and 30 mM Niacin	97.1	97.1	96.7	94.9	2.5	2.5	2.9	4.1
200	30 mM Meglumine and 30 mM Niacin	97.2	97.1	96.7	95.2	2.4	2.5	2.9	3.8
200	30 mM Lysine and 30 mM Niacin	97.2	97.1	96.7	95.2	2.4	2.5	2.9	3.8
200	30 mM Arginine·HCl and 30 mM Niacinamide	97.1	97.1	96.6	95.3	2.5	2.5	3.0	3.7
200	30 mM Histidine and 30 mM Niacinamide	97.1	97.1	96.7	94.8	2.5	2.5	2.9	4.2
200	30 mM Meglumine and 30 mM Niacinamide	97.2	97.1	96.7	94.9	2.4	2.5	2.9	4.1
200	30 mM Lysine·HCl and 30 mM Niacinamide	97.2	97.1	96.8	94.8	2.4	2.5	2.8	4.2
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	97.2	97.2	96.7	94.5	2.4	2.4	2.9	4.5
200	Water (Blank), pH 6.5	96.9	96.6	95.9	93.6	2.7	3.0	3.7	5.4
100	30 mM Arginine and 30 mM Niacin	97.4	97.3	97.2	96.3	2.2	2.8	2.3	2.3
100	30 mM Histidine and 30 mM Niacin	97.4	97.3	97.2	96.0	2.2	2.8	2.3	2.3
100	30 mM Meglumine and 30 mM Niacin	97.4	97.3	97.2	96.3	2.2	2.8	2.3	2.3
100	30 mM Lysine and 30 mM Niacin	97.4	97.3	97.2	96.2	2.2	2.8	2.3	2.3
100	30 mM Arginine·HCl and 30 mM Niacinamide	97.4	97.3	97.2	96.3	2.2	2.8	2.3	2.8
100	30 mM Histidine and 30 mM Niacinamide	97.4	97.3	97.2	96.0	2.2	2.8	2.3	2.2
100	30 mM Meglumine and 30 mM Niacinamide	97.4	97.3	97.2	96.0	2.2	2.8	2.3	2.3
100	30 mM Lysine·HCl and 30 mM Niacinamide	97.4	97.3	97.2	95.8	2.2	2.8	2.3	2.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	97.4	97.3	97.2	95.7	2.2	2.2	2.5	3.3
100	Water (Blank), pH 6.5	97.3	97.2	97.1	94.9	2.3	2.4	2.5	4.2

Table 123 SE-UPLC results of formulated Adalimumab in 20 mM Tris buffer, pH 7.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	96.9	96.9	96.2	94.6	2.7	2.7	3.4	4.4
300	140 mM Histidine and 140 mM Niacin	96.9	96.9	96.2	94.8	2.7	2.7	3.4	4.2
300	140 mM Meglumine and 140 mM Niacin	96.9	96.9	96.2	93.7	2.7	2.7	3.4	5.3
300	140 mM Lysine and 140 mM Niacin	96.9	96.9	96.3	93.9	2.7	2.7	3.3	5.1
300	70 mM Arginine-HCl and 140 mM Niacinamide	96.9	96.9	96.3	93.9	2.7	2.7	3.3	5.1
300	140 mM Histidine and 140 mM Niacinamide	96.9	96.9	96.2	94.1	2.7	2.7	3.4	4.9
300	140 mM Meglumine and 140 mM Niacinamide	96.9	96.9	96.2	94.1	2.7	2.7	3.4	4.9
300	70 mM Lysine-HCl and 140 mM Niacinamide	96.9	96.9	96.2	93.7	2.7	2.7	3.4	5.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	96.8	96.8	95.8	93.0	2.8	2.8	3.8	6.1
300	Water (Blank), pH 7.0	96.2	96.0	94.9	90.8	3.4	3.6	4.7	8.3
200	140 mM Arginine and 140 mM Niacin	97.2	97.1	96.7	95.3	2.4	2.5	2.9	3.7
200	140 mM Histidine and 140 mM Niacin	97.1	97.1	96.7	95.2	2.5	2.5	2.9	3.8
200	140 mM Meglumine and 140 mM Niacin	97.2	97.1	96.7	95.4	2.4	2.5	2.9	3.6
200	140 mM Lysine and 140 mM Niacin	97.2	97.1	96.8	95.4	2.4	2.5	2.8	3.6
200	70 mM Arginine-HCl and 140 mM Niacinamide	97.1	97.1	96.7	95.4	2.5	2.5	2.9	3.6
200	140 mM Histidine and 140 mM Niacinamide	97.1	97.1	96.7	94.9	2.5	2.5	2.9	4.1
200	140 mM Meglumine and 140 mM Niacinamide	97.2	97.1	96.7	95.1	2.4	2.5	2.9	3.9
200	70 mM Lysine-HCl and 140 mM Niacinamide	97.2	97.1	96.7	95.2	2.4	2.5	2.9	3.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	97.1	97.1	96.5	94.1	2.5	2.5	3.1	4.9
200	Water (Blank), pH 7.0	96.8	96.4	95.6	93.2	2.8	3.2	4.0	5.8
100	140 mM Arginine and 140 mM Niacin	97.4	97.3	97.2	96.2	2.2	2.3	2.4	2.8
100	140 mM Histidine and 140 mM Niacin	97.4	97.3	97.2	95.8	2.2	2.3	2.4	3.2
100	140 mM Meglumine and 140 mM Niacin	97.4	97.3	97.2	96.0	2.2	2.3	2.4	3.0
100	140 mM Lysine and 140 mM Niacin	97.4	97.3	97.2	96.0	2.2	2.3	2.4	3.0
100	70 mM Arginine-HCl and 140 mM Niacinamide	97.4	97.3	97.2	96.1	2.2	2.3	2.4	2.9
100	140 mM Histidine and 140 mM Niacinamide	97.4	97.3	97.2	95.8	2.2	2.3	2.4	3.2
100	140 mM Meglumine and 140 mM Niacinamide	97.4	97.3	97.2	95.8	2.2	2.3	2.4	3.2
100	70 mM Lysine-HCl and 140 mM Niacinamide	97.4	97.3	97.2	95.8	2.2	2.3	2.4	3.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	97.3	97.3	97.1	95.4	2.3	2.3	2.6	3.6
100	Water (Blank), pH 7.0	97.1	97.1	97.0	94.5	2.5	2.5	2.6	4.6

Table 124 SE-UPLC results of formulated Adalimumab in 50 mM Tris buffer, pH 7.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing Formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	96.9	96.9	96.1	94.2	2.7	2.7	3.5	4.8
300	300 mM Histidine and 300 mM Niacin	96.9	96.9	96.0	94.4	2.7	2.7	3.6	4.6
300	300 mM Meglumine and 300 mM Niacin	96.9	96.9	96.0	93.7	2.7	2.7	3.6	5.3
300	300 mM Lysine and 300 mM Niacin	96.9	96.9	96.2	93.6	2.7	2.7	3.4	5.4
300	140 mM Arginine·HCl and 300 mM Niacinamide	96.9	96.9	96.2	93.8	2.7	2.7	3.4	5.2
300	300 mM Histidine and 300 mM Niacinamide	96.9	96.9	96.0	93.9	2.7	2.7	3.6	5.1
300	300 mM Meglumine and 300 mM Niacinamide	96.9	96.9	96.0	93.6	2.7	2.7	3.6	5.4
300	140 mM Lysine·HCl and 300 mM Niacinamide	96.9	96.9	96.1	93.4	2.7	2.7	3.5	5.6
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	96.9	96.9	95.8	92.9	2.7	2.7	3.8	6.1
300	Water (Blank), pH 7.5	96.1	96.0	95.0	90.5	3.5	3.6	4.6	8.5
200	300 mM Arginine and 300 mM Niacin	97.2	97.1	96.5	94.7	2.4	2.5	3.1	4.3
200	300 mM Histidine and 300 mM Niacin	97.1	97.1	96.5	94.5	2.5	2.5	3.1	4.5
200	300 mM Meglumine and 300 mM Niacin	97.2	97.1	96.5	95.1	2.4	2.5	3.1	3.9
200	300 mM Lysine and 300 mM Niacin	97.2	97.1	96.6	94.9	2.4	2.5	3.0	4.1
200	140 mM Arginine·HCl and 300 mM Niacinamide	97.1	97.1	96.6	94.9	2.5	2.5	3.0	4.1
200	300 mM Histidine and 300 mM Niacinamide	97.1	97.1	96.5	94.3	2.5	2.5	3.1	4.7
200	300 mM Meglumine and 300 mM Niacinamide	97.2	97.1	96.5	94.6	2.4	2.5	3.1	4.4
200	140 mM Lysine·HCl and 300 mM Niacinamide	97.2	97.1	96.6	94.7	2.4	2.5	3.0	4.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	97.0	97.0	96.4	94.0	2.6	2.6	3.2	5.0
200	Water (Blank), pH 7.5	96.6	96.6	95.6	92.8	3.0	3.0	4.0	6.2
100	300 mM Arginine and 300 mM Niacin	97.4	97.3	97.1	95.6	2.2	2.3	2.5	3.4
100	300 mM Histidine and 300 mM Niacin	97.4	97.3	97.1	95.2	2.2	2.3	2.5	3.8
100	300 mM Meglumine and 300 mM Niacin	97.4	97.3	97.1	95.6	2.2	2.3	2.5	3.4
100	300 mM Lysine and 300 mM Niacin	97.4	97.3	97.1	95.4	2.2	2.3	2.5	3.6
100	140 mM Arginine·HCl and 300 mM Niacinamide	97.4	97.3	97.1	95.7	2.2	2.3	2.5	3.3
100	300 mM Histidine and 300 mM Niacinamide	97.4	97.3	97.1	95.3	2.2	2.3	2.5	3.7
100	300 mM Meglumine and 300 mM Niacinamide	97.4	97.3	97.1	95.3	2.2	2.3	2.5	3.7
100	140 mM Lysine·HCl and 300 mM Niacinamide	97.4	97.3	97.1	95.3	2.2	2.3	2.5	3.7
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	97.3	97.3	97.1	95.0	2.3	2.3	2.5	4.0
100	Water (Blank), pH 7.5	97.1	97.1	96.8	93.7	2.5	2.5	2.8	5.3

Table 125 SE-UPLC results of formulated Adalimumab in 5 mM Succinate buffer, pH 4.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	96.6	96.5	95.6	93.4	3.0	3.1	4.0	5.6
300	30 mM Histidine and 30 mM Niacin	96.6	96.5	95.9	93.6	3.0	3.1	3.7	5.4
300	30 mM Meglumine and 30 mM Niacin	96.6	96.5	95.5	93.7	3.0	3.1	4.1	5.3
300	30 mM Lysine and 30 mM Niacin	96.6	96.5	95.9	92.9	3.0	3.1	3.7	6.1
300	30 mM Arginine-HCl and 30 mM Niacinamide	96.6	96.5	95.7	92.9	3.0	3.1	3.9	6.1
300	30 mM Histidine and 30 mM Niacinamide	96.6	96.5	95.8	93.1	3.0	3.1	3.8	5.9
300	30 mM Meglumine and 30 mM Niacinamide	96.6	96.5	95.8	93.7	3.0	3.1	3.8	5.3
300	30 mM Lysine-HCl and 30 mM Niacinamide	96.6	96.5	95.5	93.6	3.0	3.1	4.1	5.4
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	96.6	96.5	95.2	90.3	3.0	3.1	4.4	8.7
300	Water (Blank), pH 4.5	96.0	95.8	94.4	88.1	3.6	3.8	5.2	10.9
200	30 mM Arginine and 30 mM Niacin	97.0	97.0	96.5	94.2	2.6	2.6	3.1	4.8
200	30 mM Histidine and 30 mM Niacin	97.0	97.0	96.5	93.8	2.6	2.6	3.1	5.2
200	30 mM Meglumine and 30 mM Niacin	97.0	97.0	96.5	93.9	2.6	2.6	3.1	5.1
200	30 mM Lysine and 30 mM Niacin	97.0	97.0	96.6	94.1	2.6	2.6	3.0	4.9
200	30 mM Arginine-HCl and 30 mM Niacinamide	97.0	97.0	96.7	94.9	2.6	2.6	2.9	4.1
200	30 mM Histidine and 30 mM Niacinamide	97.0	97.0	96.6	94.1	2.6	2.6	3.0	4.9
200	30 mM Meglumine and 30 mM Niacinamide	97.0	97.0	96.7	93.9	2.6	2.6	2.9	5.1
200	30 mM Lysine-HCl and 30 mM Niacinamide	97.0	97.0	96.6	94.0	2.6	2.6	3.0	5.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	97.0	97.0	96.0	92.2	2.6	2.6	3.6	6.8
200	Water (Blank), pH 4.5	96.6	96.5	95.0	91.6	3.0	3.1	4.6	7.4
100	30 mM Arginine and 30 mM Niacin	97.4	97.3	96.6	95.9	2.2	2.3	3.0	3.1
100	30 mM Histidine and 30 mM Niacin	97.4	97.3	97.1	95.6	2.2	2.3	2.5	3.4
100	30 mM Meglumine and 30 mM Niacin	97.4	97.3	96.8	95.4	2.2	2.3	2.8	3.6
100	30 mM Lysine and 30 mM Niacin	97.4	97.3	96.8	95.4	2.2	2.3	2.8	3.6
100	30 mM Arginine-HCl and 30 mM Niacinamide	97.4	97.3	97.3	95.4	2.2	2.3	2.3	3.6
100	30 mM Histidine and 30 mM Niacinamide	97.4	97.3	96.9	95.4	2.2	2.3	2.7	3.6
100	30 mM Meglumine and 30 mM Niacinamide	97.4	97.3	96.9	95.4	2.2	2.3	2.7	3.6
100	30 mM Lysine-HCl and 30 mM Niacinamide	97.4	97.3	96.9	95.5	2.2	2.3	2.7	3.5
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	97.4	97.3	96.5	94.0	2.2	2.3	3.1	5.0
100	Water (Blank), pH 4.5	97.1	97.1	96.1	93.5	2.5	2.5	3.5	5.5

Table 126 SE-UPLC results of formulated Adalimumab in 20 mM Succinate buffer, pH 5.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	96.8	96.7	96.4	95.2	2.8	2.9	3.2	3.8
300	140 mM Histidine and 140 mM Niacin	96.8	96.7	96.5	95.1	2.8	2.9	3.1	3.9
300	140 mM Meglumine and 140 mM Niacin	96.8	96.7	96.4	95.1	2.8	2.9	3.2	3.9
300	140 mM Lysine and 140 mM Niacin	96.8	96.7	96.5	95.1	2.8	2.9	3.1	3.9
300	70 mM Arginine·HCl and 140 mM Niacinamide	96.8	96.7	96.5	95.1	2.8	2.9	3.1	3.9
300	140 mM Histidine and 140 mM Niacinamide	96.8	96.7	96.5	95.1	2.8	2.9	3.1	3.9
300	140 mM Meglumine and 140 mM Niacinamide	96.8	96.7	96.4	95.0	2.8	2.9	3.2	4.0
300	70 mM Lysine·HCl and 140 mM Niacinamide	96.8	96.7	96.4	95.4	2.8	2.9	3.2	3.6
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	96.8	96.7	96.0	92.8	2.8	2.9	3.6	6.2
300	Water (Blank), pH 5.5	96.2	96.0	94.9	90.5	3.4	3.6	4.7	8.5
200	140 mM Arginine and 140 mM Niacin	97.0	97.0	96.7	95.1	2.6	2.6	2.9	3.9
200	140 mM Histidine and 140 mM Niacin	97.0	97.0	96.7	95.3	2.6	2.6	2.9	3.7
200	140 mM Meglumine and 140 mM Niacin	97.0	97.0	96.9	95.1	2.6	2.6	2.7	3.9
200	140 mM Lysine and 140 mM Niacin	97.0	97.0	96.7	95.2	2.6	2.6	2.9	3.8
200	70 mM Arginine·HCl and 140 mM Niacinamide	97.0	97.0	96.7	95.3	2.6	2.6	2.9	3.7
200	140 mM Histidine and 140 mM Niacinamide	97.0	97.0	96.8	95.3	2.6	2.6	2.8	3.7
200	140 mM Meglumine and 140 mM Niacinamide	97.0	97.0	96.7	95.6	2.6	2.6	2.9	3.4
200	70 mM Lysine·HCl and 140 mM Niacinamide	97.0	97.0	96.7	95.4	2.6	2.6	2.9	3.6
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	97.0	97.0	96.3	93.6	2.6	2.6	3.3	5.4
200	Water (Blank), pH 5.5	96.6	96.5	95.6	92.6	3.0	3.1	4.0	6.4
100	140 mM Arginine and 140 mM Niacin	97.4	97.3	97.3	96.6	2.2	2.3	2.3	2.4
100	140 mM Histidine and 140 mM Niacin	97.4	97.4	97.3	96.1	2.2	2.2	2.3	2.9
100	140 mM Meglumine and 140 mM Niacin	97.4	97.4	97.3	96.4	2.2	2.2	2.3	2.6
100	140 mM Lysine and 140 mM Niacin	97.4	97.3	97.3	96.4	2.2	2.3	2.3	2.6
100	70 mM Arginine·HCl and 140 mM Niacinamide	97.4	97.4	97.4	96.3	2.2	2.2	2.2	2.7
100	140 mM Histidine and 140 mM Niacinamide	97.4	97.3	97.2	96.2	2.2	2.3	2.4	2.8
100	140 mM Meglumine and 140 mM Niacinamide	97.4	97.4	97.3	96.3	2.2	2.2	2.3	2.7
100	70 mM Lysine·HCl and 140 mM Niacinamide	97.4	97.3	97.2	96.4	2.2	2.3	2.4	2.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	97.4	97.3	97.1	95.4	2.2	2.3	2.5	3.6
100	Water (Blank), pH 5.5	97.1	97.1	96.9	94.5	2.5	2.5	2.7	4.5

Table 127 SE-UPLC results of formulated Adalimumab in 50 mM Succinate buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing Formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	96.9	96.9	96.3	95.0	2.7	2.7	3.3	4.0
300	300 mM Histidine and 300 mM Niacin	96.9	96.9	96.2	95.0	2.7	2.7	3.4	4.0
300	300 mM Meglumine and 300 mM Niacin	96.9	96.9	96.4	95.2	2.7	2.7	3.2	3.8
300	300 mM Lysine and 300 mM Niacin	96.9	96.9	96.4	95.0	2.7	2.7	3.2	4.0
300	140 mM Arginine-HCl and 300 mM Niacinamide	96.9	96.9	96.6	95.2	2.7	2.7	3.0	3.8
300	300 mM Histidine and 300 mM Niacinamide	96.9	96.9	96.3	95.5	2.7	2.7	3.3	3.5
300	300 mM Meglumine and 300 mM Niacinamide	96.9	96.9	96.4	95.2	2.7	2.7	3.2	3.8
300	140 mM Lysine-HCl and 300 mM Niacinamide	96.9	96.9	96.1	95.2	2.7	2.7	3.5	3.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.9	96.9	96.0	93.3	2.7	2.7	3.6	5.8
300	Water (Blank), pH 6.0	96.3	96.1	95.1	91.1	3.3	3.5	4.5	8.0
200	300 mM Arginine and 300 mM Niacin	97.2	97.2	96.8	95.6	2.4	2.4	2.8	3.4
200	300 mM Histidine and 300 mM Niacin	97.2	97.2	97.0	95.5	2.4	2.4	2.6	3.5
200	300 mM Meglumine and 300 mM Niacin	97.2	97.2	97.1	95.5	2.4	2.4	2.5	3.5
200	300 mM Lysine and 300 mM Niacin	97.2	97.2	96.9	95.5	2.4	2.4	2.7	3.5
200	140 mM Arginine-HCl and 300 mM Niacinamide	97.2	97.2	96.8	95.4	2.4	2.4	2.8	3.6
200	300 mM Histidine and 300 mM Niacinamide	97.2	97.2	97.0	95.8	2.4	2.4	2.6	3.2
200	300 mM Meglumine and 300 mM Niacinamide	97.2	97.2	96.8	95.8	2.4	2.4	2.8	3.2
200	140 mM Lysine-HCl and 300 mM Niacinamide	97.2	97.2	96.9	95.8	2.4	2.4	2.7	3.2
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.1	97.2	96.6	94.3	2.5	2.4	3.0	4.7
200	Water (Blank), pH 6.0	96.9	96.5	95.8	93.4	2.7	3.1	3.8	5.6
100	300 mM Arginine and 300 mM Niacin	97.4	97.3	97.2	96.7	2.2	2.3	2.4	2.3
100	300 mM Histidine and 300 mM Niacin	97.4	97.3	97.2	96.7	2.2	2.3	2.4	2.3
100	300 mM Meglumine and 300 mM Niacin	97.4	97.4	97.3	96.7	2.2	2.2	2.3	2.3
100	300 mM Lysine and 300 mM Niacin	97.4	97.3	97.2	96.7	2.2	2.3	2.4	2.3
100	140 mM Arginine-HCl and 300 mM Niacinamide	97.4	97.3	97.2	96.4	2.2	2.3	2.4	2.6
100	300 mM Histidine and 300 mM Niacinamide	97.4	97.3	97.2	96.8	2.2	2.3	2.4	2.2
100	300 mM Meglumine and 300 mM Niacinamide	97.4	97.3	97.2	96.7	2.2	2.3	2.4	2.3
100	140 mM Lysine-HCl and 300 mM Niacinamide	97.4	97.3	97.2	96.6	2.2	2.3	2.4	2.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.4	97.3	97.2	95.6	2.2	2.2	2.5	3.4
100	Water (Blank), pH 6.0	97.2	97.2	97.0	94.7	2.4	2.4	2.6	4.4

Example 9: Effect of viscosity-reducing and stabilizing formulations on Trastuzumab stability at various temperatures.

[00105] This example tested the effect of viscosity-reducing and stabilizing formulations on Trastuzumab stability and compared it with the lead formulation (25 mM Phosphate, 81.2 mM of Nicotinic acid and 29.4 mM Tryptophan) in WO2018211517.

[00106] Materials and Methods

[00107] The Trastuzumab (Herceptin®) samples were produced by WuXi Biologics, as described in Example 3, and formulated as shown in Tables 128-145. The prepared samples were aseptically filtered with 0.22 µm PVDF membrane filters before filling. After filtration, samples were filled with a pipette to 2 mL vials, and the fill volume was 1.0 mL. Then the vials were stoppered and sealed and subjected to 5°C, 25°C and 40°C chambers to start the stability assessment. Furthermore, there was a control group comprising 25 mM phosphate buffer at pH 6.0, with 81.2 mM Nicotinic acid and 29.4 mM Tryptophan (matching the lead formulation 25 mM phosphate buffer at pH 6.0 along with 10 mg/mL Nicotinic acid (acid form) and 6 mg/mL Tryptophan from Examples 14 and 16-21 in WO2018211517). After preparing the control group samples, the pH was adjusted to the target value using hydrochloric acid and sodium hydroxide. An additional control group, consisting solely of MilliQ water and the protein, was prepared as a blank. The pH of the blank group was also adjusted to match the target pH using the same method. To ascertain Trastuzumab's concentration in the groups, absorbance at 280 nm combined with SE-UPLC was gauged against corresponding buffers containing a viscosity-reducing and stabilizing agent for excipient-containing samples, and absorbance at 280 nm was measured for the protein solution without a viscosity-reducing and stabilizing formulation. For Trastuzumab without excipients, the buffer alone (i.e., devoid of excipients) served as a blank for protein concentration calculation. The extinction coefficient was measured at $1.48 \text{ (mg/mL)}^{-1} \cdot \text{cm}^{-1}$.

[00108] The test for protein stability was carried out over a 4-week period by SE-UPLC. Samples were prepared as described above. As shown in Tables 128-145, after 4 weeks, the monomer content of Trastuzumab formulated with the tested viscosity-reducing and stabilizing formulations was higher than or close to 90% even at 40°C, comparable or better than the lead formulation in WO2018211517, regardless of the used buffers, indicating good stabilization effect of the tested viscosity-reducing and stabilizing formulations.

Table 128 SE-UPLC results of formulated Trastuzumab in 5 mM Histidine buffer, pH 5.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	96.3	96.1	94.8	91.7	3.7	3.9	5.0	7.5
300	30 mM Histidine and 30 mM Niacin	96.8	96.8	95.4	91.5	3.2	3.2	4.4	7.6
300	30 mM Meglumine and 30 mM Niacin	96.3	96.3	95.4	90.4	3.7	3.7	4.4	8.9
300	30 mM Lysine and 30 mM Niacin	96.7	96.5	95.6	90.5	3.3	3.5	4.3	8.6
300	30 mM Arginine-HCl and 30 mM Niacinamide	96.3	96.3	95.3	90.1	3.7	3.7	4.5	9.1
300	30 mM Histidine and 30 mM Niacinamide	96.8	96.7	95.6	90.7	3.2	3.3	4.2	8.4
300	30 mM Meglumine and 30 mM Niacinamide	96.5	96.5	95.0	90.6	3.5	3.5	4.9	8.7
300	30 mM Lysine-HCl and 30 mM Niacinamide	96.8	96.6	95.7	90.9	3.2	3.4	4.2	8.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	95.8	95.7	94.1	89.3	4.2	4.3	5.8	9.8
300	Water (Blank), pH 5.0	95.4	95.3	93.0	86.9	4.6	4.7	6.8	12.0
200	30 mM Arginine and 30 mM Niacin	97.4	97.4	96.8	93.9	2.6	2.6	3.1	5.6
200	30 mM Histidine and 30 mM Niacin	97.7	97.7	97.2	94.2	2.3	2.3	2.6	5.2
200	30 mM Meglumine and 30 mM Niacin	97.7	97.6	97.3	94.5	2.3	2.4	2.5	4.8
200	30 mM Lysine and 30 mM Niacin	97.4	97.3	96.8	93.6	2.6	2.7	3.0	5.8
200	30 mM Arginine-HCl and 30 mM Niacinamide	97.3	97.3	96.9	94.1	2.7	2.7	2.8	5.4
200	30 mM Histidine and 30 mM Niacinamide	97.7	97.6	96.8	94.0	2.3	2.4	2.9	5.4
200	30 mM Meglumine and 30 mM Niacinamide	97.3	97.2	96.4	94.3	2.7	2.8	3.5	5.0
200	30 mM Lysine-HCl and 30 mM Niacinamide	97.7	97.7	97.2	94.0	2.3	2.3	2.7	5.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	96.9	96.9	95.7	92.5	3.1	3.1	4.2	7.0
200	Water (Blank), pH 5.0	96.6	96.5	94.9	90.8	3.4	3.5	4.9	8.3
100	30 mM Arginine and 30 mM Niacin	97.6	97.6	97.2	94.9	2.4	2.4	2.5	4.6
100	30 mM Histidine and 30 mM Niacin	97.7	97.7	97.2	95.3	2.3	2.3	2.5	4.2
100	30 mM Meglumine and 30 mM Niacin	97.6	97.6	97.1	94.9	2.4	2.4	2.7	4.6
100	30 mM Lysine and 30 mM Niacin	97.8	97.7	97.2	95.6	2.2	2.3	2.7	4.1
100	30 mM Arginine-HCl and 30 mM Niacinamide	97.7	97.7	97.3	95.5	2.3	2.3	2.6	4.0
100	30 mM Histidine and 30 mM Niacinamide	97.8	97.7	97.4	95.3	2.2	2.3	2.5	4.4
100	30 mM Meglumine and 30 mM Niacinamide	97.9	97.9	97.3	96.0	2.1	2.1	2.4	3.5
100	30 mM Lysine-HCl and 30 mM Niacinamide	97.8	97.8	97.4	95.1	2.2	2.2	2.5	4.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	97.3	97.3	96.6	94.4	2.7	2.7	3.3	5.2
100	Water (Blank), pH 5.0	97.5	97.5	96.2	93.2	2.5	2.5	3.6	6.0

Table 129 SE-UPLC results of formulated Trastuzumab in 20 mM Histidine buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	96.7	96.6	94.4	90.4	3.3	3.4	5.5	8.7
300	140 mM Histidine and 140 mM Niacin	96.5	96.4	94.9	90.3	3.5	2.6	4.9	8.5
300	140 mM Meglumine and 140 mM Niacin	97.0	96.8	95.1	90.0	3.0	3.2	4.7	9.0
300	140 mM Lysine and 140 mM Niacin	96.9	96.7	94.4	90.2	3.1	3.3	5.5	8.9
300	70 mM Arginine·HCl and 140 mM Niacinamide	96.8	96.6	95.0	90.7	3.2	3.4	4.9	8.4
300	140 mM Histidine and 140 mM Niacinamide	96.4	96.3	94.7	90.6	3.6	3.7	5.1	8.4
300	140 mM Meglumine and 140 mM Niacinamide	96.6	96.5	95.0	90.8	3.4	3.5	4.8	8.3
300	70 mM Lysine·HCl and 140 mM Niacinamide	97.2	97.1	95.3	91.5	1.8	1.9	4.5	7.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.0	95.9	94.4	89.7	4.0	4.1	5.4	9.5
300	Water (Blank), pH 6.0	95.7	95.5	93.2	87.4	4.2	4.4	6.5	11.4
200	140 mM Arginine and 140 mM Niacin	97.8	97.8	96.8	94.3	2.2	2.2	3.1	5.0
200	140 mM Histidine and 140 mM Niacin	97.5	97.5	96.7	93.7	2.5	2.5	3.2	5.3
200	140 mM Meglumine and 140 mM Niacin	97.9	97.9	96.4	94.0	2.1	2.1	3.5	5.4
200	140 mM Lysine and 140 mM Niacin	97.6	97.6	96.5	93.5	2.4	2.4	3.4	5.7
200	70 mM Arginine·HCl and 140 mM Niacinamide	97.1	97.1	96.0	94.5	2.9	2.9	3.9	4.7
200	140 mM Histidine and 140 mM Niacinamide	97.9	97.9	96.2	93.3	2.1	2.1	3.7	6.0
200	140 mM Meglumine and 140 mM Niacinamide	97.7	97.7	96.3	93.9	2.3	2.3	3.5	5.2
200	70 mM Lysine·HCl and 140 mM Niacinamide	97.3	97.3	96.0	93.9	2.7	2.7	3.8	5.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.2	97.2	96.0	93.1	2.8	2.8	3.8	6.2
200	Water (Blank), pH 6.0	97.0	97.0	95.1	91.7	2.9	2.9	4.7	7.4
100	140 mM Arginine and 140 mM Niacin	98.2	98.2	97.2	96.2	1.8	1.8	2.7	3.3
100	140 mM Histidine and 140 mM Niacin	97.8	97.8	97.0	95.3	2.2	2.2	2.9	4.2
100	140 mM Meglumine and 140 mM Niacin	98.4	98.4	97.5	96.4	1.6	1.6	2.4	3.1
100	140 mM Lysine and 140 mM Niacin	98.3	98.3	96.9	95.7	1.7	1.7	2.9	3.7
100	70 mM Arginine·HCl and 140 mM Niacinamide	98.0	98.0	97.1	95.9	2.0	2.0	2.7	3.5
100	140 mM Histidine and 140 mM Niacinamide	97.9	97.9	96.9	95.4	2.1	2.1	3.0	4.1
100	140 mM Meglumine and 140 mM Niacinamide	98.3	98.3	96.8	95.5	1.7	1.7	3.0	4.0
100	70 mM Lysine·HCl and 140 mM Niacinamide	98.1	98.1	97.3	95.9	1.9	1.9	2.5	3.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.9	97.9	97.0	94.8	2.1	2.1	2.9	4.6
100	Water (Blank), pH 6.0	97.7	97.7	96.3	94.1	2.3	2.3	3.5	5.0

Table 130 SE-UPLC results of formulated Trastuzumab in 50 mM Histidine buffer, pH 7.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	96.0	95.9	94.9	91.1	4.0	4.1	4.9	8.2
300	300 mM Histidine and 300 mM Niacin	96.1	95.9	94.7	91.0	3.9	4.1	5.1	8.1
300	300 mM Meglumine and 300 mM Niacin	95.6	95.4	94.8	89.7	4.4	4.6	5.0	9.5
300	300 mM Lysine and 300 mM Niacin	95.7	95.6	94.6	90.8	4.3	4.4	5.2	8.3
300	140 mM Arginine·HCl and 300 mM Niacinamide	96.0	95.9	94.5	91.1	4.0	4.1	5.3	7.9
300	300 mM Histidine and 300 mM Niacinamide	95.8	95.7	94.5	91.0	4.2	4.3	5.3	8.3
300	300 mM Meglumine and 300 mM Niacinamide	96.1	95.9	94.9	91.0	3.9	4.1	4.9	8.3
300	140 mM Lysine·HCl and 300 mM Niacinamide	95.6	95.5	94.5	90.9	4.4	4.5	5.4	8.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	95.6	95.5	93.9	89.0	4.4	4.5	5.9	10.0
300	Water (Blank), pH 7.0	95.2	95.0	92.8	86.5	4.7	4.9	7.0	12.3
200	300 mM Arginine and 300 mM Niacin	96.9	96.8	95.9	93.3	3.1	3.2	4.0	6.0
200	300 mM Histidine and 300 mM Niacin	96.9	96.8	96.2	93.1	3.1	3.2	3.7	6.2
200	300 mM Meglumine and 300 mM Niacin	96.8	96.8	96.0	92.9	3.2	3.2	3.8	6.4
200	300 mM Lysine and 300 mM Niacin	97.3	97.2	96.4	93.3	2.7	2.8	3.5	6.2
200	140 mM Arginine·HCl and 300 mM Niacinamide	97.1	97.1	96.6	93.3	2.9	2.9	3.1	6.1
200	300 mM Histidine and 300 mM Niacinamide	96.9	96.9	96.3	93.4	3.1	3.1	3.6	6.0
200	300 mM Meglumine and 300 mM Niacinamide	97.0	96.9	96.5	93.7	3.0	3.1	3.2	5.7
200	140 mM Lysine·HCl and 300 mM Niacinamide	97.3	97.3	96.5	94.1	2.7	2.7	3.3	5.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	96.8	96.8	95.5	92.2	3.2	3.2	4.3	7.1
200	Water (blank), pH 7.0	96.5	96.4	94.7	90.5	3.5	3.6	5.0	8.5
100	300 mM Arginine and 300 mM Niacin	97.5	97.5	97.1	95.1	2.5	2.5	2.8	4.4
100	300 mM Histidine and 300 mM Niacin	97.4	97.3	96.9	95.4	2.6	2.7	3.0	4.3
100	300 mM Meglumine and 300 mM Niacin	97.5	97.5	97.0	95.3	2.5	2.5	2.8	4.3
100	300 mM Lysine and 300 mM Niacin	97.5	97.4	97.0	94.8	2.5	2.6	2.9	4.7
100	140 mM Arginine·HCl and 300 mM Niacinamide	97.3	97.3	96.8	94.6	2.7	2.7	3.0	5.1
100	300 mM Histidine and 300 mM Niacinamide	97.4	97.3	96.9	95.3	2.6	2.7	2.8	4.2
100	300 mM Meglumine and 300 mM Niacinamide	97.3	97.3	96.7	95.3	2.7	2.7	3.0	4.3
100	140 mM Lysine·HCl and 300 mM Niacinamide	97.3	97.3	96.9	94.8	2.7	2.7	3.0	4.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	97.2	97.2	96.5	94.2	2.8	2.8	3.4	5.2
100	Water (blank), pH 7.0	97.0	97.0	96.0	93.0	3.0	3.0	3.9	6.1

Table 131 SE-UPLC results of formulated Trastuzumab in 5 mM Acetate buffer, pH 4.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	95.9	95.7	94.5	89.0	4.1	4.3	5.2	10.3
300	30 mM Histidine and 30 mM Niacin	95.5	95.4	94.1	89.0	4.5	4.6	5.6	10.3
300	30 mM Meglumine and 30 mM Niacin	95.7	95.6	94.2	89.0	4.3	4.4	5.6	10.1
300	30 mM Lysine and 30 mM Niacin	95.5	95.3	94.3	89.8	4.5	4.7	5.5	9.5
300	30 mM Arginine-HCl and 30 mM Niacinamide	95.4	95.3	93.9	89.7	4.6	4.7	5.8	9.6
300	30 mM Histidine and 30 mM Niacinamide	95.9	95.8	94.1	88.7	4.1	4.2	5.6	10.5
300	30 mM Meglumine and 30 mM Niacinamide	95.6	95.4	93.9	89.6	4.4	4.6	5.8	9.7
300	30 mM Lysine-HCl and 30 mM Niacinamide	95.9	95.7	94.1	89.2	4.1	4.3	5.7	10.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	95.4	95.2	93.4	87.8	4.6	4.8	6.3	11.2
300	Water (Blank), pH 4.5	95.0	94.7	92.7	85.3	5.0	5.3	6.9	13.4
200	30 mM Arginine and 30 mM Niacin	96.6	96.5	95.8	92.1	3.4	3.5	4.0	7.0
200	30 mM Histidine and 30 mM Niacin	96.6	96.5	95.5	92.0	3.4	3.5	4.3	7.2
200	30 mM Meglumine and 30 mM Niacin	96.8	96.7	95.7	92.6	3.2	3.3	4.1	6.7
200	30 mM Lysine and 30 mM Niacin	96.8	96.8	95.9	93.1	3.2	3.2	3.8	6.1
200	30 mM Arginine-HCl and 30 mM Niacinamide	96.8	96.7	96.1	92.3	3.2	3.3	3.7	6.8
200	30 mM Histidine and 30 mM Niacinamide	96.7	96.6	95.6	92.8	3.3	3.4	4.1	6.5
200	30 mM Meglumine and 30 mM Niacinamide	96.9	96.9	95.8	92.3	3.1	3.1	4.1	6.8
200	30 mM Lysine-HCl and 30 mM Niacinamide	96.9	96.8	96.0	93.0	3.1	3.2	3.8	6.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	96.5	96.4	95.1	91.4	3.5	3.6	4.7	7.7
200	Water (blank), pH 4.5	96.2	96.0	94.2	90.2	3.8	4.0	5.4	8.8
100	30 mM Arginine and 30 mM Niacin	97.2	97.1	96.9	93.8	2.8	2.9	2.8	5.6
100	30 mM Histidine and 30 mM Niacin	97.1	97.1	96.6	93.6	2.9	2.9	3.2	5.8
100	30 mM Meglumine and 30 mM Niacin	97.1	97.0	96.8	93.8	2.9	3.0	2.9	5.6
100	30 mM Lysine and 30 mM Niacin	97.1	97.1	96.6	94.4	2.9	2.9	3.3	4.8
100	30 mM Arginine-HCl and 30 mM Niacinamide	97.1	97.0	96.7	94.2	2.9	3.0	3.0	5.0
100	30 mM Histidine and 30 mM Niacinamide	97.1	97.1	96.7	94.4	2.9	2.9	3.1	4.8
100	30 mM Meglumine and 30 mM Niacinamide	97.0	96.9	96.6	94.2	3.0	3.1	3.1	5.1
100	30 mM Lysine-HCl and 30 mM Niacinamide	97.3	97.2	96.8	94.2	2.7	2.8	3.1	5.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	97.0	96.9	96.1	93.3	3.0	3.1	3.7	5.9
100	Water (blank), pH 4.5	96.8	96.6	95.4	92.1	3.2	3.4	4.3	7.0

Table 132 SE-UPLC results of formulated Trastuzumab in 20 mM Acetate buffer, pH 5.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	96.7	96.5	95.9	92.2	3.3	3.5	3.9	7.1
300	140 mM Histidine and 140 mM Niacin	96.4	96.4	95.7	91.2	3.6	3.6	4.2	8.0
300	140 mM Meglumine and 140 mM Niacin	96.4	96.4	95.7	91.0	3.6	3.6	4.1	8.2
300	140 mM Lysine and 140 mM Niacin	96.3	96.2	95.3	90.6	3.7	3.8	4.6	8.4
300	70 mM Arginine·HCl and 140 mM Niacinamide	96.3	96.3	95.6	90.5	3.7	3.7	4.3	8.5
300	140 mM Histidine and 140 mM Niacinamide	96.8	96.6	95.3	90.7	3.2	3.4	4.5	8.3
300	140 mM Meglumine and 140 mM Niacinamide	96.5	96.3	95.7	91.8	3.5	3.7	4.1	7.5
300	70 mM Lysine·HCl and 140 mM Niacinamide	96.7	96.5	95.5	91.6	3.3	3.5	4.3	7.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	95.8	95.7	94.1	89.3	4.2	4.3	5.8	9.8
300	Water (Blank), pH 5.0	95.4	95.3	93.0	86.9	4.6	4.7	6.8	12.0
200	140 mM Arginine and 140 mM Niacin	97.4	97.4	96.4	93.7	2.6	2.6	3.5	5.6
200	140 mM Histidine and 140 mM Niacin	97.6	97.6	97.2	94.5	2.4	2.4	2.5	4.8
200	140 mM Meglumine and 140 mM Niacin	97.6	97.5	96.8	93.7	2.4	2.5	3.0	5.8
200	140 mM Lysine and 140 mM Niacin	97.3	97.2	96.7	93.8	2.7	2.8	3.0	5.6
200	70 mM Arginine·HCl and 140 mM Niacinamide	97.7	97.7	97.0	94.5	2.3	2.3	2.9	4.8
200	140 mM Histidine and 140 mM Niacinamide	97.6	97.5	96.7	93.6	2.4	2.5	3.1	5.7
200	140 mM Meglumine and 140 mM Niacinamide	97.3	97.2	96.7	94.3	2.7	2.8	3.1	5.0
200	70 mM Lysine·HCl and 140 mM Niacinamide	97.5	97.5	96.8	94.5	2.5	2.5	3.1	5.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	96.9	96.9	95.7	92.5	3.1	3.1	4.2	7.0
200	Water (blank), pH 5.0	96.6	96.5	94.9	90.8	3.4	3.5	4.9	8.3
100	140 mM Arginine and 140 mM Niacin	97.8	97.7	97.3	95.5	2.2	2.3	2.5	4.2
100	140 mM Histidine and 140 mM Niacin	97.6	97.6	97.0	95.2	2.4	2.4	2.7	4.5
100	140 mM Meglumine and 140 mM Niacin	97.7	97.6	97.1	95.1	2.3	2.4	2.6	4.5
100	140 mM Lysine and 140 mM Niacin	97.8	97.7	97.2	95.3	2.2	2.3	2.5	4.3
100	70 mM Arginine·HCl and 140 mM Niacinamide	97.7	97.6	97.1	95.1	2.3	2.4	2.8	4.5
100	140 mM Histidine and 140 mM Niacinamide	97.8	97.7	97.3	95.9	2.2	2.3	2.6	3.7
100	140 mM Meglumine and 140 mM Niacinamide	97.6	97.5	97.2	95.1	2.4	2.5	2.6	4.6
100	70 mM Lysine·HCl and 140 mM Niacinamide	97.6	97.6	97.1	95.0	2.4	2.4	2.8	4.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	97.3	97.3	96.6	94.4	2.7	2.7	3.3	5.2
100	Water (blank), pH 5.0	97.5	97.5	96.2	93.2	2.5	2.5	3.6	6.0

Table 133 SE-UPLC results of formulated Trastuzumab in 50 mM Acetate buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing Formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	96.8	96.7	94.5	90.5	3.2	3.3	5.4	8.6
300	300 mM Histidine and 300 mM Niacin	96.6	96.5	94.3	90.4	3.4	3.5	5.6	8.8
300	300 mM Meglumine and 300 mM Niacin	97.1	97.0	95.0	90.2	2.9	3.0	4.9	8.2
300	300 mM Lysine and 300 mM Niacin	96.7	96.6	94.8	90.3	3.3	3.4	5.0	8.5
300	140 mM Arginine·HCl and 300 mM Niacinamide	96.5	96.4	94.6	90.6	3.5	3.6	5.3	8.3
300	300 mM Histidine and 300 mM Niacinamide	97.4	97.2	95.5	91.0	2.6	2.8	4.4	6.9
300	300 mM Meglumine and 300 mM Niacinamide	97.0	96.9	95.2	90.1	3.0	3.1	4.7	8.0
300	140 mM Lysine·HCl and 300 mM Niacinamide	96.2	96.1	94.5	89.8	3.8	3.9	5.3	9.2
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.0	95.9	94.4	89.7	4.0	4.1	5.4	9.5
300	Water (Blank), pH 6.0	95.7	95.5	93.2	87.4	4.2	4.4	6.5	11.4
200	300 mM Arginine and 300 mM Niacin	98.0	98.0	96.9	94.7	2.0	2.0	3.0	5.5
200	300 mM Histidine and 300 mM Niacin	97.4	97.4	96.6	93.8	2.6	2.6	3.3	5.6
200	300 mM Meglumine and 300 mM Niacin	97.8	97.8	96.3	94.2	2.2	2.2	3.6	5.1
200	300 mM Lysine and 300 mM Niacin	97.5	97.5	96.4	93.4	2.5	2.5	3.5	5.8
200	140 mM Arginine·HCl and 300 mM Niacinamide	97.2	97.2	96.5	94.1	2.8	2.8	3.4	5.3
200	300 mM Histidine and 300 mM Niacinamide	97.6	97.6	96.7	93.6	2.4	2.4	3.2	4.9
200	300 mM Meglumine and 300 mM Niacinamide	97.1	97.1	96.8	94.0	2.9	2.9	3.1	5.2
200	140 mM Lysine·HCl and 300 mM Niacinamide	97.3	97.3	96.2	93.5	2.7	2.7	3.7	6.2
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.2	97.2	96.0	93.1	2.8	2.8	3.8	6.2
200	Water (Blank), pH 6.0	97.0	97.0	95.1	91.7	2.9	2.9	4.7	7.4
100	300 mM Arginine and 300 mM Niacin	98.1	98.1	97.4	96.1	1.9	1.9	2.5	3.4
100	300 mM Histidine and 300 mM Niacin	97.7	97.7	96.6	95.1	2.3	2.3	3.3	4.0
100	300 mM Meglumine and 300 mM Niacin	98.5	98.5	97.3	96.3	1.5	1.5	2.6	3.2
100	300 mM Lysine and 300 mM Niacin	98.0	98.0	96.7	95.6	2.0	2.0	3.2	3.8
100	140 mM Arginine·HCl and 300 mM Niacinamide	97.8	97.8	97.4	95.5	2.2	2.2	2.5	4.3
100	300 mM Histidine and 300 mM Niacinamide	98.2	98.2	97.6	96.5	1.8	1.8	2.3	3.1
100	300 mM Meglumine and 300 mM Niacinamide	98.4	98.4	97.2	95.8	1.6	1.6	2.7	3.5
100	140 mM Lysine·HCl and 300 mM Niacinamide	98.3	98.3	97.1	95.2	1.7	1.7	2.8	3.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.9	97.9	97.0	94.8	2.1	2.1	2.9	4.6
100	Water (Blank), pH 6.0	97.7	97.7	96.3	94.1	2.3	2.3	3.5	5.0

Table 134 SE-UPLC results of formulated Trastuzumab in 5 mM Citrate buffer, pH 4.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	95.8	95.7	94.5	89.6	4.2	4.3	5.3	9.5
300	30 mM Histidine and 30 mM Niacin	95.8	95.7	94.6	89.7	4.2	4.3	5.1	9.4
300	30 mM Meglumine and 30 mM Niacin	95.4	95.3	93.8	89.3	4.6	4.7	6.0	9.9
300	30 mM Lysine and 30 mM Niacin	95.4	95.2	93.9	88.1	4.6	4.8	5.8	11.2
300	30 mM Arginine-HCl and 30 mM Niacinamide	95.6	95.4	94.0	89.1	4.4	4.6	5.7	10.1
300	30 mM Histidine and 30 mM Niacinamide	95.7	95.6	94.4	89.2	4.3	4.4	5.3	10.0
300	30 mM Meglumine and 30 mM Niacinamide	95.6	95.4	93.9	89.1	4.4	4.6	5.8	10.2
300	30 mM Lysine-HCl and 30 mM Niacinamide	95.6	95.4	94.1	88.8	4.4	4.6	5.7	10.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	95.4	95.2	93.4	87.8	4.6	4.8	6.3	11.2
300	Water (Blank), pH 4.5	95.0	94.7	92.7	85.3	5.0	5.3	6.9	13.4
200	30 mM Arginine and 30 mM Niacin	96.8	96.8	95.8	92.3	3.2	3.2	4.1	7.0
200	30 mM Histidine and 30 mM Niacin	96.9	96.8	96.1	92.7	3.1	3.2	3.6	6.4
200	30 mM Meglumine and 30 mM Niacin	96.5	96.5	95.7	92.3	3.5	3.5	4.2	6.9
200	30 mM Lysine and 30 mM Niacin	96.6	96.5	95.8	92.1	3.4	3.5	4.0	7.0
200	30 mM Arginine-HCl and 30 mM Niacinamide	96.7	96.7	95.7	92.5	3.3	3.3	4.1	6.6
200	30 mM Histidine and 30 mM Niacinamide	96.9	96.8	96.0	93.0	3.1	3.2	3.7	6.1
200	30 mM Meglumine and 30 mM Niacinamide	96.8	96.7	95.7	92.4	3.2	3.3	4.1	6.9
200	30 mM Lysine-HCl and 30 mM Niacinamide	96.6	96.6	95.7	92.8	3.4	3.4	4.0	6.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	96.5	96.4	95.1	91.4	3.5	3.6	4.7	7.7
200	Water (blank), pH 4.5	96.2	96.0	94.2	90.2	3.8	4.0	5.4	8.8
100	30 mM Arginine and 30 mM Niacin	97.2	97.2	96.8	94.2	2.8	2.8	3.1	5.1
100	30 mM Histidine and 30 mM Niacin	97.0	97.0	96.6	93.6	3.0	3.0	3.3	5.7
100	30 mM Meglumine and 30 mM Niacin	97.3	97.2	96.9	94.1	2.7	2.8	2.8	5.1
100	30 mM Lysine and 30 mM Niacin	97.2	97.2	96.8	94.1	2.8	2.8	3.1	5.1
100	30 mM Arginine-HCl and 30 mM Niacinamide	97.3	97.2	97.0	94.1	2.7	2.8	2.8	5.3
100	30 mM Histidine and 30 mM Niacinamide	97.2	97.2	96.8	94.5	2.8	2.8	2.9	4.8
100	30 mM Meglumine and 30 mM Niacinamide	97.1	97.0	96.6	93.6	2.9	3.0	3.1	5.7
100	30 mM Lysine-HCl and 30 mM Niacinamide	97.2	97.2	96.7	94.5	2.8	2.8	3.1	4.7
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	97.0	96.9	96.1	93.3	3.0	3.1	3.7	5.9
100	Water (blank), pH 4.5	96.8	96.6	95.4	92.1	3.2	3.4	4.3	7.0

Table 135 SE-UPLC results of formulated Trastuzumab in 20 mM Citrate buffer, pH 5.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	96.8	96.6	96.0	92.0	3.2	3.4	3.7	7.2
300	140 mM Histidine and 140 mM Niacin	96.7	96.6	95.5	91.2	3.3	3.4	4.3	8.2
300	140 mM Meglumine and 140 mM Niacin	96.4	96.3	95.1	90.7	3.6	3.7	4.6	8.3
300	140 mM Lysine and 140 mM Niacin	96.7	96.6	95.5	90.8	3.3	3.4	4.4	8.7
300	70 mM Arginine·HCl and 140 mM Niacinamide	96.6	96.4	95.3	90.7	3.4	3.6	4.5	8.8
300	140 mM Histidine and 140 mM Niacinamide	96.8	96.7	95.6	91.7	3.2	3.3	4.2	7.4
300	140 mM Meglumine and 140 mM Niacinamide	96.6	96.5	95.0	91.8	3.4	3.5	4.9	7.5
300	70 mM Lysine·HCl and 140 mM Niacinamide	96.6	96.4	95.8	92.6	3.4	3.6	3.9	6.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	96.3	96.1	94.8	90.2	3.8	3.9	5.2	9.0
300	Water (Blank), pH 5.5	95.5	95.4	93.5	88.1	4.1	4.3	6.0	10.2
200	140 mM Arginine and 140 mM Niacin	97.8	97.7	96.5	93.8	2.2	2.3	3.4	5.3
200	140 mM Histidine and 140 mM Niacin	97.9	97.8	97.1	93.9	2.1	2.2	2.7	5.6
200	140 mM Meglumine and 140 mM Niacin	97.6	97.5	97.1	95.0	2.4	2.5	2.6	4.6
200	140 mM Lysine and 140 mM Niacin	97.7	97.7	96.8	95.0	2.3	2.3	2.9	4.6
200	70 mM Arginine·HCl and 140 mM Niacinamide	97.8	97.8	97.0	94.1	2.2	2.2	2.9	5.6
200	140 mM Histidine and 140 mM Niacinamide	97.6	97.6	96.5	94.0	2.4	2.4	3.3	5.5
200	140 mM Meglumine and 140 mM Niacinamide	97.4	97.3	96.8	93.9	2.6	2.7	2.9	5.5
200	70 mM Lysine·HCl and 140 mM Niacinamide	97.6	97.5	96.6	95.0	2.4	2.5	3.3	4.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	97.4	97.4	96.3	93.5	2.7	2.7	4.0	6.5
200	Water (Blank), pH 5.5	97.1	97.1	95.5	92.0	3.0	3.0	4.5	7.0
100	140 mM Arginine and 140 mM Niacin	98.2	98.1	97.2	96.2	1.8	1.9	2.6	3.5
100	140 mM Histidine and 140 mM Niacin	98.1	98.0	96.9	96.8	1.9	2.0	2.9	2.9
100	140 mM Meglumine and 140 mM Niacin	98.0	98.0	96.9	96.8	2.0	2.0	3.0	2.8
100	140 mM Lysine and 140 mM Niacin	98.3	98.3	97.2	95.2	1.7	1.7	2.7	4.0
100	70 mM Arginine·HCl and 140 mM Niacinamide	98.3	98.2	96.8	95.6	1.7	1.8	2.9	4.0
100	140 mM Histidine and 140 mM Niacinamide	98.0	97.9	97.0	95.7	2.0	2.1	2.9	3.6
100	140 mM Meglumine and 140 mM Niacinamide	98.1	98.0	97.3	96.0	1.9	2.0	2.5	3.2
100	70 mM Lysine·HCl and 140 mM Niacinamide	98.0	97.9	97.0	96.3	2.0	2.1	2.8	3.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	98.0	98.0	96.8	95.2	2.0	2.0	3.1	4.4
100	Water (Blank), pH 5.5	97.5	97.5	96.5	93.9	2.4	2.4	3.2	5.2

Table 136 SE-UPLC results of formulated Trastuzumab in 50 mM Citrate buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing Formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	96.9	96.8	94.7	90.7	3.1	3.2	5.2	8.4
300	300 mM Histidine and 300 mM Niacin	96.4	96.3	94.2	90.1	3.6	3.7	5.7	8.7
300	300 mM Meglumine and 300 mM Niacin	97.2	97.1	95.3	90.9	2.8	2.9	4.6	8.1
300	300 mM Lysine and 300 mM Niacin	96.6	96.5	94.4	90.2	3.4	3.5	5.4	8.5
300	140 mM Arginine·HCl and 300 mM Niacinamide	97.5	97.4	95.6	91.2	2.5	2.6	4.3	7.8
300	300 mM Histidine and 300 mM Niacinamide	97.1	97.0	95.1	90.6	2.9	3.0	4.7	8.3
300	300 mM Meglumine and 300 mM Niacinamide	96.3	96.2	94.6	90.0	3.7	3.8	5.3	8.9
300	140 mM Lysine·HCl and 300 mM Niacinamide	97.4	97.4	95.2	91.5	2.6	2.6	4.6	7.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.0	95.9	94.4	89.7	4.0	4.1	5.4	9.5
300	Water (Blank), pH 6.0	95.7	95.5	93.2	87.4	4.2	4.4	6.5	11.4
200	300 mM Arginine and 300 mM Niacin	98.2	98.2	97.1	95.0	1.8	1.8	2.8	4.4
200	300 mM Histidine and 300 mM Niacin	97.6	97.6	96.5	93.7	2.4	2.4	3.4	5.7
200	300 mM Meglumine and 300 mM Niacin	97.9	97.9	96.4	94.3	2.1	2.1	3.5	5.2
200	300 mM Lysine and 300 mM Niacin	97.3	97.3	96.7	93.9	2.7	2.7	3.2	5.6
200	140 mM Arginine·HCl and 300 mM Niacinamide	97.7	97.7	96.3	93.4	2.3	2.3	3.6	5.5
200	300 mM Histidine and 300 mM Niacinamide	97.0	97.0	96.2	94.1	3.0	3.0	3.7	5.2
200	300 mM Meglumine and 300 mM Niacinamide	97.8	97.8	96.8	94.5	2.2	2.2	3.1	5.0
200	140 mM Lysine·HCl and 300 mM Niacinamide	97.4	97.4	96.1	93.3	2.6	2.6	3.8	6.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.2	97.2	96.0	93.1	2.8	2.8	3.8	6.2
200	Water (Blank), pH 6.0	97.0	97.0	95.1	91.7	2.9	2.9	4.7	7.4
100	300 mM Arginine and 300 mM Niacin	98.3	98.3	97.5	96.0	1.7	1.7	2.4	3.5
100	300 mM Histidine and 300 mM Niacin	97.6	97.6	96.5	95.0	2.4	2.4	3.4	4.4
100	300 mM Meglumine and 300 mM Niacin	98.1	98.1	97.2	95.9	1.9	1.9	2.7	3.3
100	300 mM Lysine and 300 mM Niacin	98.6	98.6	97.7	96.2	1.4	1.4	2.2	3.3
100	140 mM Arginine·HCl and 300 mM Niacinamide	97.9	97.9	96.8	95.4	2.1	2.1	3.1	4.0
100	300 mM Histidine and 300 mM Niacinamide	98.4	98.4	97.1	95.7	1.6	1.6	2.8	3.6
100	300 mM Meglumine and 300 mM Niacinamide	98.2	98.2	97.3	96.4	1.8	1.8	2.6	3.0
100	140 mM Lysine·HCl and 300 mM Niacinamide	97.5	97.5	96.7	95.3	2.5	2.5	3.2	4.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.9	97.9	97.0	94.8	2.1	2.1	2.9	4.6
100	Water (Blank), pH 6.0	97.7	97.7	96.3	94.1	2.3	2.3	3.5	5.0

Table 137 SE-UPLC results of formulated Trastuzumab in 5 mM Phosphate buffer, pH 6.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	97.1	97.0	95.3	91.6	2.9	3.0	4.6	7.6
300	30 mM Histidine and 30 mM Niacin	97.2	97.2	96.0	90.7	2.8	2.8	3.9	8.6
300	30 mM Meglumine and 30 mM Niacin	97.2	97.2	96.1	92.8	2.8	2.8	3.6	6.3
300	30 mM Lysine and 30 mM Niacin	96.8	96.7	95.5	90.8	3.2	3.3	4.3	8.1
300	30 mM Arginine-HCl and 30 mM Niacinamide	96.8	96.8	95.7	90.7	3.2	3.2	4.1	8.7
300	30 mM Histidine and 30 mM Niacinamide	97.1	97.0	95.6	90.8	2.9	3.0	4.3	8.6
300	30 mM Meglumine and 30 mM Niacinamide	96.8	96.6	95.4	91.0	3.2	3.4	4.5	8.2
300	30 mM Lysine-HCl and 30 mM Niacinamide	97.0	97.0	96.0	90.9	3.0	3.0	3.9	8.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	96.7	96.5	94.9	90.5	3.6	3.7	5.3	8.8
300	Water (Blank), pH 6.5	95.8	95.7	93.9	88.5	4.0	4.2	6.1	10.0
200	30 mM Arginine and 30 mM Niacin	97.4	97.4	96.9	94.4	2.6	2.6	3.0	5.2
200	30 mM Histidine and 30 mM Niacin	97.6	97.6	96.4	93.9	2.4	2.4	3.5	5.8
200	30 mM Meglumine and 30 mM Niacin	97.3	97.3	96.7	95.2	2.7	2.7	3.1	4.5
200	30 mM Lysine and 30 mM Niacin	97.3	97.2	96.8	95.0	2.7	2.8	2.9	4.7
200	30 mM Arginine-HCl and 30 mM Niacinamide	97.5	97.4	96.7	94.0	2.5	2.6	3.0	5.6
200	30 mM Histidine and 30 mM Niacinamide	97.3	97.2	96.8	94.9	2.7	2.8	2.9	4.4
200	30 mM Meglumine and 30 mM Niacinamide	97.6	97.6	96.9	94.3	2.4	2.4	2.8	5.1
200	30 mM Lysine-HCl and 30 mM Niacinamide	97.5	97.5	96.7	94.3	2.5	2.5	3.2	4.9
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.2	97.2	96.1	93.8	2.8	2.8	4.2	6.8
200	Water (Blank), pH 6.5	96.9	96.9	95.3	91.0	3.2	3.2	4.4	6.7
100	30 mM Arginine and 30 mM Niacin	97.8	97.7	97.5	95.6	2.2	2.3	2.2	3.6
100	30 mM Histidine and 30 mM Niacin	98.1	98.1	97.3	94.9	1.9	1.9	2.6	4.3
100	30 mM Meglumine and 30 mM Niacin	98.1	98.1	97.2	94.7	1.9	1.9	2.6	4.9
100	30 mM Lysine and 30 mM Niacin	97.8	97.8	97.0	94.3	2.2	2.2	2.9	5.0
100	30 mM Arginine-HCl and 30 mM Niacinamide	97.9	97.8	97.0	95.2	2.1	2.2	2.7	3.9
100	30 mM Histidine and 30 mM Niacinamide	98.0	98.0	97.0	94.7	2.0	2.0	2.8	4.5
100	30 mM Meglumine and 30 mM Niacinamide	98.0	98.0	96.7	94.7	2.0	2.0	3.1	5.0
100	30 mM Lysine-HCl and 30 mM Niacinamide	98.1	98.1	97.2	94.1	1.9	1.9	2.5	5.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	97.8	97.8	96.7	94.0	2.3	2.3	3.4	5.6
100	Water (Blank), pH 6.5	97.4	97.4	96.4	93.1	2.6	2.6	3.0	5.1

Table 138 SE-UPLC results of formulated Trastuzumab in 20 mM Phosphate buffer, pH 7.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	95.6	95.5	94.2	89.6	4.4	4.5	5.6	9.7
300	140 mM Histidine and 140 mM Niacin	95.9	95.8	94.4	91.3	4.1	4.2	5.5	7.8
300	140 mM Meglumine and 140 mM Niacin	95.7	95.7	94.3	90.9	4.3	4.3	5.6	8.1
300	140 mM Lysine and 140 mM Niacin	95.6	95.6	94.8	90.5	4.4	4.4	5.0	8.7
300	70 mM Arginine·HCl and 140 mM Niacinamide	95.6	95.6	94.2	89.7	4.4	4.4	5.6	9.4
300	140 mM Histidine and 140 mM Niacinamide	96.0	96.0	95.3	89.8	4.0	4.0	4.6	9.5
300	140 mM Meglumine and 140 mM Niacinamide	96.1	96.1	94.7	89.8	3.9	3.9	5.2	9.4
300	70 mM Lysine·HCl and 140 mM Niacinamide	95.6	95.5	94.7	90.9	4.4	4.5	5.1	8.2
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	95.6	95.5	93.9	89.0	4.4	4.5	5.9	10.0
300	Water (Blank), pH 7.0	95.2	95.0	92.8	86.5	4.7	4.9	7.0	12.3
200	140 mM Arginine and 140 mM Niacin	97.2	97.1	96.2	93.1	2.8	2.9	3.7	6.3
200	140 mM Histidine and 140 mM Niacin	97.3	97.2	96.7	93.4	2.7	2.8	3.0	6.1
200	140 mM Meglumine and 140 mM Niacin	97.3	97.3	96.4	93.9	2.7	2.7	3.3	5.4
200	140 mM Lysine and 140 mM Niacin	97.1	97.1	96.0	93.1	2.9	2.9	3.8	6.3
200	70 mM Arginine·HCl and 140 mM Niacinamide	96.9	96.8	95.9	93.7	3.1	3.2	4.0	5.8
200	140 mM Histidine and 140 mM Niacinamide	97.1	97.1	96.1	92.8	2.9	2.9	3.6	6.5
200	140 mM Meglumine and 140 mM Niacinamide	96.9	96.9	96.2	92.8	3.1	3.1	3.7	6.5
200	70 mM Lysine·HCl and 140 mM Niacinamide	97.1	97.0	96.5	93.7	2.9	3.0	3.3	5.7
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	96.8	96.8	95.5	92.2	3.2	3.2	4.3	7.1
200	Water (blank), pH 7.0	96.5	96.4	94.7	90.5	3.5	3.6	5.0	8.5
100	140 mM Arginine and 140 mM Niacin	97.2	97.1	96.8	94.6	2.8	2.9	3.1	5.1
100	140 mM Histidine and 140 mM Niacin	97.5	97.5	96.9	94.9	2.5	2.5	2.8	4.7
100	140 mM Meglumine and 140 mM Niacin	97.2	97.1	96.8	95.0	2.8	2.9	3.1	4.7
100	140 mM Lysine and 140 mM Niacin	97.2	97.1	96.8	95.1	2.8	2.9	3.0	4.5
100	70 mM Arginine·HCl and 140 mM Niacinamide	97.5	97.4	96.9	94.9	2.5	2.6	3.0	4.7
100	140 mM Histidine and 140 mM Niacinamide	97.4	97.4	96.9	95.3	2.6	2.6	3.0	4.2
100	140 mM Meglumine and 140 mM Niacinamide	97.5	97.5	96.9	95.0	2.5	2.5	3.0	4.5
100	70 mM Lysine·HCl and 140 mM Niacinamide	97.2	97.1	96.8	94.5	2.8	2.9	2.9	5.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	97.2	97.2	96.5	94.2	2.8	2.8	3.4	5.2
100	Water (blank), pH 7.0	97.0	97.0	96.0	93.0	3.0	3.0	3.9	6.1

Table 139 SE-UPLC results of formulated Trastuzumab in 50 mM Phosphate buffer, pH 7.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing Formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	95.8	95.7	94.1	89.6	4.2	4.3	5.6	9.7
300	300 mM Histidine and 300 mM Niacin	95.8	95.7	94.6	88.5	4.2	4.3	5.2	10.9
300	300 mM Meglumine and 300 mM Niacin	95.6	95.5	94.2	88.4	4.4	4.5	5.5	10.9
300	300 mM Lysine and 300 mM Niacin	95.3	95.2	93.5	87.8	4.7	4.8	6.2	11.4
300	140 mM Arginine·HCl and 300 mM Niacinamide	95.6	95.4	93.8	88.5	4.4	4.6	6.0	10.8
300	300 mM Histidine and 300 mM Niacinamide	95.8	95.6	94.6	89.3	4.2	4.4	5.1	9.9
300	300 mM Meglumine and 300 mM Niacinamide	95.5	95.3	94.3	88.1	4.5	4.7	5.4	11.2
300	140 mM Lysine·HCl and 300 mM Niacinamide	95.7	95.5	94.2	89.8	4.3	4.5	5.6	9.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	95.3	95.1	93.3	87.5	4.7	4.9	6.5	11.6
300	Water (Blank), pH 7.5	94.9	94.6	92.1	85.0	5.1	5.4	7.5	13.9
200	300 mM Arginine and 300 mM Niacin	96.7	96.6	96.0	92.1	3.3	3.4	3.9	7.3
200	300 mM Histidine and 300 mM Niacin	96.6	96.5	95.8	92.1	3.4	3.5	4.0	7.3
200	300 mM Meglumine and 300 mM Niacin	96.7	96.6	95.6	92.9	3.3	3.4	4.1	6.3
200	300 mM Lysine and 300 mM Niacin	96.4	96.3	95.3	91.8	3.6	3.7	4.6	7.6
200	140 mM Arginine·HCl and 300 mM Niacinamide	96.5	96.5	95.7	92.2	3.5	3.5	4.0	7.1
200	300 mM Histidine and 300 mM Niacinamide	96.7	96.6	95.9	92.3	3.3	3.4	3.9	7.1
200	300 mM Meglumine and 300 mM Niacinamide	96.7	96.7	95.6	91.8	3.3	3.3	4.2	7.6
200	140 mM Lysine·HCl and 300 mM Niacinamide	96.7	96.7	95.7	91.8	3.3	3.3	4.2	7.4
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	96.4	96.3	95.0	91.2	3.6	3.7	4.8	8.0
200	Water (Blank), pH 7.5	96.1	95.9	94.0	90.0	3.9	4.1	5.6	8.9
100	300 mM Arginine and 300 mM Niacin	97.2	97.1	96.9	94.2	2.8	2.9	2.9	5.1
100	300 mM Histidine and 300 mM Niacin	97.1	97.0	96.7	94.2	2.9	3.0	3.0	5.1
100	300 mM Meglumine and 300 mM Niacin	96.9	96.8	96.5	93.9	3.1	3.2	3.3	5.5
100	300 mM Lysine and 300 mM Niacin	97.2	97.1	96.9	94.4	2.8	2.9	2.8	5.0
100	140 mM Arginine·HCl and 300 mM Niacinamide	97.0	96.9	96.6	93.6	3.0	3.1	3.1	5.7
100	300 mM Histidine and 300 mM Niacinamide	97.2	97.2	96.8	93.9	2.8	2.8	3.0	5.4
100	300 mM Meglumine and 300 mM Niacinamide	97.2	97.1	96.9	94.1	2.8	2.9	2.9	5.2
100	140 mM Lysine·HCl and 300 mM Niacinamide	97.0	96.9	96.5	93.5	3.0	3.1	3.3	5.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	96.9	96.8	96.0	93.1	3.1	3.2	3.8	6.2
100	Water (Blank), pH 7.5	96.7	96.5	95.3	92.0	3.3	3.5	4.4	7.1

Table 140 SE-UPLC results of formulated Trastuzumab in 5 mM Tris buffer, pH 6.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	97.2	97.1	95.3	92.6	2.8	2.9	4.5	6.4
300	30 mM Histidine and 30 mM Niacin	96.9	96.9	95.4	92.0	3.1	3.1	4.3	7.3
300	30 mM Meglumine and 30 mM Niacin	96.9	96.8	95.5	91.9	3.1	3.2	4.2	7.0
300	30 mM Lysine and 30 mM Niacin	96.8	96.7	95.9	92.5	3.2	3.3	3.9	6.8
300	30 mM Arginine·HCl and 30 mM Niacinamide	96.9	96.9	95.6	91.1	3.1	3.1	4.2	7.8
300	30 mM Histidine and 30 mM Niacinamide	97.2	97.0	95.9	92.8	2.8	3.0	3.9	6.6
300	30 mM Meglumine and 30 mM Niacinamide	97.0	96.9	95.8	90.5	3.0	3.1	3.9	8.7
300	30 mM Lysine·HCl and 30 mM Niacinamide	97.0	96.8	95.6	90.5	3.0	3.2	4.3	8.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	96.7	96.5	94.9	90.5	3.6	3.7	5.3	8.8
300	Water (Blank), pH 6.5	95.8	95.7	93.9	88.5	4.0	4.2	6.1	10.0
200	30 mM Arginine and 30 mM Niacin	97.3	97.3	96.6	94.5	2.7	2.7	3.1	4.7
200	30 mM Histidine and 30 mM Niacin	97.5	97.4	96.6	93.8	2.5	2.6	3.3	5.6
200	30 mM Meglumine and 30 mM Niacin	97.3	97.3	96.7	94.9	2.7	2.7	3.2	4.4
200	30 mM Lysine and 30 mM Niacin	97.3	97.3	96.4	93.8	2.7	2.7	3.4	5.7
200	30 mM Arginine·HCl and 30 mM Niacinamide	97.5	97.4	96.9	94.9	2.5	2.6	2.9	4.3
200	30 mM Histidine and 30 mM Niacinamide	97.7	97.7	96.4	94.7	2.3	2.3	3.5	5.0
200	30 mM Meglumine and 30 mM Niacinamide	97.5	97.5	96.5	95.1	2.5	2.5	3.3	4.0
200	30 mM Lysine·HCl and 30 mM Niacinamide	97.2	97.1	96.9	94.1	2.8	2.9	2.9	5.5
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	97.2	97.2	96.1	93.8	2.8	2.8	4.2	6.8
200	Water (Blank), pH 6.5	96.9	96.9	95.3	91.0	3.2	3.2	4.4	6.7
100	30 mM Arginine and 30 mM Niacin	98.1	98.0	96.9	95.5	1.9	2.0	2.9	4.0
100	30 mM Histidine and 30 mM Niacin	98.1	98.1	96.9	94.5	1.9	1.9	2.8	5.2
100	30 mM Meglumine and 30 mM Niacin	98.1	98.1	97.3	95.0	1.9	1.9	2.6	4.4
100	30 mM Lysine and 30 mM Niacin	98.0	97.9	96.9	94.5	2.0	2.1	2.9	4.7
100	30 mM Arginine·HCl and 30 mM Niacinamide	98.1	98.0	97.0	94.7	1.9	2.0	2.8	4.6
100	30 mM Histidine and 30 mM Niacinamide	98.0	98.0	97.5	94.5	2.0	2.0	2.4	4.7
100	30 mM Meglumine and 30 mM Niacinamide	98.1	98.0	97.0	94.9	1.9	2.0	2.9	4.4
100	30 mM Lysine·HCl and 30 mM Niacinamide	97.8	97.8	97.0	94.6	2.2	2.2	2.9	5.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	97.8	97.8	96.7	94.0	2.3	2.3	3.4	5.6
100	Water (Blank), pH 6.5	97.4	97.4	96.4	93.1	2.6	2.6	3.0	5.1

Table 141 SE-UPLC results of formulated Trastuzumab in 20 mM Tris buffer, pH 7.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	96.0	95.9	94.7	90.3	4.0	4.1	5.2	8.7
300	140 mM Histidine and 140 mM Niacin	95.7	95.7	94.5	89.4	4.3	4.3	5.3	9.6
300	140 mM Meglumine and 140 mM Niacin	95.6	95.6	94.7	90.5	4.4	4.4	5.1	8.6
300	140 mM Lysine and 140 mM Niacin	95.7	95.6	94.5	90.1	4.3	4.4	5.4	8.9
300	70 mM Arginine·HCl and 140 mM Niacinamide	96.1	95.9	94.7	90.4	3.9	4.1	5.2	8.9
300	140 mM Histidine and 140 mM Niacinamide	95.9	95.7	94.6	89.9	4.1	4.3	5.3	9.2
300	140 mM Meglumine and 140 mM Niacinamide	96.1	95.9	94.6	89.9	3.9	4.1	5.3	9.3
300	70 mM Lysine·HCl and 140 mM Niacinamide	95.6	95.4	94.9	90.7	4.4	4.6	5.0	8.4
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	95.6	95.5	93.9	89.0	4.4	4.5	5.9	10.0
300	Water (Blank), pH 7.0	95.2	95.0	92.8	86.5	4.7	4.9	7.0	12.3
200	140 mM Arginine and 140 mM Niacin	97.0	97.0	96.4	93.6	3.0	3.0	3.3	5.7
200	140 mM Histidine and 140 mM Niacin	97.0	97.0	96.0	93.3	3.0	3.0	3.7	6.2
200	140 mM Meglumine and 140 mM Niacin	97.3	97.3	96.2	93.4	2.7	2.7	3.7	6.1
200	140 mM Lysine and 140 mM Niacin	97.1	97.0	96.2	93.1	2.9	3.0	3.5	6.4
200	70 mM Arginine·HCl and 140 mM Niacinamide	97.3	97.2	96.3	93.4	2.7	2.8	3.6	6.1
200	140 mM Histidine and 140 mM Niacinamide	97.3	97.3	96.2	93.2	2.7	2.7	3.6	6.3
200	140 mM Meglumine and 140 mM Niacinamide	97.0	97.0	96.4	93.4	3.0	3.0	3.4	6.0
200	70 mM Lysine·HCl and 140 mM Niacinamide	96.8	96.7	95.8	93.4	3.2	3.3	3.9	6.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	96.8	96.8	95.5	92.2	3.2	3.2	4.3	7.1
200	Water (blank), pH 7.0	96.5	96.4	94.7	90.5	3.5	3.6	5.0	8.5
100	140 mM Arginine and 140 mM Niacin	97.5	97.4	97.0	94.8	2.5	2.6	2.7	4.7
100	140 mM Histidine and 140 mM Niacin	97.5	97.5	96.9	95.1	2.5	2.5	2.9	4.6
100	140 mM Meglumine and 140 mM Niacin	97.2	97.2	96.6	94.5	2.8	2.8	3.2	5.1
100	140 mM Lysine and 140 mM Niacin	97.3	97.3	96.7	94.7	2.7	2.7	3.1	4.9
100	70 mM Arginine·HCl and 140 mM Niacinamide	97.4	97.4	96.9	94.7	2.6	2.6	2.9	4.8
100	140 mM Histidine and 140 mM Niacinamide	97.3	97.3	96.8	94.8	2.7	2.7	3.1	4.9
100	140 mM Meglumine and 140 mM Niacinamide	97.4	97.3	97.0	95.4	2.6	2.7	2.7	4.3
100	70 mM Lysine·HCl and 140 mM Niacinamide	97.5	97.5	97.0	94.9	2.5	2.5	2.7	4.7
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	97.2	97.2	96.5	94.2	2.8	2.8	3.4	5.2
100	Water (blank), pH 7.0	97.0	97.0	96.0	93.0	3.0	3.0	3.9	6.1

Table 142 SE-UPLC results of formulated Trastuzumab in 50 mM Tris buffer, pH 7.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25° C	40° C	T0	5°C	25° C	40° C
300	300 mM Arginine and 300 mM Niacin	95.5	95.3	93.7	89.6	4.5	4.7	6.1	9.6
300	300 mM Histidine and 300 mM Niacin	95.7	95.5	94.4	88.5	4.3	4.5	5.4	10.9
300	300 mM Meglumine and 300 mM Niacin	95.8	95.7	94.1	89.0	4.2	4.3	5.6	10.4
300	300 mM Lysine and 300 mM Niacin	95.5	95.3	94.2	89.3	4.5	4.7	5.6	9.9
300	140 mM Arginine·HCl and 300 mM Niacinamide	95.4	95.3	93.7	89.2	4.6	4.7	6.1	10.2
300	300 mM Histidine and 300 mM Niacinamide	95.5	95.3	94.1	89.3	4.5	4.7	5.7	10.1
300	300 mM Meglumine and 300 mM Niacinamide	95.4	95.2	94.1	88.6	4.6	4.8	5.6	10.8
300	140 mM Lysine·HCl and 300 mM Niacinamide	95.8	95.6	94.2	89.4	4.2	4.4	5.6	9.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	95.3	95.1	93.3	87.5	4.7	4.9	6.5	11.6
300	Water (Blank), pH 7.5	94.9	94.6	92.1	85.0	5.1	5.4	7.5	13.9
200	300 mM Arginine and 300 mM Niacin	96.5	96.5	95.6	92.7	3.5	3.5	4.3	6.5
200	300 mM Histidine and 300 mM Niacin	96.8	96.8	96.1	92.1	3.2	3.2	3.6	7.2
200	300 mM Meglumine and 300 mM Niacin	96.5	96.4	95.7	92.3	3.5	3.6	4.1	7.0
200	300 mM Lysine and 300 mM Niacin	96.8	96.8	96.0	92.5	3.2	3.2	3.7	6.9
200	140 mM Arginine·HCl and 300 mM Niacinamide	96.6	96.5	95.5	91.8	3.4	3.5	4.2	7.6
200	300 mM Histidine and 300 mM Niacinamide	96.7	96.6	95.9	92.5	3.3	3.4	3.9	6.9
200	300 mM Meglumine and 300 mM Niacinamide	96.8	96.7	95.7	92.3	3.2	3.3	4.0	6.9
200	140 mM Lysine·HCl and 300 mM Niacinamide	96.7	96.7	95.6	92.6	3.3	3.3	4.2	6.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	96.4	96.3	95.0	91.2	3.6	3.7	4.8	8.0
200	Water (Blank), pH 7.5	96.1	95.9	94.0	90.0	3.9	4.1	5.6	8.9
100	300 mM Arginine and 300 mM Niacin	97.1	97.1	96.8	93.9	2.9	2.9	3.0	5.4
100	300 mM Histidine and 300 mM Niacin	96.9	96.9	96.4	94.0	3.1	3.1	3.3	5.3
100	300 mM Meglumine and 300 mM Niacin	97.0	97.0	96.6	94.0	3.0	3.0	3.2	5.4
100	300 mM Lysine and 300 mM Niacin	97.1	97.0	96.8	94.1	2.9	3.0	2.9	5.3
100	140 mM Arginine·HCl and 300 mM Niacinamide	96.9	96.8	96.4	93.9	3.1	3.2	3.3	5.4
100	300 mM Histidine and 300 mM Niacinamide	97.2	97.2	96.7	93.8	2.8	2.8	3.2	5.6
100	300 mM Meglumine and 300 mM Niacinamide	97.2	97.2	96.9	93.7	2.8	2.8	2.8	5.8
100	140 mM Lysine·HCl and 300 mM Niacinamide	97.2	97.2	96.9	94.1	2.8	2.8	2.9	5.3
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	96.9	96.8	96.0	93.1	3.1	3.2	3.8	6.2
100	Water (Blank), pH 7.5	96.7	96.5	95.3	92.0	3.3	3.5	4.4	7.1

Table 143 SE-UPLC results of formulated Trastuzumab in 5 mM Succinate buffer, pH 4.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	95.5	95.4	94.1	89.5	4.5	4.6	5.7	9.8
300	30 mM Histidine and 30 mM Niacin	95.9	95.8	94.4	89.2	4.1	4.2	5.4	10.0
300	30 mM Meglumine and 30 mM Niacin	95.9	95.7	94.7	88.6	4.1	4.3	5.1	10.7
300	30 mM Lysine and 30 mM Niacin	95.4	95.2	94.1	88.8	4.6	4.8	5.6	10.4
300	30 mM Arginine-HCl and 30 mM Niacinamide	95.5	95.3	93.9	88.4	4.5	4.7	5.9	10.9
300	30 mM Histidine and 30 mM Niacinamide	95.6	95.4	93.9	88.9	4.4	4.6	5.9	10.3
300	30 mM Meglumine and 30 mM Niacinamide	95.6	95.4	94.0	88.6	4.4	4.6	5.7	10.6
300	30 mM Lysine-HCl and 30 mM Niacinamide	95.7	95.5	93.9	90.0	4.3	4.5	5.8	9.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	95.4	95.2	93.4	87.8	4.6	4.8	6.3	11.2
300	Water (Blank), pH 4.5	95.0	94.7	92.7	85.3	5.0	5.3	6.9	13.4
200	30 mM Arginine and 30 mM Niacin	96.6	96.5	95.6	91.9	3.4	3.5	4.2	7.4
200	30 mM Histidine and 30 mM Niacin	96.7	96.7	96.0	92.4	3.3	3.3	3.7	6.9
200	30 mM Meglumine and 30 mM Niacin	96.5	96.4	95.8	92.8	3.5	3.6	4.0	6.4
200	30 mM Lysine and 30 mM Niacin	96.7	96.7	95.7	92.4	3.3	3.3	4.2	6.8
200	30 mM Arginine-HCl and 30 mM Niacinamide	96.7	96.6	95.7	92.4	3.3	3.4	4.2	6.8
200	30 mM Histidine and 30 mM Niacinamide	96.9	96.8	95.8	93.1	3.1	3.2	3.9	6.2
200	30 mM Meglumine and 30 mM Niacinamide	96.8	96.8	95.9	92.6	3.2	3.2	3.8	6.5
200	30 mM Lysine-HCl and 30 mM Niacinamide	96.8	96.8	96.1	92.7	3.2	3.2	3.8	6.6
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	96.5	96.4	95.1	91.4	3.5	3.6	4.7	7.7
200	Water (Blank), pH 4.5	96.2	96.0	94.2	90.2	3.8	4.0	5.4	8.8
100	30 mM Arginine and 30 mM Niacin	97.0	96.9	96.6	94.0	3.0	3.1	3.1	5.3
100	30 mM Histidine and 30 mM Niacin	97.3	97.2	97.0	94.4	2.7	2.8	2.9	4.8
100	30 mM Meglumine and 30 mM Niacin	97.3	97.2	96.9	94.0	2.7	2.8	2.9	5.2
100	30 mM Lysine and 30 mM Niacin	97.3	97.3	96.9	94.2	2.7	2.7	2.9	5.1
100	30 mM Arginine-HCl and 30 mM Niacinamide	97.2	97.2	96.9	93.9	2.8	2.8	3.0	5.4
100	30 mM Histidine and 30 mM Niacinamide	97.1	97.0	96.8	93.7	2.9	3.0	3.1	5.5
100	30 mM Meglumine and 30 mM Niacinamide	97.0	97.0	96.5	93.8	3.0	3.0	3.3	5.6
100	30 mM Lysine-HCl and 30 mM Niacinamide	97.3	97.3	97.0	94.3	2.7	2.7	2.8	5.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	97.0	96.9	96.1	93.3	3.0	3.1	3.7	5.9
100	Water (Blank), pH 4.5	96.8	96.6	95.4	92.1	3.2	3.4	4.3	7.0

Table 144 SE-UPLC results of formulated Trastuzumab in 20 mM Succinate buffer, pH 5.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	96.7	96.7	95.9	90.4	3.3	3.3	3.9	8.9
300	140 mM Histidine and 140 mM Niacin	96.3	96.1	95.5	92.5	3.7	3.9	4.3	6.8
300	140 mM Meglumine and 140 mM Niacin	96.6	96.6	95.1	91.6	3.4	3.4	4.8	7.4
300	140 mM Lysine and 140 mM Niacin	96.3	96.3	95.9	91.4	3.7	3.7	3.9	7.9
300	70 mM Arginine·HCl and 140 mM Niacinamide	96.6	96.6	95.8	92.4	3.4	3.4	4.0	7.1
300	140 mM Histidine and 140 mM Niacinamide	96.4	96.3	95.2	91.7	3.6	3.7	4.5	7.8
300	140 mM Meglumine and 140 mM Niacinamide	96.7	96.6	95.4	91.1	3.3	3.4	4.5	8.4
300	70 mM Lysine·HCl and 140 mM Niacinamide	96.3	96.1	95.4	92.2	3.7	3.9	4.5	6.9
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	96.3	96.1	94.8	90.2	3.8	3.9	5.2	9.0
300	Water (Blank), pH 5.5	95.5	95.4	93.5	88.1	4.1	4.3	6.0	10.2
200	140 mM Arginine and 140 mM Niacin	97.7	97.7	97.1	94.2	2.3	2.3	2.7	5.3
200	140 mM Histidine and 140 mM Niacin	97.8	97.8	97.0	94.5	2.2	2.2	2.9	4.8
200	140 mM Meglumine and 140 mM Niacin	97.5	97.5	96.5	93.6	2.5	2.5	3.4	6.1
200	140 mM Lysine and 140 mM Niacin	97.5	97.4	96.6	94.9	2.5	2.6	3.2	4.6
200	70 mM Arginine·HCl and 140 mM Niacinamide	97.6	97.6	96.7	93.8	2.4	2.4	3.2	5.6
200	140 mM Histidine and 140 mM Niacinamide	97.8	97.7	96.7	93.9	2.2	2.3	3.2	5.4
200	140 mM Meglumine and 140 mM Niacinamide	97.9	97.9	96.8	93.9	2.1	2.1	3.0	5.6
200	70 mM Lysine·HCl and 140 mM Niacinamide	97.5	97.5	96.6	93.8	2.5	2.5	3.3	5.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	97.4	97.4	96.3	93.5	2.7	2.7	4.0	6.5
200	Water (Blank), pH 5.5	97.1	97.1	95.5	92.0	3.0	3.0	4.5	7.0
100	140 mM Arginine and 140 mM Niacin	98.1	98.1	97.5	95.7	1.9	1.9	2.3	3.9
100	140 mM Histidine and 140 mM Niacin	98.2	98.2	97.4	96.1	1.8	1.8	2.4	3.2
100	140 mM Meglumine and 140 mM Niacin	98.2	98.2	97.1	96.6	1.8	1.8	2.8	3.1
100	140 mM Lysine and 140 mM Niacin	98.3	98.2	97.5	95.7	1.7	1.8	2.2	3.9
100	70 mM Arginine·HCl and 140 mM Niacinamide	98.3	98.2	97.6	96.5	1.7	1.8	2.2	2.8
100	140 mM Histidine and 140 mM Niacinamide	98.3	98.2	97.5	96.1	1.7	1.8	2.4	3.0
100	140 mM Meglumine and 140 mM Niacinamide	98.2	98.1	97.3	96.3	1.8	1.9	2.5	3.1
100	70 mM Lysine·HCl and 140 mM Niacinamide	98.3	98.2	97.2	96.3	1.7	1.8	2.7	3.3
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	98.0	98.0	96.8	95.2	2.0	2.0	3.1	4.4
100	Water (Blank), pH 5.5	97.5	97.5	96.5	93.9	2.4	2.4	3.2	5.2

Table 145 SE-UPLC results of formulated Trastuzumab in 50 mM Succinate buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing Formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	96.0	95.9	95.1	91.4	4.0	4.1	4.7	8.1
300	300 mM Histidine and 300 mM Niacin	96.2	96.2	94.9	91.5	3.8	3.8	5.0	7.7
300	300 mM Meglumine and 300 mM Niacin	96.0	95.8	95.2	91.8	4.0	4.2	4.5	7.4
300	300 mM Lysine and 300 mM Niacin	96.3	96.1	95.4	90.2	3.7	3.9	4.4	8.9
300	140 mM Arginine·HCl and 300 mM Niacinamide	96.0	96.0	95.3	90.6	4.0	4.0	4.4	8.4
300	300 mM Histidine and 300 mM Niacinamide	96.5	96.4	95.6	90.8	3.5	3.6	4.3	8.3
300	300 mM Meglumine and 300 mM Niacinamide	96.3	96.2	95.4	90.7	3.7	3.8	4.3	8.2
300	140 mM Lysine·HCl and 300 mM Niacinamide	96.3	96.1	95.2	92.0	3.7	3.9	4.6	6.9
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.0	95.9	94.4	89.7	4.0	4.1	5.4	9.5
300	Water (Blank), pH 6.0	95.7	95.5	93.2	87.4	4.2	4.4	6.5	11.4
200	300 mM Arginine and 300 mM Niacin	97.7	97.6	96.6	93.7	2.3	2.4	3.2	5.5
200	300 mM Histidine and 300 mM Niacin	97.6	97.6	96.2	94.4	2.4	2.4	3.6	5.3
200	300 mM Meglumine and 300 mM Niacin	97.2	97.2	96.2	93.7	2.8	2.8	3.5	5.6
200	300 mM Lysine and 300 mM Niacin	97.5	97.4	96.6	93.9	2.5	2.6	3.1	5.2
200	140 mM Arginine·HCl and 300 mM Niacinamide	97.5	97.4	96.2	94.1	2.5	2.6	3.5	5.1
200	300 mM Histidine and 300 mM Niacinamide	97.4	97.4	96.8	93.2	2.6	2.6	3.0	6.0
200	300 mM Meglumine and 300 mM Niacinamide	97.5	97.4	96.5	94.6	2.5	2.6	3.4	4.5
200	140 mM Lysine·HCl and 300 mM Niacinamide	97.4	97.3	96.7	93.1	2.6	2.7	3.1	6.4
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.2	97.2	96.0	93.1	2.8	2.8	3.8	6.2
200	Water (Blank), pH 6.0	97.0	97.0	95.1	91.7	2.9	2.9	4.7	7.4
100	300 mM Arginine and 300 mM Niacin	98.1	98.0	97.4	95.5	1.9	2.0	2.5	4.2
100	300 mM Histidine and 300 mM Niacin	98.2	98.1	97.1	95.8	1.8	1.9	2.7	3.6
100	300 mM Meglumine and 300 mM Niacin	98.0	98.0	97.7	95.9	2.0	2.0	2.2	3.4
100	300 mM Lysine and 300 mM Niacin	98.1	98.1	97.3	96.0	1.9	1.9	2.5	3.7
100	140 mM Arginine·HCl and 300 mM Niacinamide	98.1	98.1	97.2	96.1	1.9	1.9	2.6	3.0
100	300 mM Histidine and 300 mM Niacinamide	98.0	98.0	97.1	94.8	2.0	2.0	2.6	4.6
100	300 mM Meglumine and 300 mM Niacinamide	98.0	97.9	97.4	95.4	2.0	2.1	2.3	4.1
100	140 mM Lysine·HCl and 300 mM Niacinamide	98.0	98.0	97.6	94.8	2.0	2.0	2.3	4.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.9	97.9	97.0	94.8	2.1	2.1	2.9	4.6
100	Water (Blank), pH 6.0	97.7	97.7	96.3	94.1	2.3	2.3	3.5	5.0

Example 10: Effect of viscosity-reducing and stabilizing formulations on ADC (Trastuzumab-MMAE, DAR8 Cysteine) stability at various temperatures.

[00109] This example tested the effect of viscosity-reducing and stabilizing formulations on Trastuzumab-MMAE stability and compared it with the lead formulation (25 mM Phosphate, 81.2 mM of Nicotinic acid and 29.4 mM Tryptophan) in WO2018211517.

[00110] Materials and Methods

[00111] The Trastuzumab-MMAE samples were produced by WuXi Biologics, as described in Example 4, and formulated as shown in Tables 146-163. The prepared samples were aseptically filtered with 0.22 μm PVDF membrane filters before filling. After filtration, samples were filled with a pipette to 2 mL vials, and the fill volume was 1.0 mL. Then the vials were stoppered and sealed and subjected to 5°C, 25°C and 40°C chambers to start the stability assessment. Furthermore, there was a control group comprising 25 mM phosphate buffer at pH 6.0, with 81.2 mM Nicotinic acid and 29.4 mM Tryptophan (matching the lead formulation 25 mM phosphate buffer at pH 6.0 along with 10 mg/mL Nicotinic acid (acid form) and 6 mg/mL Tryptophan from Examples 14 and 16-21 in WO2018211517). After preparing the control group samples, the pH was adjusted to the target value using hydrochloric acid and sodium hydroxide. An additional control group, consisting solely of MilliQ water and the Trastuzumab-MMAE, was prepared as a blank. The pH of the blank group was also adjusted to match the target pH using the same method. To ascertain Trastuzumab-MMAE's concentration in the groups, absorbance at 280 nm combined with SE-UPLC was gauged against corresponding buffers containing a viscosity-reducing and stabilizing agent for excipient-containing samples, and absorbance at 280 nm was measured for the Trastuzumab-MMAE solution without a viscosity-reducing and stabilizing formulation. For Trastuzumab-MMAE without excipients, the buffer alone (i.e., devoid of excipients) served as a blank for protein concentration calculation. The extinction coefficient was measured at 1.48 (mg/mL)⁻¹·cm⁻¹.

[00112] The test for protein stability was carried out over a 4-week period by SE-UPLC. Samples were prepared as described above. As shown in Tables 146-163, after 4 weeks, the monomer content of Trastuzumab-MMAE at a concentration from 100 to 300 mg/mL formulated with the tested viscosity-reducing and stabilizing formulations was higher than or close to 90% even at 40°C, comparable or better than the lead formulation in WO2018211517, regardless of the

used buffers, indicating good stabilization effect of the tested viscosity-reducing and stabilizing formulations.

Table 146 SE-UPLC results of formulated Trastuzumab-MMAE in 5 mM Histidine buffer, pH 5.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid, 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	96.9	96.9	95.8	91.6	3.1	3.1	4.0	7.7
300	30 mM Histidine and 30 mM Niacin	96.6	96.6	95.3	90.8	3.4	3.4	4.5	8.5
300	30 mM Meglumine and 30 mM Niacin	96.7	96.7	96.0	92.2	3.3	3.3	3.9	7.1
300	30 mM Lysine and 30 mM Niacin	96.9	96.8	96.0	91.7	3.1	3.2	3.9	7.4
300	30 mM Arginine-HCl and 30 mM Niacinamide	96.6	96.5	95.7	91.9	3.4	3.5	4.2	7.4
300	30 mM Histidine and 30 mM Niacinamide	97.0	96.9	95.7	91.1	3.0	3.1	4.2	7.9
300	30 mM Meglumine and 30 mM Niacinamide	97.1	97.0	96.3	92.3	2.9	3.0	3.6	6.8
300	30 mM Lysine-HCl and 30 mM Niacinamide	97.1	96.9	95.8	91.3	2.9	3.1	4.0	7.7
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	96.1	96.0	94.3	88.6	3.9	4.0	5.5	10.5
300	Water (Blank), pH 5.0	95.8	95.6	93.8	86.3	4.1	4.3	6.0	12.9
200	30 mM Arginine and 30 mM Niacin	97.1	97.1	96.6	93.2	2.9	2.9	3.1	6.2
200	30 mM Histidine and 30 mM Niacin	97.1	97.1	96.4	93.6	2.9	2.9	3.5	5.9
200	30 mM Meglumine and 30 mM Niacin	97.2	97.1	96.7	93.4	2.8	2.9	3.1	6.1
200	30 mM Lysine and 30 mM Niacin	97.0	96.9	96.1	93.6	3.0	3.1	3.7	5.8
200	30 mM Arginine-HCl and 30 mM Niacinamide	96.9	96.8	95.9	92.2	3.1	3.2	3.8	7.1
200	30 mM Histidine and 30 mM Niacinamide	96.9	96.9	96.0	93.0	3.1	3.1	3.9	6.5
200	30 mM Meglumine and 30 mM Niacinamide	97.2	97.2	96.6	93.5	2.8	2.8	3.3	5.9
200	30 mM Lysine-HCl and 30 mM Niacinamide	97.1	97.1	96.4	93.2	2.9	2.9	3.3	6.2
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	96.5	96.5	95.0	91.7	3.4	3.4	4.8	7.4
200	Water (blank), pH 5.0	96.2	96.2	94.5	90.3	3.7	3.7	5.3	8.8
100	30 mM Arginine and 30 mM Niacin	97.8	97.8	97.3	95.8	2.2	2.2	2.6	3.9
100	30 mM Histidine and 30 mM Niacin	97.7	97.6	97.2	95.0	2.3	2.4	2.5	4.5
100	30 mM Meglumine and 30 mM Niacin	98.0	97.9	97.5	95.5	2.0	2.1	2.4	4.2
100	30 mM Lysine and 30 mM Niacin	97.7	97.7	97.3	95.6	2.3	2.3	2.6	4.0
100	30 mM Arginine-HCl and 30 mM Niacinamide	97.9	97.9	97.4	95.5	2.1	2.1	2.3	4.1
100	30 mM Histidine and 30 mM Niacinamide	97.7	97.7	97.3	95.2	2.3	2.3	2.5	4.4
100	30 mM Meglumine and 30 mM Niacinamide	98.0	97.9	97.6	95.6	2.0	2.1	2.3	4.1
100	30 mM Lysine-HCl and 30 mM Niacinamide	97.7	97.6	97.3	95.4	2.3	2.4	2.5	4.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	97.4	97.3	96.2	93.6	2.5	2.6	3.7	5.7
100	Water (blank), pH 5.0	96.8	96.7	95.4	92.8	2.1	2.2	4.4	6.4

Table 147 SE-UPLC results of formulated Trastuzumab-MMAE in 20 mM Histidine buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid, 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	97.2	97.2	95.8	92.3	2.8	2.8	4.1	6.7
300	140 mM Histidine and 140 mM Niacin	96.9	96.9	95.7	92.7	3.1	3.1	4.1	6.6
300	140 mM Meglumine and 140 mM Niacin	97.1	96.9	95.8	93.0	2.9	3.1	4.1	6.3
300	140 mM Lysine and 140 mM Niacin	97.2	97.2	95.9	92.3	2.8	2.8	4.0	6.9
300	70 mM Arginine·HCl and 140 mM Niacinamide	96.8	96.8	95.8	92.1	3.2	3.2	4.1	6.9
300	140 mM Histidine and 140 mM Niacinamide	96.8	96.8	95.5	92.1	3.2	3.2	4.4	6.9
300	140 mM Meglumine and 140 mM Niacinamide	97.0	96.8	96.2	92.8	3.0	3.2	3.7	6.5
300	70 mM Lysine·HCl and 140 mM Niacinamide	96.8	96.8	95.8	92.5	3.2	3.2	4.0	6.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.3	96.2	94.7	89.3	3.6	3.7	4.2	9.9
300	Water (Blank), pH 6.0	95.9	95.7	94.1	88.2	4.0	4.2	5.5	11.0
200	140 mM Arginine and 140 mM Niacin	97.9	97.8	97.1	95.1	2.1	2.2	2.7	4.3
200	140 mM Histidine and 140 mM Niacin	97.7	97.6	97.0	94.6	2.3	2.4	2.7	4.8
200	140 mM Meglumine and 140 mM Niacin	97.6	97.6	96.7	95.1	2.4	2.4	3.0	4.2
200	140 mM Lysine and 140 mM Niacin	97.5	97.5	96.6	94.7	2.5	2.5	3.2	4.8
200	70 mM Arginine·HCl and 140 mM Niacinamide	97.5	97.5	96.7	94.8	2.5	2.5	3.2	4.7
200	140 mM Histidine and 140 mM Niacinamide	97.8	97.7	97.0	95.2	2.2	2.3	2.8	4.1
200	140 mM Meglumine and 140 mM Niacinamide	97.7	97.6	96.9	95.0	2.3	2.4	3.0	4.4
200	70 mM Lysine·HCl and 140 mM Niacinamide	97.8	97.8	96.9	95.1	2.2	2.2	3.0	4.4
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.1	97.0	96.0	93.2	2.8	2.9	3.9	5.9
200	Water (blank), pH 6.0	96.6	96.6	95.3	91.9	3.3	3.3	4.5	7.4
100	140 mM Arginine and 140 mM Niacin	98.4	98.4	97.9	96.3	1.6	1.6	2.0	3.3
100	140 mM Histidine and 140 mM Niacin	98.2	98.2	97.7	96.4	1.8	1.8	2.2	3.2
100	140 mM Meglumine and 140 mM Niacin	98.2	98.2	97.7	96.3	1.8	1.8	2.0	3.2
100	140 mM Lysine and 140 mM Niacin	98.3	98.2	97.8	96.3	1.7	1.8	1.9	3.2
100	70 mM Arginine·HCl and 140 mM Niacinamide	98.1	98.0	97.6	95.9	1.9	2.0	2.3	3.7
100	140 mM Histidine and 140 mM Niacinamide	98.3	98.3	98.0	96.3	1.7	1.7	1.8	3.2
100	140 mM Meglumine and 140 mM Niacinamide	98.4	98.3	98.0	96.4	1.6	1.7	1.8	3.3
100	70 mM Lysine·HCl and 140 mM Niacinamide	98.2	98.1	97.8	96.3	1.8	1.9	2.0	3.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.8	97.8	97.2	94.8	2.1	2.1	2.7	4.4
100	Water (blank), pH 6.0	97.3	97.3	96.2	93.6	2.6	2.6	3.7	5.6

Table 148 SE-UPLC results of formulated Trastuzumab-MMAE in 50 mM Histidine buffer, pH 7.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid, 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C C	40°C C	T0	5°C	25°C C	40°C C
300	300 mM Arginine and 300 mM Niacin	96.0	95.9	94.4	88.1	4.0	4.1	5.3	11.3
300	300 mM Histidine and 300 mM Niacin	96.4	96.2	95.4	88.7	3.6	3.8	4.4	10.7
300	300 mM Meglumine and 300 mM Niacin	96.4	96.3	95.1	88.5	3.6	3.7	4.6	10.8
300	300 mM Lysine and 300 mM Niacin	96.0	95.9	95.0	88.9	4.0	4.1	4.7	10.3
300	140 mM Arginine·HCl and 300 mM Niacinamide	96.2	96.1	95.0	88.0	3.8	3.9	4.8	11.4
300	300 mM Histidine and 300 mM Niacinamide	96.3	96.1	94.7	88.2	3.7	3.9	5.1	11.1
300	300 mM Meglumine and 300 mM Niacinamide	96.4	96.2	94.8	88.1	3.6	3.8	4.9	11.1
300	140 mM Lysine·HCl and 300 mM Niacinamide	96.3	96.2	94.9	87.9	3.7	3.8	4.8	11.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	95.7	95.5	93.9	87.6	4.2	4.4	6.0	11.6
300	Water (Blank), pH 7.0	95.1	95.0	92.5	85.4	5.3	5.5	7.6	13.7
200	300 mM Arginine and 300 mM Niacin	97.1	97.1	96.3	92.8	2.9	2.9	3.5	6.5
200	300 mM Histidine and 300 mM Niacin	97.2	97.1	96.4	93.2	2.8	2.9	3.5	6.1
200	300 mM Meglumine and 300 mM Niacin	97.0	97.0	96.1	93.0	3.0	3.0	3.6	6.2
200	300 mM Lysine and 300 mM Niacin	97.3	97.2	96.5	93.0	2.7	2.8	3.2	6.4
200	140 mM Arginine·HCl and 300 mM Niacinamide	96.9	96.8	96.1	92.5	3.1	3.2	3.8	6.8
200	300 mM Histidine and 300 mM Niacinamide	97.1	97.0	96.3	92.8	2.9	3.0	3.5	6.6
200	300 mM Meglumine and 300 mM Niacinamide	97.3	97.3	96.4	93.2	2.7	2.7	3.4	6.2
200	140 mM Lysine·HCl and 300 mM Niacinamide	97.1	97.0	96.1	92.8	2.9	3.0	3.8	6.5
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	96.7	96.6	95.5	92.0	3.6	3.7	4.8	7.2
200	Water (blank), pH 7.0	96.0	95.8	94.6	90.7	3.9	4.1	5.3	8.4
100	300 mM Arginine and 300 mM Niacin	97.4	97.4	96.9	94.6	2.6	2.6	3.0	4.7
100	300 mM Histidine and 300 mM Niacin	97.5	97.4	96.8	94.8	2.5	2.6	2.9	4.6
100	300 mM Meglumine and 300 mM Niacin	97.4	97.4	96.8	94.5	2.6	2.6	3.0	5.0
100	300 mM Lysine and 300 mM Niacin	97.3	97.3	96.7	94.2	2.7	2.7	3.2	5.1
100	140 mM Arginine·HCl and 300 mM Niacinamide	97.4	97.4	96.8	94.4	2.6	2.6	3.0	5.0
100	300 mM Histidine and 300 mM Niacinamide	97.6	97.5	97.0	94.7	2.4	2.5	2.9	4.7
100	300 mM Meglumine and 300 mM Niacinamide	97.5	97.5	96.8	94.4	2.5	2.5	2.9	5.0
100	140 mM Lysine·HCl and 300 mM Niacinamide	97.3	97.3	96.8	94.6	2.7	2.7	2.9	4.7
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	97.3	97.3	96.5	94.0	2.6	2.6	3.3	5.2
100	Water (blank), pH 7.0	97.0	96.9	96.0	92.8	2.9	3.0	3.8	6.4

Table 149 SE-UPLC results of formulated Trastuzumab-MMAE in 5 mM Acetate buffer, pH 4.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid, 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	95.8	95.7	94.8	90.7	4.2	4.3	5.0	8.5
300	30 mM Histidine and 30 mM Niacin	95.7	95.5	94.0	89.0	4.3	4.5	5.8	10.4
300	30 mM Meglumine and 30 mM Niacin	95.8	95.7	94.2	88.7	4.2	4.3	5.6	10.7
300	30 mM Lysine and 30 mM Niacin	95.7	95.5	94.7	90.2	4.3	4.5	5.1	9.2
300	30 mM Arginine-HCl and 30 mM Niacinamide	95.5	95.4	94.0	88.4	4.5	4.6	5.8	10.8
300	30 mM Histidine and 30 mM Niacinamide	95.7	95.6	94.2	89.3	4.3	4.4	5.5	9.9
300	30 mM Meglumine and 30 mM Niacinamide	95.7	95.6	94.5	88.7	4.3	4.4	5.3	10.7
300	30 mM Lysine-HCl and 30 mM Niacinamide	95.4	95.2	93.6	88.3	4.6	4.8	6.2	10.6
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	95.3	95.1	93.2	87.0	4.6	4.8	6.7	12.3
300	Water (Blank), pH 4.5	94.8	94.5	92.1	85.0	4.9	5.2	7.6	14.0
200	30 mM Arginine and 30 mM Niacin	96.7	96.7	96.0	91.8	3.3	3.3	3.9	7.6
200	30 mM Histidine and 30 mM Niacin	96.8	96.7	96.1	92.5	3.2	3.3	3.6	6.7
200	30 mM Meglumine and 30 mM Niacin	96.5	96.4	95.8	91.6	3.5	3.6	3.9	7.6
200	30 mM Lysine and 30 mM Niacin	96.6	96.5	96.0	92.5	3.4	3.5	3.9	6.7
200	30 mM Arginine-HCl and 30 mM Niacinamide	96.6	96.6	95.7	92.4	3.4	3.4	4.1	7.0
200	30 mM Histidine and 30 mM Niacinamide	96.6	96.6	95.9	92.5	3.4	3.4	4.0	6.9
200	30 mM Meglumine and 30 mM Niacinamide	96.5	96.5	95.3	92.5	3.5	3.5	4.6	6.7
200	30 mM Lysine-HCl and 30 mM Niacinamide	96.4	96.4	95.7	91.9	3.6	3.6	4.1	7.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	96.4	96.3	95.0	91.7	3.5	3.6	4.9	7.6
200	Water (blank), pH 4.5	95.9	95.7	94.3	90.2	3.9	4.1	5.5	9.0
100	30 mM Arginine and 30 mM Niacin	97.3	97.2	96.6	94.3	2.7	2.8	3.3	5.0
100	30 mM Histidine and 30 mM Niacin	97.2	97.1	96.7	93.7	2.8	2.9	3.0	5.8
100	30 mM Meglumine and 30 mM Niacin	97.2	97.2	96.5	94.1	2.8	2.8	3.2	5.4
100	30 mM Lysine and 30 mM Niacin	97.1	97.0	96.6	93.8	2.9	3.0	3.3	5.6
100	30 mM Arginine-HCl and 30 mM Niacinamide	97.3	97.2	96.8	94.5	2.7	2.8	3.0	4.8
100	30 mM Histidine and 30 mM Niacinamide	97.2	97.2	96.7	94.2	2.8	2.8	3.2	5.2
100	30 mM Meglumine and 30 mM Niacinamide	97.1	97.0	96.7	94.4	2.9	3.0	3.1	5.0
100	30 mM Lysine-HCl and 30 mM Niacinamide	97.4	97.3	96.8	94.5	2.6	2.7	3.1	5.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	97.1	97.0	96.1	93.7	2.8	2.9	3.7	5.7
100	Water (blank), pH 4.5	96.6	96.5	95.4	92.0	3.2	3.3	4.4	7.2

Table 150 SE-UPLC results of formulated Trastuzumab-MMAE in 20 mM Acetate buffer, pH 5.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid, 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	96.8	96.6	95.4	89.4	3.2	3.4	4.3	9.9
300	140 mM Histidine and 140 mM Niacin	96.4	96.3	95.2	89.1	3.6	3.7	4.6	10.3
300	140 mM Meglumine and 140 mM Niacin	96.6	96.5	95.7	90.4	3.4	3.5	4.0	9.9
300	140 mM Lysine and 140 mM Niacin	96.6	96.4	95.4	89.6	3.4	3.6	4.4	9.7
300	70 mM Arginine·HCl and 140 mM Niacinamide	96.6	96.4	95.8	90.3	3.4	3.6	4.0	8.9
300	140 mM Histidine and 140 mM Niacinamide	96.6	96.5	95.8	89.7	3.4	3.5	3.9	9.5
300	140 mM Meglumine and 140 mM Niacinamide	96.7	96.5	95.4	89.0	3.3	3.5	4.4	10.4
300	70 mM Lysine·HCl and 140 mM Niacinamide	96.4	96.3	94.9	88.9	3.6	3.7	4.9	10.4
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	96.1	96.0	94.3	88.6	3.9	4.0	5.5	10.5
300	Water (Blank), pH 5.0	95.8	95.6	93.8	86.3	4.1	4.3	6.0	12.9
200	140 mM Arginine and 140 mM Niacin	96.7	96.7	95.7	92.9	3.3	3.3	4.1	6.3
200	140 mM Histidine and 140 mM Niacin	96.8	96.8	95.7	93.3	3.2	3.2	4.0	6.0
200	140 mM Meglumine and 140 mM Niacin	97.1	97.1	96.2	93.1	2.9	2.9	3.6	6.1
200	140 mM Lysine and 140 mM Niacin	96.8	96.7	95.5	92.5	3.2	3.3	4.4	6.7
200	70 mM Arginine·HCl and 140 mM Niacinamide	97.0	96.9	95.9	92.8	3.0	3.1	3.9	6.4
200	140 mM Histidine and 140 mM Niacinamide	96.8	96.7	95.6	92.4	3.2	3.3	4.1	7.0
200	140 mM Meglumine and 140 mM Niacinamide	96.7	96.7	95.4	92.3	3.3	3.3	4.3	6.9
200	70 mM Lysine·HCl and 140 mM Niacinamide	96.8	96.8	95.8	93.1	3.2	3.2	3.9	6.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	96.5	96.5	95.0	91.7	3.4	3.4	4.8	7.4
200	Water (blank), pH 5.0	96.2	96.2	94.5	90.3	3.7	3.7	5.3	8.8
100	140 mM Arginine and 140 mM Niacin	97.4	97.3	96.8	94.1	2.6	2.7	2.9	5.4
100	140 mM Histidine and 140 mM Niacin	97.7	97.7	96.8	94.1	2.3	2.3	3.0	5.4
100	140 mM Meglumine and 140 mM Niacin	97.6	97.5	96.7	94.8	2.4	2.5	3.1	4.7
100	140 mM Lysine and 140 mM Niacin	97.5	97.4	96.7	94.2	2.5	2.6	3.0	5.1
100	70 mM Arginine·HCl and 140 mM Niacinamide	97.5	97.4	96.8	94.4	2.5	2.6	3.0	5.1
100	140 mM Histidine and 140 mM Niacinamide	97.5	97.5	96.8	94.7	2.5	2.5	3.1	4.6
100	140 mM Meglumine and 140 mM Niacinamide	97.5	97.5	96.9	94.2	2.5	2.5	2.9	5.1
100	70 mM Lysine·HCl and 140 mM Niacinamide	97.4	97.4	96.7	93.9	2.6	2.6	3.2	5.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	97.4	97.3	96.2	93.6	2.5	2.6	3.7	5.7
100	Water (blank), pH 5.0	96.8	96.7	95.4	92.8	2.1	2.2	4.4	6.4

Table 151 SE-UPLC results of formulated Trastuzumab-MMAE in 50 mM Acetate buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid, 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	96.9	96.7	95.5	88.3	3.1	3.3	4.2	11.0
300	300 mM Histidine and 300 mM Niacin	96.6	96.5	95.2	88.0	3.4	3.5	4.5	11.3
300	300 mM Meglumine and 300 mM Niacin	97.0	96.8	95.6	89.4	3.0	3.2	4.1	10.0
300	300 mM Lysine and 300 mM Niacin	97.0	96.8	95.7	88.4	3.0	3.2	4.0	10.9
300	140 mM Arginine-HCl and 300 mM Niacinamide	96.9	96.7	95.8	89.3	3.1	3.3	4.0	9.9
300	300 mM Histidine and 300 mM Niacinamide	96.9	96.7	96.1	89.3	3.1	3.3	3.6	9.9
300	300 mM Meglumine and 300 mM Niacinamide	96.9	96.8	95.4	88.3	3.1	3.2	4.3	11.0
300	140 mM Lysine-HCl and 300 mM Niacinamide	96.9	96.8	95.7	88.9	3.1	3.2	4.0	10.4
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.3	96.2	94.7	89.3	3.6	3.7	4.2	9.9
300	Water (Blank), pH 6.0	95.9	95.7	94.1	88.2	4.0	4.2	5.5	11.0
200	300 mM Arginine and 300 mM Niacin	97.5	97.4	96.7	93.9	2.5	2.6	3.2	5.5
200	300 mM Histidine and 300 mM Niacin	97.5	97.4	96.7	94.3	2.5	2.6	3.1	5.1
200	300 mM Meglumine and 300 mM Niacin	97.5	97.5	96.6	94.2	2.5	2.5	3.3	5.0
200	300 mM Lysine and 300 mM Niacin	97.7	97.6	96.9	94.1	2.3	2.4	2.9	5.2
200	140 mM Arginine-HCl and 300 mM Niacinamide	97.4	97.3	96.9	94.2	2.6	2.7	3.0	5.1
200	300 mM Histidine and 300 mM Niacinamide	97.7	97.6	96.9	94.4	2.3	2.4	3.0	5.0
200	300 mM Meglumine and 300 mM Niacinamide	97.6	97.6	97.0	94.2	2.4	2.4	2.9	5.0
200	140 mM Lysine-HCl and 300 mM Niacinamide	97.3	97.2	96.7	93.7	2.7	2.8	3.2	5.7
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.1	97.0	96.0	93.2	2.8	2.9	3.9	5.9
200	Water (blank), pH 6.0	96.6	96.6	95.3	91.9	3.3	3.3	4.5	7.4
100	300 mM Arginine and 300 mM Niacin	97.9	97.8	97.5	95.5	2.1	2.2	2.3	4.0
100	300 mM Histidine and 300 mM Niacin	98.1	98.1	97.7	95.4	1.9	1.9	2.0	4.0
100	300 mM Meglumine and 300 mM Niacin	98.0	98.0	97.6	95.5	2.0	2.0	2.1	3.9
100	300 mM Lysine and 300 mM Niacin	98.1	98.0	97.7	95.6	1.9	2.0	2.1	3.8
100	140 mM Arginine-HCl and 300 mM Niacinamide	97.8	97.8	97.4	95.3	2.2	2.2	2.3	4.0
100	300 mM Histidine and 300 mM Niacinamide	98.1	98.0	97.7	95.4	1.9	2.0	2.0	4.1
100	300 mM Meglumine and 300 mM Niacinamide	97.8	97.7	97.5	95.0	2.2	2.3	2.2	4.4
100	140 mM Lysine-HCl and 300 mM Niacinamide	98.1	98.0	97.6	95.5	1.9	2.0	2.1	3.8
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.8	97.8	97.2	94.8	2.1	2.1	2.7	4.4
100	Water (blank), pH 6.0	97.3	97.3	96.2	93.6	2.6	2.6	3.7	5.6

Table 152 SE-UPLC results of formulated Trastuzumab-MMAE in 5 mM Citrate buffer, pH 4.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	95.4	95.3	93.6	88.9	4.6	4.7	6.1	10.3
300	30 mM Histidine and 30 mM Niacin	95.7	95.5	94.6	89.0	4.3	4.5	5.1	10.4
300	30 mM Meglumine and 30 mM Niacin	95.5	95.3	93.8	89.2	4.5	4.7	6.0	10.0
300	30 mM Lysine and 30 mM Niacin	95.5	95.4	93.9	88.2	4.5	4.6	5.8	11.2
300	30 mM Arginine-HCl and 30 mM Niacinamide	95.3	95.1	94.2	88.8	4.7	4.9	5.6	10.6
300	30 mM Histidine and 30 mM Niacinamide	95.7	95.6	94.9	90.0	4.3	4.4	4.8	9.4
300	30 mM Meglumine and 30 mM Niacinamide	95.4	95.2	93.7	88.0	4.6	4.8	6.1	11.4
300	30 mM Lysine-HCl and 30 mM Niacinamide	95.5	95.4	93.8	89.5	4.5	4.6	5.9	9.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	95.3	95.1	93.2	87.0	4.6	4.8	6.7	12.3
300	Water (Blank), pH 4.5	94.8	94.5	92.1	85.0	4.9	5.2	7.6	14.0
200	30 mM Arginine and 30 mM Niacin	96.4	96.3	95.6	91.9	3.6	3.7	4.3	7.4
200	30 mM Histidine and 30 mM Niacin	96.8	96.8	95.8	91.9	3.2	3.2	3.9	7.5
200	30 mM Meglumine and 30 mM Niacin	96.7	96.6	96.0	92.2	3.3	3.4	3.7	7.2
200	30 mM Lysine and 30 mM Niacin	96.8	96.7	95.8	92.4	3.2	3.3	4.0	7.0
200	30 mM Arginine-HCl and 30 mM Niacinamide	96.7	96.7	95.5	92.2	3.3	3.3	4.3	7.1
200	30 mM Histidine and 30 mM Niacinamide	96.7	96.7	95.6	92.1	3.3	3.3	4.2	7.2
200	30 mM Meglumine and 30 mM Niacinamide	96.6	96.5	96.0	92.6	3.4	3.5	3.8	6.7
200	30 mM Lysine-HCl and 30 mM Niacinamide	96.8	96.7	95.7	92.2	3.2	3.3	4.0	7.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	96.4	96.3	95.0	91.7	3.5	3.6	4.9	7.6
200	Water (blank), pH 4.5	95.9	95.7	94.3	90.2	3.9	4.1	5.5	9.0
100	30 mM Arginine and 30 mM Niacin	97.1	97.0	96.5	94.2	2.9	3.0	3.2	5.1
100	30 mM Histidine and 30 mM Niacin	97.2	97.2	96.9	93.9	2.8	2.8	3.0	5.6
100	30 mM Meglumine and 30 mM Niacin	97.2	97.1	96.9	94.2	2.8	2.9	2.9	5.3
100	30 mM Lysine and 30 mM Niacin	97.3	97.3	97.0	93.9	2.7	2.7	2.7	5.5
100	30 mM Arginine-HCl and 30 mM Niacinamide	97.4	97.4	96.9	94.5	2.6	2.6	2.8	4.9
100	30 mM Histidine and 30 mM Niacinamide	97.1	97.1	96.6	94.3	2.9	2.9	3.1	5.2
100	30 mM Meglumine and 30 mM Niacinamide	97.3	97.2	96.6	94.6	2.7	2.8	3.2	4.7
100	30 mM Lysine-HCl and 30 mM Niacinamide	97.4	97.3	96.8	93.9	2.6	2.7	3.0	5.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	97.1	97.0	96.1	93.7	2.8	2.9	3.7	5.7
100	Water (blank), pH 4.5	96.6	96.5	95.4	92.0	3.2	3.3	4.4	7.2

Table 153 SE-UPLC results of formulated Trastuzumab-MMAE in 20 mM Citrate buffer, pH 5.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid, 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	97.1	97.0	96.4	91.0	2.9	3.0	3.3	8.3
300	140 mM Histidine and 140 mM Niacin	97.0	96.9	95.9	90.6	3.0	3.1	3.8	8.7
300	140 mM Meglumine and 140 mM Niacin	97.1	97.0	95.9	90.0	2.9	3.0	3.8	9.3
300	140 mM Lysine and 140 mM Niacin	97.1	97.0	96.4	91.0	2.9	3.0	3.3	8.4
300	70 mM Arginine·HCl and 140 mM Niacinamide	96.7	96.5	95.6	89.7	3.3	3.5	4.1	9.7
300	140 mM Histidine and 140 mM Niacinamide	96.7	96.5	95.7	90.0	3.3	3.5	4.1	9.2
300	140 mM Meglumine and 140 mM Niacinamide	96.8	96.7	96.1	90.2	3.2	3.3	3.6	9.1
300	70 mM Lysine·HCl and 140 mM Niacinamide	97.0	96.9	95.9	90.7	3.0	3.1	3.8	8.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	96.4	96.1	94.8	89.3	3.4	3.7	5.0	9.9
300	Water (Blank), pH 5.5	95.8	95.6	94.0	87.8	4.0	4.2	5.8	11.4
200	140 mM Arginine and 140 mM Niacin	97.6	97.5	97.1	94.1	2.4	2.5	2.7	5.2
200	140 mM Histidine and 140 mM Niacin	97.8	97.8	97.3	94.3	2.2	2.2	2.5	5.0
200	140 mM Meglumine and 140 mM Niacin	97.4	97.3	96.9	94.1	2.6	2.7	3.0	5.2
200	140 mM Lysine and 140 mM Niacin	97.5	97.5	96.7	93.9	2.5	2.5	3.1	5.3
200	70 mM Arginine·HCl and 140 mM Niacinamide	97.6	97.6	97.1	93.9	2.4	2.4	2.8	5.5
200	140 mM Histidine and 140 mM Niacinamide	97.4	97.3	96.9	93.8	2.6	2.7	2.8	5.5
200	140 mM Meglumine and 140 mM Niacinamide	97.7	97.7	97.0	94.2	2.3	2.3	2.9	5.2
200	70 mM Lysine·HCl and 140 mM Niacinamide	97.5	97.4	96.8	93.8	2.5	2.6	3.0	5.6
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	97.2	97.1	95.9	93.4	2.7	2.8	4.0	5.9
200	Water (blank), pH 5.5	96.5	96.3	94.4	92.0	3.4	3.6	5.5	7.3
100	140 mM Arginine and 140 mM Niacin	98.1	98.0	97.6	95.0	1.9	2.0	2.1	4.4
100	140 mM Histidine and 140 mM Niacin	98.1	98.1	97.6	95.3	1.9	1.9	2.1	4.2
100	140 mM Meglumine and 140 mM Niacin	98.1	98.1	97.8	95.4	1.9	1.9	2.1	4.1
100	140 mM Lysine and 140 mM Niacin	98.2	98.1	97.8	95.3	1.8	1.9	2.0	4.1
100	70 mM Arginine·HCl and 140 mM Niacinamide	97.9	97.8	97.4	94.9	2.1	2.2	2.4	4.6
100	140 mM Histidine and 140 mM Niacinamide	98.1	98.0	97.8	95.1	1.9	2.0	2.0	4.2
100	140 mM Meglumine and 140 mM Niacinamide	98.2	98.2	97.8	95.3	1.8	1.8	2.1	4.2
100	70 mM Lysine·HCl and 140 mM Niacinamide	97.9	97.9	97.4	95.2	2.1	2.1	2.5	4.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	97.9	97.9	97.3	94.9	2.0	2.0	2.6	4.3
100	Water (blank), pH 5.5	97.4	97.3	96.3	93.7	2.5	2.6	3.6	5.5

Table 154 SE-UPLC results of formulated Trastuzumab-MMAE in 50 mM Citrate buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid, 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing Formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	96.6	96.5	95.2	89.5	3.4	3.5	4.5	9.9
300	300 mM Histidine and 300 mM Niacin	96.8	96.6	95.9	90.8	3.2	3.4	3.8	8.6
300	300 mM Meglumine and 300 mM Niacin	96.7	96.6	95.6	90.4	3.3	3.4	4.2	9.0
300	300 mM Lysine and 300 mM Niacin	96.8	96.7	95.5	90.1	3.2	3.3	4.3	9.3
300	140 mM Arginine·HCl and 300 mM Niacinamide	97.0	96.9	95.8	90.6	3.0	3.1	4.0	8.6
300	300 mM Histidine and 300 mM Niacinamide	96.8	96.7	95.9	89.7	3.2	3.3	3.9	9.7
300	300 mM Meglumine and 300 mM Niacinamide	96.9	96.8	95.9	90.0	3.1	3.2	3.8	9.3
300	140 mM Lysine·HCl and 300 mM Niacinamide	96.9	96.8	95.8	89.8	3.1	3.2	4.0	9.4
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.3	96.2	94.7	89.3	3.6	3.7	4.2	9.9
300	Water (Blank), pH 6.0	95.9	95.7	94.1	88.2	4.0	4.2	5.5	11.0
200	300 mM Arginine and 300 mM Niacin	97.4	97.4	96.7	94.2	2.6	2.6	3.2	5.0
200	300 mM Histidine and 300 mM Niacin	97.3	97.3	96.4	94.0	2.7	2.7	3.4	5.4
200	300 mM Meglumine and 300 mM Niacin	97.4	97.4	96.6	94.2	2.6	2.6	3.1	5.0
200	300 mM Lysine and 300 mM Niacin	97.3	97.2	96.8	94.1	2.7	2.8	3.0	5.2
200	140 mM Arginine·HCl and 300 mM Niacinamide	97.7	97.7	97.1	94.3	2.3	2.3	2.6	5.1
200	300 mM Histidine and 300 mM Niacinamide	97.5	97.4	96.8	94.1	2.5	2.6	2.9	5.2
200	300 mM Meglumine and 300 mM Niacinamide	97.3	97.2	96.8	93.8	2.7	2.8	3.1	5.4
200	140 mM Lysine·HCl and 300 mM Niacinamide	97.5	97.4	96.6	94.3	2.5	2.6	3.2	5.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.1	97.0	96.0	93.2	2.8	2.9	3.9	5.9
200	Water (blank), pH 6.0	96.6	96.6	95.3	91.9	3.3	3.3	4.5	7.4
100	300 mM Arginine and 300 mM Niacin	97.8	97.7	97.5	95.1	2.2	2.3	2.4	4.4
100	300 mM Histidine and 300 mM Niacin	97.9	97.8	97.5	95.5	2.1	2.2	2.3	4.0
100	300 mM Meglumine and 300 mM Niacin	98.0	98.0	97.7	95.6	2.0	2.0	2.1	3.8
100	300 mM Lysine and 300 mM Niacin	97.8	97.7	97.5	95.2	2.2	2.3	2.2	4.2
100	140 mM Arginine·HCl and 300 mM Niacinamide	98.1	98.0	97.8	95.5	1.9	2.0	2.0	4.0
100	300 mM Histidine and 300 mM Niacinamide	97.8	97.8	97.3	95.0	2.2	2.2	2.5	4.5
100	300 mM Meglumine and 300 mM Niacinamide	97.8	97.7	97.4	95.4	2.2	2.3	2.5	4.0
100	140 mM Lysine·HCl and 300 mM Niacinamide	97.9	97.9	97.6	95.1	2.1	2.1	2.3	4.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.8	97.8	97.2	94.8	2.1	2.1	2.7	4.4
100	Water (blank), pH 6.0	97.3	97.3	96.2	93.6	2.6	2.6	3.7	5.6

Table 155 SE-UPLC results of formulated Trastuzumab-MMAE in 5 mM Phosphate buffer, pH 6.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid, 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	97.2	97.1	96.6	91.3	2.8	2.9	3.2	8.1
300	30 mM Histidine and 30 mM Niacin	96.9	96.7	95.8	90.6	3.1	3.3	4.0	8.6
300	30 mM Meglumine and 30 mM Niacin	97.2	97.1	96.0	90.5	2.8	2.9	3.7	8.7
300	30 mM Lysine and 30 mM Niacin	96.9	96.8	96.0	90.6	3.1	3.2	3.7	8.6
300	30 mM Arginine-HCl and 30 mM Niacinamide	97.0	96.8	96.3	91.2	3.0	3.2	3.4	8.1
300	30 mM Histidine and 30 mM Niacinamide	97.2	97.0	96.3	90.9	2.8	3.0	3.4	8.5
300	30 mM Meglumine and 30 mM Niacinamide	97.0	96.9	96.0	90.3	3.0	3.1	3.8	9.1
300	30 mM Lysine-HCl and 30 mM Niacinamide	97.0	96.9	96.4	91.1	3.0	3.1	3.3	8.2
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	96.6	96.4	95.2	89.5	3.3	3.5	4.7	9.7
300	Water (Blank), pH 6.5	95.5	95.3	93.6	88.0	4.4	4.6	6.3	11.1
200	30 mM Arginine and 30 mM Niacin	97.8	97.7	97.3	94.5	2.2	2.3	2.4	4.8
200	30 mM Histidine and 30 mM Niacin	98.0	98.0	97.2	94.2	2.0	2.0	2.6	5.1
200	30 mM Meglumine and 30 mM Niacin	97.7	97.7	97.2	94.4	2.3	2.3	2.7	4.8
200	30 mM Lysine and 30 mM Niacin	97.7	97.7	97.1	94.2	2.3	2.3	2.8	5.0
200	30 mM Arginine-HCl and 30 mM Niacinamide	98.0	98.0	97.2	94.4	2.0	2.0	2.6	4.9
200	30 mM Histidine and 30 mM Niacinamide	97.8	97.8	97.2	94.0	2.2	2.2	2.6	5.3
200	30 mM Meglumine and 30 mM Niacinamide	97.7	97.7	96.9	94.2	2.3	2.3	2.9	5.1
200	30 mM Lysine-HCl and 30 mM Niacinamide	98.0	97.9	97.5	94.6	2.0	2.1	2.4	4.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	97.4	97.3	96.5	93.3	3.0	3.0	3.4	5.7
200	Water (blank), pH 6.5	96.7	96.6	95.4	91.8	3.2	3.3	4.5	7.5
100	30 mM Arginine and 30 mM Niacin	98.3	98.3	97.9	95.3	1.7	1.7	2.0	4.0
100	30 mM Histidine and 30 mM Niacin	98.6	98.5	98.1	95.6	1.4	1.5	1.8	3.7
100	30 mM Meglumine and 30 mM Niacin	98.6	98.5	98.3	95.9	1.4	1.5	1.5	3.5
100	30 mM Lysine and 30 mM Niacin	98.5	98.4	98.0	95.5	1.5	1.6	1.9	3.9
100	30 mM Arginine-HCl and 30 mM Niacinamide	98.6	98.5	98.3	95.6	1.4	1.5	1.4	3.7
100	30 mM Histidine and 30 mM Niacinamide	98.3	98.2	98.0	95.2	1.7	1.8	1.8	4.1
100	30 mM Meglumine and 30 mM Niacinamide	98.5	98.5	98.1	95.8	1.5	1.5	1.8	3.5
100	30 mM Lysine-HCl and 30 mM Niacinamide	98.5	98.5	98.2	95.7	1.5	1.5	1.7	3.7
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	98.3	98.3	97.6	95.0	1.6	1.6	2.3	4.3
100	Water (blank), pH 6.5	97.1	97.0	96.0	93.2	2.8	2.9	3.8	6.0

Table 156 SE-UPLC results of formulated Trastuzumab-MMAE in 20 mM Phosphate buffer, pH 7.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid, 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	96.4	96.3	95.0	88.2	3.6	3.7	4.8	11.1
300	140 mM Histidine and 140 mM Niacin	96.1	96.0	94.7	87.6	3.9	4.0	5.0	11.8
300	140 mM Meglumine and 140 mM Niacin	96.1	96.0	94.7	88.1	3.9	4.0	5.0	11.3
300	140 mM Lysine and 140 mM Niacin	96.1	95.9	94.5	87.2	3.9	4.1	5.2	12.2
300	70 mM Arginine·HCl and 140 mM Niacinamide	96.1	96.0	95.1	88.6	3.9	4.0	4.6	10.7
300	140 mM Histidine and 140 mM Niacinamide	96.2	96.0	94.8	88.0	3.8	4.0	4.9	11.4
300	140 mM Meglumine and 140 mM Niacinamide	96.0	95.9	94.9	88.6	4.0	4.1	4.8	10.7
300	70 mM Lysine·HCl and 140 mM Niacinamide	96.1	96.0	94.6	88.2	3.9	4.0	5.1	11.0
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	95.7	95.5	93.9	87.6	4.2	4.4	6.0	11.6
300	Water (Blank), pH 7.0	95.1	95.0	92.5	85.4	5.3	5.5	7.6	13.7
200	140 mM Arginine and 140 mM Niacin	97.0	97.0	96.0	93.0	3.0	3.0	3.7	6.3
200	140 mM Histidine and 140 mM Niacin	97.1	97.0	96.3	92.8	2.9	3.0	3.6	6.4
200	140 mM Meglumine and 140 mM Niacin	97.0	96.9	96.2	92.7	3.0	3.1	3.6	6.5
200	140 mM Lysine and 140 mM Niacin	97.3	97.3	96.3	92.9	2.7	2.7	3.4	6.3
200	70 mM Arginine·HCl and 140 mM Niacinamide	97.2	97.1	96.6	92.9	2.8	2.9	3.1	6.3
200	140 mM Histidine and 140 mM Niacinamide	96.9	96.9	96.1	92.9	3.1	3.1	3.8	6.4
200	140 mM Meglumine and 140 mM Niacinamide	97.2	97.1	96.5	92.9	2.8	2.9	3.2	6.5
200	70 mM Lysine·HCl and 140 mM Niacinamide	97.2	97.1	96.6	92.8	2.8	2.9	3.2	6.5
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	96.7	96.6	95.5	92.0	3.6	3.7	4.8	7.2
200	Water (blank), pH 7.0	96.0	95.8	94.6	90.7	3.9	4.1	5.3	8.4
100	140 mM Arginine and 140 mM Niacin	97.6	97.6	97.1	94.6	2.4	2.4	2.6	4.7
100	140 mM Histidine and 140 mM Niacin	97.3	97.2	96.6	94.2	2.7	2.8	3.2	5.2
100	140 mM Meglumine and 140 mM Niacin	97.5	97.4	97.0	94.7	2.5	2.6	2.8	4.6
100	140 mM Lysine and 140 mM Niacin	97.4	97.3	96.8	94.4	2.6	2.7	3.0	5.0
100	70 mM Arginine·HCl and 140 mM Niacinamide	97.4	97.4	96.8	94.3	2.6	2.6	3.1	5.0
100	140 mM Histidine and 140 mM Niacinamide	97.6	97.5	97.0	94.7	2.4	2.5	2.7	4.8
100	140 mM Meglumine and 140 mM Niacinamide	97.5	97.4	96.8	94.4	2.5	2.6	3.0	5.1
100	70 mM Lysine·HCl and 140 mM Niacinamide	97.3	97.3	96.8	94.3	2.7	2.7	3.0	5.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	97.3	97.3	96.5	94.0	2.6	2.6	3.3	5.2
100	Water (blank), pH 7.0	97.0	96.9	96.0	92.8	2.9	3.0	3.8	6.4

Table 157 SE-UPLC results of formulated Trastuzumab-MMAE in 50 mM Phosphate buffer, pH 7.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid, 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C C	40°C C	T0	5°C	25°C C	40°C C
300	300 mM Arginine and 300 mM Niacin	95.8	95.7	94.0	89.0	4.2	4.3	5.8	10.3
300	300 mM Histidine and 300 mM Niacin	95.5	95.3	93.7	88.0	4.5	4.7	6.1	11.4
300	300 mM Meglumine and 300 mM Niacin	95.6	95.4	94.0	88.6	4.4	4.6	5.8	10.8
300	300 mM Lysine and 300 mM Niacin	95.8	95.7	94.2	89.2	4.2	4.3	5.6	10.2
300	140 mM Arginine·HCl and 300 mM Niacinamide	96.0	95.9	94.4	89.8	4.0	4.1	5.4	9.6
300	300 mM Histidine and 300 mM Niacinamide	95.8	95.7	94.4	89.7	4.2	4.3	5.4	9.5
300	300 mM Meglumine and 300 mM Niacinamide	95.9	95.7	94.1	89.2	4.1	4.3	5.7	10.2
300	140 mM Lysine·HCl and 300 mM Niacinamide	95.7	95.6	93.9	88.3	4.3	4.4	5.9	11.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	95.5	95.2	93.5	87.2	4.4	4.7	6.3	11.8
300	Water (Blank), pH 7.5	94.7	94.4	91.9	85.3	5.2	5.5	7.7	13.5
200	300 mM Arginine and 300 mM Niacin	96.2	96.2	95.3	91.4	3.8	3.8	4.5	7.8
200	300 mM Histidine and 300 mM Niacin	96.2	96.1	95.4	91.8	3.8	3.9	4.3	7.4
200	300 mM Meglumine and 300 mM Niacin	96.2	96.2	95.1	91.1	3.8	3.8	4.7	8.3
200	300 mM Lysine and 300 mM Niacin	96.6	96.5	95.6	92.1	3.4	3.5	4.2	7.3
200	140 mM Arginine·HCl and 300 mM Niacinamide	96.6	96.5	95.9	92.6	3.4	3.5	3.9	6.8
200	300 mM Histidine and 300 mM Niacinamide	96.6	96.5	95.7	92.5	3.4	3.5	4.0	6.7
200	300 mM Meglumine and 300 mM Niacinamide	96.4	96.4	95.6	91.9	3.6	3.6	4.3	7.3
200	140 mM Lysine·HCl and 300 mM Niacinamide	96.4	96.3	95.7	91.7	3.6	3.7	4.1	7.7
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	96.2	96.1	94.8	91.5	3.8	3.9	5.0	7.6
200	Water (blank), pH 7.5	96.0	95.8	94.1	89.9	3.9	4.1	5.5	9.1
100	300 mM Arginine and 300 mM Niacin	97.2	97.1	96.9	94.3	2.8	2.9	2.9	5.0
100	300 mM Histidine and 300 mM Niacin	97.0	96.9	96.5	94.0	3.0	3.1	3.3	5.4
100	300 mM Meglumine and 300 mM Niacin	97.2	97.1	96.7	94.1	2.8	2.9	3.2	5.4
100	300 mM Lysine and 300 mM Niacin	97.2	97.2	96.8	94.5	2.8	2.8	2.9	4.9
100	140 mM Arginine·HCl and 300 mM Niacinamide	97.1	97.1	96.7	93.6	2.9	2.9	3.2	5.8
100	300 mM Histidine and 300 mM Niacinamide	97.0	97.0	96.5	94.0	3.0	3.0	3.4	5.4
100	300 mM Meglumine and 300 mM Niacinamide	97.3	97.2	97.0	94.2	2.7	2.8	2.9	5.3
100	140 mM Lysine·HCl and 300 mM Niacinamide	97.2	97.1	96.9	93.9	2.8	2.9	2.9	5.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	97.0	96.9	96.2	93.4	3.0	3.1	3.6	5.7
100	Water (blank), pH 7.5	96.8	96.6	95.5	92.3	3.1	3.3	4.1	6.8

Table 158 SE-UPLC results of formulated Trastuzumab-MMAE in 5 mM Tris buffer, pH 6.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid, 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	97.1	96.9	96.0	90.6	2.9	3.1	3.8	8.8
300	30 mM Histidine and 30 mM Niacin	97.0	96.8	95.8	90.6	3.0	3.2	4.0	8.6
300	30 mM Meglumine and 30 mM Niacin	96.9	96.8	95.9	89.9	3.1	3.2	3.8	9.5
300	30 mM Lysine and 30 mM Niacin	96.9	96.7	95.7	90.5	3.1	3.3	4.0	8.9
300	30 mM Arginine·HCl and 30 mM Niacinamide	96.9	96.8	95.8	89.6	3.1	3.2	4.0	9.8
300	30 mM Histidine and 30 mM Niacinamide	97.0	96.9	96.4	91.2	3.0	3.1	3.4	8.1
300	30 mM Meglumine and 30 mM Niacinamide	96.9	96.7	96.3	90.3	3.1	3.3	3.4	8.9
300	30 mM Lysine·HCl and 30 mM Niacinamide	96.9	96.8	96.1	90.6	3.1	3.2	3.6	8.7
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	96.6	96.4	95.2	89.5	3.3	3.5	4.7	9.7
300	Water (Blank), pH 6.5	95.5	95.3	93.6	88.0	4.4	4.6	6.3	11.1
200	30 mM Arginine and 30 mM Niacin	97.9	97.8	97.2	94.1	2.1	2.2	2.7	5.1
200	30 mM Histidine and 30 mM Niacin	97.9	97.9	97.1	94.3	2.1	2.1	2.7	5.1
200	30 mM Meglumine and 30 mM Niacin	97.6	97.6	97.1	93.8	2.4	2.4	2.6	5.6
200	30 mM Lysine and 30 mM Niacin	97.9	97.8	97.2	94.5	2.1	2.2	2.6	4.8
200	30 mM Arginine·HCl and 30 mM Niacinamide	97.9	97.9	97.2	94.2	2.1	2.1	2.5	5.1
200	30 mM Histidine and 30 mM Niacinamide	97.6	97.6	96.8	93.8	2.4	2.4	2.9	5.6
200	30 mM Meglumine and 30 mM Niacinamide	97.6	97.5	96.9	94.0	2.4	2.5	3.0	5.4
200	30 mM Lysine·HCl and 30 mM Niacinamide	97.9	97.9	97.3	94.2	2.1	2.1	2.6	5.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	97.4	97.3	96.5	93.3	3.0	3.0	3.4	5.7
200	Water (blank), pH 6.5	96.7	96.6	95.4	91.8	3.2	3.3	4.5	7.5
100	30 mM Arginine and 30 mM Niacin	98.5	98.5	98.1	95.4	1.5	1.5	1.6	4.0
100	30 mM Histidine and 30 mM Niacin	98.6	98.5	98.3	95.8	1.4	1.5	1.6	3.7
100	30 mM Meglumine and 30 mM Niacin	98.6	98.5	98.3	95.6	1.4	1.5	1.5	3.8
100	30 mM Lysine and 30 mM Niacin	98.3	98.3	97.8	95.5	1.7	1.7	2.0	4.0
100	30 mM Arginine·HCl and 30 mM Niacinamide	98.3	98.2	98.0	95.2	1.7	1.8	1.7	4.2
100	30 mM Histidine and 30 mM Niacinamide	98.3	98.3	97.8	95.3	1.7	1.7	2.1	4.1
100	30 mM Meglumine and 30 mM Niacinamide	98.4	98.4	98.1	95.3	1.6	1.6	1.7	4.2
100	30 mM Lysine·HCl and 30 mM Niacinamide	98.4	98.4	97.9	95.5	1.6	1.6	2.0	3.8
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	98.3	98.3	97.6	95.0	1.6	1.6	2.3	4.3
100	Water (blank), pH 6.5	97.1	97.0	96.0	93.2	2.8	2.9	3.8	6.0

Table 159 SE-UPLC results of formulated Trastuzumab-MMAE in 20 mM Tris buffer, pH 7.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid, 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	96.4	96.2	95.1	88.7	3.6	3.8	4.6	10.5
300	140 mM Histidine and 140 mM Niacin	96.4	96.3	95.1	87.9	3.6	3.7	4.7	11.5
300	140 mM Meglumine and 140 mM Niacin	96.0	95.8	94.8	87.7	4.0	4.2	5.0	11.7
300	140 mM Lysine and 140 mM Niacin	96.2	96.1	94.8	88.4	3.8	3.9	5.0	11.0
300	70 mM Arginine·HCl and 140 mM Niacinamide	96.1	95.9	95.1	88.4	3.9	4.1	4.6	11.0
300	140 mM Histidine and 140 mM Niacinamide	96.0	95.9	94.8	88.0	4.0	4.1	5.0	11.2
300	140 mM Meglumine and 140 mM Niacinamide	96.4	96.2	95.1	87.8	3.6	3.8	4.6	11.5
300	70 mM Lysine·HCl and 140 mM Niacinamide	96.4	96.3	95.4	88.3	3.6	3.7	4.4	11.0
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	95.7	95.5	93.9	87.6	4.2	4.4	6.0	11.6
300	Water (Blank), pH 7.0	95.1	95.0	92.5	85.4	5.3	5.5	7.6	13.7
200	140 mM Arginine and 140 mM Niacin	97.0	97.0	96.2	92.9	3.0	3.0	3.6	6.5
200	140 mM Histidine and 140 mM Niacin	96.9	96.9	96.3	92.7	3.1	3.1	3.6	6.5
200	140 mM Meglumine and 140 mM Niacin	97.1	97.0	96.1	92.7	2.9	3.0	3.8	6.7
200	140 mM Lysine and 140 mM Niacin	97.1	97.0	96.1	92.8	2.9	3.0	3.8	6.6
200	70 mM Arginine·HCl and 140 mM Niacinamide	96.9	96.8	96.0	92.6	3.1	3.2	3.8	6.6
200	140 mM Histidine and 140 mM Niacinamide	97.0	97.0	96.2	92.7	3.0	3.0	3.5	6.7
200	140 mM Meglumine and 140 mM Niacinamide	97.3	97.2	96.5	93.0	2.7	2.8	3.3	6.2
200	70 mM Lysine·HCl and 140 mM Niacinamide	97.0	96.9	96.4	92.9	3.0	3.1	3.4	6.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	96.7	96.6	95.5	92.0	3.6	3.7	4.8	7.2
200	Water (blank), pH 7.0	96.0	95.8	94.6	90.7	3.9	4.1	5.3	8.4
100	140 mM Arginine and 140 mM Niacin	97.3	97.3	96.7	94.2	2.7	2.7	3.1	5.1
100	140 mM Histidine and 140 mM Niacin	97.3	97.2	96.7	94.3	2.7	2.8	3.1	5.0
100	140 mM Meglumine and 140 mM Niacin	97.4	97.3	96.9	94.3	2.6	2.7	2.8	5.0
100	140 mM Lysine and 140 mM Niacin	97.6	97.5	96.9	94.6	2.4	2.5	3.0	4.8
100	70 mM Arginine·HCl and 140 mM Niacinamide	97.4	97.3	96.9	94.6	2.6	2.7	2.9	4.7
100	140 mM Histidine and 140 mM Niacinamide	97.5	97.4	96.8	94.8	2.5	2.6	3.0	4.5
100	140 mM Meglumine and 140 mM Niacinamide	97.4	97.3	96.7	94.4	2.6	2.7	3.2	5.1
100	70 mM Lysine·HCl and 140 mM Niacinamide	97.4	97.3	96.7	94.3	2.6	2.7	3.2	5.0
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	97.3	97.3	96.5	94.0	2.6	2.6	3.3	5.2
100	Water (blank), pH 7.0	97.0	96.9	96.0	92.8	2.9	3.0	3.8	6.4

Table 160 SE-UPLC results of formulated Trastuzumab-MMAE in 50 mM Tris buffer, pH 7.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid, 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing Formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	95.7	95.6	94.5	89.9	4.3	4.4	5.3	9.5
300	300 mM Histidine and 300 mM Niacin	95.5	95.3	94.1	89.7	4.5	4.7	5.7	9.7
300	300 mM Meglumine and 300 mM Niacin	95.6	95.4	94.1	88.8	4.4	4.6	5.7	10.5
300	300 mM Lysine and 300 mM Niacin	95.8	95.7	94.0	89.5	4.2	4.3	5.7	9.8
300	140 mM Arginine·HCl and 300 mM Niacinamide	95.7	95.5	94.0	88.2	4.3	4.5	5.7	11.1
300	300 mM Histidine and 300 mM Niacinamide	95.7	95.5	94.4	89.6	4.3	4.5	5.3	9.8
300	300 mM Meglumine and 300 mM Niacinamide	95.5	95.3	93.7	88.4	4.5	4.7	6.0	10.8
300	140 mM Lysine·HCl and 300 mM Niacinamide	95.9	95.7	94.7	89.5	4.1	4.3	5.0	9.7
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	95.5	95.2	93.5	87.2	4.4	4.7	6.3	11.8
300	Water (Blank), pH 7.5	94.7	94.4	91.9	85.3	5.2	5.5	7.7	13.5
200	300 mM Arginine and 300 mM Niacin	96.6	96.5	95.5	92.3	3.4	3.5	4.2	6.9
200	300 mM Histidine and 300 mM Niacin	96.4	96.3	95.6	93.0	3.6	3.7	4.1	6.2
200	300 mM Meglumine and 300 mM Niacin	96.5	96.4	95.4	92.6	3.5	3.6	4.4	6.7
200	300 mM Lysine and 300 mM Niacin	96.5	96.4	95.4	92.5	3.5	3.6	4.5	6.8
200	140 mM Arginine·HCl and 300 mM Niacinamide	96.2	96.2	95.3	91.8	3.8	3.8	4.5	7.4
200	300 mM Histidine and 300 mM Niacinamide	96.5	96.5	95.4	92.7	3.5	3.5	4.3	6.7
200	300 mM Meglumine and 300 mM Niacinamide	96.5	96.4	95.2	91.6	3.5	3.6	4.5	7.6
200	140 mM Lysine·HCl and 300 mM Niacinamide	96.2	96.1	95.3	91.9	3.8	3.9	4.5	7.3
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	96.2	96.1	94.8	91.5	3.8	3.9	5.0	7.6
200	Water (blank), pH 7.5	96.0	95.8	94.1	89.9	3.9	4.1	5.5	9.1
100	300 mM Arginine and 300 mM Niacin	97.1	97.0	96.6	94.2	2.9	3.0	3.3	5.3
100	300 mM Histidine and 300 mM Niacin	97.3	97.3	97.0	94.3	2.7	2.7	2.8	5.2
100	300 mM Meglumine and 300 mM Niacin	97.0	97.0	96.5	93.5	3.0	3.0	3.3	6.0
100	300 mM Lysine and 300 mM Niacin	97.2	97.2	96.9	94.5	2.8	2.8	2.8	4.9
100	140 mM Arginine·HCl and 300 mM Niacinamide	97.2	97.2	96.9	94.3	2.8	2.8	2.8	5.1
100	300 mM Histidine and 300 mM Niacinamide	97.3	97.2	96.9	94.5	2.7	2.8	2.8	4.8
100	300 mM Meglumine and 300 mM Niacinamide	97.1	97.1	96.6	94.2	2.9	2.9	3.2	5.2
100	140 mM Lysine·HCl and 300 mM Niacinamide	97.3	97.2	96.8	94.3	2.7	2.8	3.0	5.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	97.0	96.9	96.2	93.4	3.0	3.1	3.6	5.7
100	Water (blank), pH 7.5	96.8	96.6	95.5	92.3	3.1	3.3	4.1	6.8

Table 161 SE-UPLC results of formulated Trastuzumab-MMAE in 5 mM Succinate buffer, pH 4.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid, 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	95.4	95.3	94.0	89.0	4.6	4.7	5.8	10.3
300	30 mM Histidine and 30 mM Niacin	95.5	95.4	93.8	88.4	4.5	4.6	5.9	10.9
300	30 mM Meglumine and 30 mM Niacin	95.8	95.7	94.0	89.4	4.2	4.3	5.7	9.9
300	30 mM Lysine and 30 mM Niacin	95.7	95.6	93.9	89.2	4.3	4.4	5.8	10.2
300	30 mM Arginine-HCl and 30 mM Niacinamide	95.6	95.5	94.4	89.3	4.4	4.5	5.3	9.9
300	30 mM Histidine and 30 mM Niacinamide	95.7	95.6	94.0	88.9	4.3	4.4	5.8	10.4
300	30 mM Meglumine and 30 mM Niacinamide	95.4	95.2	94.2	88.3	4.6	4.8	5.5	11.0
300	30 mM Lysine-HCl and 30 mM Niacinamide	95.6	95.5	94.6	90.2	4.4	4.5	5.2	9.2
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	95.3	95.1	93.2	87.0	4.6	4.8	6.7	12.3
300	Water (Blank), pH 4.5	94.8	94.5	92.1	85.0	4.9	5.2	7.6	14.0
200	30 mM Arginine and 30 mM Niacin	96.5	96.4	95.8	91.9	3.5	3.6	4.1	7.3
200	30 mM Histidine and 30 mM Niacin	96.4	96.3	95.3	91.9	3.6	3.7	4.6	7.4
200	30 mM Meglumine and 30 mM Niacin	96.6	96.5	95.7	91.8	3.4	3.5	4.0	7.5
200	30 mM Lysine and 30 mM Niacin	96.5	96.5	95.9	92.0	3.5	3.5	4.0	7.4
200	30 mM Arginine-HCl and 30 mM Niacinamide	96.6	96.5	95.6	92.6	3.4	3.5	4.2	6.7
200	30 mM Histidine and 30 mM Niacinamide	96.8	96.7	96.1	92.6	3.2	3.3	3.6	6.7
200	30 mM Meglumine and 30 mM Niacinamide	96.4	96.4	95.3	91.8	3.6	3.6	4.4	7.5
200	30 mM Lysine-HCl and 30 mM Niacinamide	96.4	96.4	95.8	92.5	3.6	3.6	3.9	6.7
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	96.4	96.3	95.0	91.7	3.5	3.6	4.9	7.6
200	Water (blank), pH 4.5	95.9	95.7	94.3	90.2	3.9	4.1	5.5	9.0
100	30 mM Arginine and 30 mM Niacin	97.2	97.2	96.8	94.4	2.8	2.8	3.1	5.1
100	30 mM Histidine and 30 mM Niacin	97.4	97.4	96.7	93.9	2.6	2.6	3.2	5.6
100	30 mM Meglumine and 30 mM Niacin	97.3	97.3	96.7	94.6	2.7	2.7	3.1	4.8
100	30 mM Lysine and 30 mM Niacin	97.3	97.2	97.0	93.9	2.7	2.8	2.7	5.4
100	30 mM Arginine-HCl and 30 mM Niacinamide	97.1	97.0	96.7	94.2	2.9	3.0	3.2	5.1
100	30 mM Histidine and 30 mM Niacinamide	97.3	97.3	96.8	94.4	2.7	2.7	2.9	5.1
100	30 mM Meglumine and 30 mM Niacinamide	97.1	97.0	96.5	94.4	2.9	3.0	3.2	4.9
100	30 mM Lysine-HCl and 30 mM Niacinamide	97.3	97.2	97.0	94.2	2.7	2.8	2.9	5.3
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	97.1	97.0	96.1	93.7	2.8	2.9	3.7	5.7
100	Water (blank), pH 4.5	96.6	96.5	95.4	92.0	3.2	3.3	4.4	7.2

Table 162 SE-UPLC results of formulated Trastuzumab-MMAE in 20 mM Succinate buffer, pH 5.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid, 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	97.1	96.9	96.1	90.8	2.9	3.1	3.6	8.4
300	140 mM Histidine and 140 mM Niacin	96.9	96.7	95.7	90.5	3.1	3.3	4.1	8.9
300	140 mM Meglumine and 140 mM Niacin	96.8	96.6	95.9	90.3	3.2	3.4	3.8	9.0
300	140 mM Lysine and 140 mM Niacin	97.1	96.9	96.1	89.8	2.9	3.1	3.6	9.6
300	70 mM Arginine·HCl and 140 mM Niacinamide	97.1	96.9	96.0	89.8	2.9	3.1	3.8	9.6
300	140 mM Histidine and 140 mM Niacinamide	96.8	96.6	95.6	89.7	3.2	3.4	4.2	9.6
300	140 mM Meglumine and 140 mM Niacinamide	97.1	97.0	96.0	89.8	2.9	3.0	3.8	9.5
300	70 mM Lysine·HCl and 140 mM Niacinamide	96.7	96.6	95.7	90.5	3.3	3.4	4.0	8.9
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	96.4	96.1	94.8	89.3	3.4	3.7	5.0	9.9
300	Water (Blank), pH 5.5	95.8	95.6	94.0	87.8	4.0	4.2	5.8	11.4
200	140 mM Arginine and 140 mM Niacin	97.6	97.5	97.0	94.2	2.4	2.5	2.8	5.0
200	140 mM Histidine and 140 mM Niacin	97.5	97.5	96.9	94.1	2.5	2.5	2.9	5.1
200	140 mM Meglumine and 140 mM Niacin	97.4	97.3	96.9	93.8	2.6	2.7	3.0	5.5
200	140 mM Lysine and 140 mM Niacin	97.8	97.7	97.0	94.1	2.2	2.3	2.7	5.1
200	70 mM Arginine·HCl and 140 mM Niacinamide	97.5	97.5	96.9	94.2	2.5	2.5	2.9	5.0
200	140 mM Histidine and 140 mM Niacinamide	97.5	97.5	96.9	93.7	2.5	2.5	3.0	5.6
200	140 mM Meglumine and 140 mM Niacinamide	97.4	97.3	96.9	94.1	2.6	2.7	2.9	5.2
200	70 mM Lysine·HCl and 140 mM Niacinamide	97.7	97.7	96.9	94.3	2.3	2.3	2.8	5.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	97.2	97.1	95.9	93.4	2.7	2.8	4.0	5.9
200	Water (blank), pH 5.5	96.5	96.3	94.4	92.0	3.4	3.6	5.5	7.3
100	140 mM Arginine and 140 mM Niacin	98.1	98.0	97.6	95.2	1.9	2.0	2.1	4.3
100	140 mM Histidine and 140 mM Niacin	97.9	97.8	97.4	94.8	2.1	2.2	2.5	4.7
100	140 mM Meglumine and 140 mM Niacin	97.9	97.9	97.4	95.1	2.1	2.1	2.5	4.3
100	140 mM Lysine and 140 mM Niacin	98.1	98.1	97.7	95.4	1.9	1.9	2.2	4.1
100	70 mM Arginine·HCl and 140 mM Niacinamide	98.0	98.0	97.5	95.3	2.0	2.0	2.3	4.0
100	140 mM Histidine and 140 mM Niacinamide	98.1	98.1	97.6	95.3	1.9	1.9	2.2	4.0
100	140 mM Meglumine and 140 mM Niacinamide	98.2	98.2	97.7	95.4	1.8	1.8	2.2	3.9
100	70 mM Lysine·HCl and 140 mM Niacinamide	98.1	98.0	97.8	95.0	1.9	2.0	2.0	4.3
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	97.9	97.9	97.3	94.9	2.0	2.0	2.6	4.3
100	Water (blank), pH 5.5	97.4	97.3	96.3	93.7	2.5	2.6	3.6	5.5

Table 163 SE-UPLC results of formulated Trastuzumab-MMAE in 50 mM Succinate buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid, 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	96.7	96.6	95.9	90.1	3.3	3.4	3.9	9.2
300	300 mM Histidine and 300 mM Niacin	96.6	96.5	95.9	89.3	3.4	3.5	3.9	9.9
300	300 mM Meglumine and 300 mM Niacin	97.0	96.9	95.8	90.3	3.0	3.1	3.9	8.9
300	300 mM Lysine and 300 mM Niacin	97.0	96.9	96.3	89.7	3.0	3.1	3.4	9.6
300	140 mM Arginine·HCl and 300 mM Niacinamide	96.6	96.4	95.6	89.9	3.4	3.6	4.2	9.4
300	300 mM Histidine and 300 mM Niacinamide	96.8	96.7	95.6	90.6	3.2	3.3	4.2	8.6
300	300 mM Meglumine and 300 mM Niacinamide	96.6	96.4	95.8	90.6	3.4	3.6	3.9	8.6
300	140 mM Lysine·HCl and 300 mM Niacinamide	97.0	96.8	95.7	90.6	3.0	3.2	4.0	8.6
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	96.3	96.2	94.7	89.3	3.6	3.7	4.2	9.9
300	Water (Blank), pH 6.0	95.9	95.7	94.1	88.2	4.0	4.2	5.5	11.0
200	300 mM Arginine and 300 mM Niacin	97.4	97.4	96.1	93.7	2.6	2.6	3.6	5.6
200	300 mM Histidine and 300 mM Niacin	97.4	97.3	96.2	93.0	2.6	2.7	3.7	6.2
200	300 mM Meglumine and 300 mM Niacin	97.5	97.4	96.8	93.3	2.5	2.6	2.9	6.1
200	300 mM Lysine and 300 mM Niacin	97.4	97.4	96.4	92.9	2.6	2.6	3.5	6.4
200	140 mM Arginine·HCl and 300 mM Niacinamide	97.6	97.6	96.6	93.6	2.4	2.4	3.2	5.6
200	300 mM Histidine and 300 mM Niacinamide	97.5	97.5	96.8	94.1	2.5	2.5	2.9	5.1
200	300 mM Meglumine and 300 mM Niacinamide	97.6	97.6	96.5	93.9	2.4	2.4	3.4	5.3
200	140 mM Lysine·HCl and 300 mM Niacinamide	97.6	97.5	96.7	93.4	2.4	2.5	3.2	6.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.1	97.0	96.0	93.6	2.8	2.9	3.9	5.6
200	Water (blank), pH 6.0	96.6	96.6	95.3	91.9	3.3	3.3	4.5	7.4
100	300 mM Arginine and 300 mM Niacin	98.1	98.1	97.1	94.5	1.9	1.9	2.7	5.0
100	300 mM Histidine and 300 mM Niacin	97.8	97.7	97.2	94.5	2.2	2.3	2.7	4.8
100	300 mM Meglumine and 300 mM Niacin	98.0	98.0	97.4	94.9	2.0	2.0	2.3	4.4
100	300 mM Lysine and 300 mM Niacin	97.8	97.7	97.0	94.4	2.2	2.3	2.9	5.1
100	140 mM Arginine·HCl and 300 mM Niacinamide	97.8	97.8	97.2	94.5	2.2	2.2	2.5	4.8
100	300 mM Histidine and 300 mM Niacinamide	97.9	97.8	97.2	95.0	2.1	2.2	2.5	4.4
100	300 mM Meglumine and 300 mM Niacinamide	97.9	97.8	96.9	95.1	2.1	2.2	2.8	4.4
100	140 mM Lysine·HCl and 300 mM Niacinamide	97.9	97.8	96.9	94.4	2.1	2.2	2.8	5.1
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	97.8	97.8	97.2	94.8	2.1	2.1	2.7	4.4
100	Water (blank), pH 6.0	97.3	97.3	96.2	93.6	2.6	2.6	3.7	5.6

Example 11: Effect of viscosity-reducing and stabilizing formulations on Aflibercept stability at various temperatures.

[00113] This example tested the effect of viscosity-reducing and stabilizing formulations on Aflibercept stability and compared it with the lead formulation (25 mM Phosphate, 81.2 mM of Nicotinic acid and 29.4 mM Tryptophan) in WO2018211517.

[00114] Materials and Methods

[00115] The Aflibercept (Eylea®) samples were produced by WuXi Biologics, as described in Example 5, and formulated as shown in Tables 164-181. The prepared samples were aseptically filtered with 0.22 µm PVDF membrane filters before filling. After filtration, samples were filled with a pipette to 2 mL vials, and the fill volume was 1.0 mL. Then the vials were stoppered and sealed and subjected to 5°C, 25°C and 40°C chambers to start the stability assessment. Furthermore, there was a control group comprising 25 mM phosphate buffer at pH 6.0, with 81.2 mM Nicotinic acid and 29.4 mM Tryptophan (matching the lead formulation 25 mM phosphate buffer at pH 6.0 along with 10 mg/mL Nicotinic acid (acid form) and 6 mg/mL Tryptophan from Examples 14 and 16-21 in WO2018211517). After preparing the control group samples, the pH was adjusted to the target value using hydrochloric acid and sodium hydroxide. An additional control group, consisting solely of MilliQ water and the protein, was prepared as a blank. The pH of the blank group was also adjusted to match the target pH using the same method. To ascertain Aflibercept's concentration in the groups, absorbance at 280 nm combined with SE-UPLC was gauged against corresponding buffers containing a viscosity-reducing and stabilizing agent for excipient-containing samples, and absorbance at 280 nm was measured for the protein solution without a viscosity-reducing and stabilizing formulation. For Aflibercept without excipients, the buffer alone (i.e., devoid of excipients) served as a blank for protein concentration calculation. The extinction coefficient was measured at $1.15 \text{ (mg/mL)}^{-1} \cdot \text{cm}^{-1}$.

[00116] The test for protein stability was carried out over a 4-week period by SE-UPLC. Samples were prepared as described above. As shown in Tables 164-181, after 4 weeks, the monomer content of Aflibercept at a concentration of 100 to 300 mg/mL formulated with the tested viscosity-reducing and stabilizing formulations was higher than 95% even at 40°C, comparable or better than the lead formulation in WO2018211517, regardless of the used buffers, indicating good stabilization effect of the tested viscosity-reducing and stabilizing formulations.

Table 164 SE-UPLC results of formulated Aflibercept in 5 mM Histidine buffer, pH 5.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	98.8	98.8	98.4	97.1	1.2	1.2	1.6	2.7
300	30 mM Histidine and 30 mM Niacin	98.8	98.8	98.4	97.2	1.2	1.2	1.6	2.7
300	30 mM Meglumine and 30 mM Niacin	98.8	98.8	98.3	97.4	1.2	1.2	1.6	2.5
300	30 mM Lysine and 30 mM Niacin	98.9	98.9	98.6	97.0	1.1	1.1	1.3	2.9
300	30 mM Arginine-HCl and 30 mM Niacinamide	98.9	98.9	98.6	97.7	1.1	1.1	1.3	2.2
300	30 mM Histidine and 30 mM Niacinamide	98.6	98.6	98.2	96.7	1.4	1.4	1.8	3.2
300	30 mM Meglumine and 30 mM Niacinamide	98.6	98.6	98.1	97.1	1.4	1.4	1.8	2.7
300	30 mM Lysine-HCl and 30 mM Niacinamide	98.8	98.8	98.3	97.7	1.2	1.2	1.7	2.2
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	98.6	98.6	98.1	96.7	1.4	1.4	1.8	3.2
300	Water (Blank), pH 5.0	98.6	98.5	97.9	95.8	1.4	1.5	1.9	3.7
200	30 mM Arginine and 30 mM Niacin	98.8	98.8	98.5	97.8	1.2	1.2	1.5	2.2
200	30 mM Histidine and 30 mM Niacin	98.8	98.8	98.6	97.9	1.2	1.2	1.4	1.9
200	30 mM Meglumine and 30 mM Niacin	99.1	99.1	98.8	98.4	0.9	0.9	1.1	1.5
200	30 mM Lysine and 30 mM Niacin	99.1	99.1	99.0	98.4	0.9	0.9	1.0	1.6
200	30 mM Arginine-HCl and 30 mM Niacinamide	98.9	98.9	98.7	98.3	1.1	1.1	1.3	1.5
200	30 mM Histidine and 30 mM Niacinamide	99.0	99.0	98.7	98.4	1.0	1.0	1.2	1.6
200	30 mM Meglumine and 30 mM Niacinamide	98.9	98.9	98.6	97.9	1.1	1.1	1.3	1.9
200	30 mM Lysine-HCl and 30 mM Niacinamide	98.8	98.8	98.6	98.2	1.2	1.2	1.3	1.7
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	98.8	98.8	98.5	97.7	1.2	1.2	1.5	2.2
200	Water (Blank), pH 5.0	98.8	98.8	98.3	97.3	1.2	1.2	1.7	2.5
100	30 mM Arginine and 30 mM Niacin	99.1	99.1	98.9	98.0	0.9	0.9	1.1	1.9
100	30 mM Histidine and 30 mM Niacin	99.1	99.1	98.9	97.7	0.9	0.9	1.0	2.2
100	30 mM Meglumine and 30 mM Niacin	99.0	99.0	98.8	97.8	1.0	1.0	1.2	2.1
100	30 mM Lysine and 30 mM Niacin	99.1	99.1	98.9	98.0	0.9	0.9	1.0	2.0
100	30 mM Arginine-HCl and 30 mM Niacinamide	99.2	99.2	99.0	97.9	0.8	0.8	0.9	2.1
100	30 mM Histidine and 30 mM Niacinamide	99.1	99.1	99.0	98.0	0.9	0.9	1.0	2.0
100	30 mM Meglumine and 30 mM Niacinamide	98.9	98.9	98.8	97.5	1.1	1.1	1.1	2.5
100	30 mM Lysine-HCl and 30 mM Niacinamide	99.0	99.0	98.8	97.8	1.0	1.0	1.2	2.2
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	98.9	98.9	98.7	98.4	1.1	1.1	1.3	1.5
100	Water (Blank), pH 5.0	98.9	98.9	98.6	97.9	1.1	1.1	1.3	1.9

Table 165 SE-UPLC results of formulated Aflibercept in 20 mM Histidine buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	99.0	99.0	98.6	97.6	1.0	1.0	1.4	2.2
300	140 mM Histidine and 140 mM Niacin	98.8	98.8	98.3	97.2	1.2	1.2	1.6	2.6
300	140 mM Meglumine and 140 mM Niacin	98.8	98.8	98.4	97.3	1.2	1.2	1.5	2.6
300	140 mM Lysine and 140 mM Niacin	99.0	99.0	98.6	97.9	1.0	1.0	1.4	1.9
300	70 mM Arginine·HCl and 140 mM Niacinamide	98.7	98.7	98.3	97.3	1.3	1.3	1.7	2.6
300	140 mM Histidine and 140 mM Niacinamide	98.7	98.7	98.4	97.4	1.3	1.3	1.6	2.4
300	140 mM Meglumine and 140 mM Niacinamide	98.8	98.8	98.5	97.1	1.2	1.2	1.4	2.8
300	70 mM Lysine·HCl and 140 mM Niacinamide	98.7	98.7	98.3	96.9	1.3	1.3	1.6	2.9
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	98.7	98.7	98.2	96.9	1.3	1.3	1.8	2.9
300	Water (Blank), pH 6.0	98.5	98.5	98.0	95.6	1.5	1.5	1.8	4.0
200	140 mM Arginine and 140 mM Niacin	98.7	98.7	98.5	97.9	1.3	1.3	1.4	2.0
200	140 mM Histidine and 140 mM Niacin	98.7	98.7	98.4	98.1	1.3	1.3	1.5	1.9
200	140 mM Meglumine and 140 mM Niacin	98.8	98.8	98.6	98.1	1.2	1.2	1.4	1.8
200	140 mM Lysine and 140 mM Niacin	99.0	99.0	98.8	98.4	1.0	1.0	1.1	1.4
200	70 mM Arginine·HCl and 140 mM Niacinamide	98.9	98.9	98.6	98.0	1.1	1.1	1.4	1.9
200	140 mM Histidine and 140 mM Niacinamide	99.0	99.0	98.7	98.1	1.0	1.0	1.2	1.9
200	140 mM Meglumine and 140 mM Niacinamide	99.0	99.0	98.9	98.2	1.0	1.0	1.0	1.8
200	70 mM Lysine·HCl and 140 mM Niacinamide	98.7	98.7	98.4	98.0	1.3	1.3	1.6	2.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	98.7	98.7	98.5	97.5	1.3	1.3	1.4	2.4
200	Water (Blank), pH 6.0	98.6	98.6	98.4	97.1	1.4	1.4	1.6	2.7
100	140 mM Arginine and 140 mM Niacin	98.8	98.8	98.7	97.4	1.2	1.2	1.4	2.6
100	140 mM Histidine and 140 mM Niacin	98.9	98.9	98.7	97.7	1.1	1.1	1.2	2.3
100	140 mM Meglumine and 140 mM Niacin	99.0	99.0	98.9	97.9	1.0	1.0	1.1	2.0
100	140 mM Lysine and 140 mM Niacin	98.9	98.9	98.8	97.7	1.1	1.1	1.2	2.2
100	70 mM Arginine·HCl and 140 mM Niacinamide	98.9	98.9	98.7	97.5	1.1	1.1	1.3	2.4
100	140 mM Histidine and 140 mM Niacinamide	99.0	99.0	98.9	97.6	1.0	1.0	1.1	2.4
100	140 mM Meglumine and 140 mM Niacinamide	99.1	99.1	99.0	97.7	0.9	0.9	1.0	2.2
100	70 mM Lysine·HCl and 140 mM Niacinamide	98.8	98.8	98.6	97.5	1.2	1.2	1.5	2.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	98.8	98.8	98.7	98.1	1.2	1.2	1.3	1.8
100	Water (Blank), pH 6.0	98.8	98.8	98.6	97.8	1.2	1.2	1.4	2.0

Table 166 SE-UPLC results of formulated Aflibercept in 50 mM Histidine buffer, pH 7.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C C	40°C C	T0	5°C	25°C C	40°C C
300	300 mM Arginine and 300 mM Niacin	98.6	98.6	98.1	96.3	1.4	1.4	1.9	3.6
300	300 mM Histidine and 300 mM Niacin	98.8	98.8	98.5	96.4	1.2	1.2	1.5	3.5
300	300 mM Meglumine and 300 mM Niacin	98.7	98.7	98.3	96.5	1.3	1.3	1.6	3.3
300	300 mM Lysine and 300 mM Niacin	98.8	98.8	98.3	96.4	1.2	1.2	1.6	3.5
300	140 mM Arginine·HCl and 300 mM Niacinamide	98.8	98.8	98.3	96.5	1.2	1.2	1.6	3.4
300	300 mM Histidine and 300 mM Niacinamide	98.9	98.9	98.4	96.5	1.1	1.1	1.6	3.4
300	300 mM Meglumine and 300 mM Niacinamide	98.6	98.6	98.3	96.5	1.4	1.4	1.6	3.4
300	140 mM Lysine·HCl and 300 mM Niacinamide	98.6	98.6	98.2	96.8	1.4	1.4	1.8	3.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	98.6	98.6	98.4	96.0	1.4	1.4	1.6	3.8
300	Water (Blank), pH 7.0	98.4	98.4	98.1	94.7	1.6	1.6	1.9	5.0
200	300 mM Arginine and 300 mM Niacin	98.6	98.6	98.3	96.8	1.4	1.4	1.7	3.0
200	300 mM Histidine and 300 mM Niacin	98.8	98.8	98.6	97.4	1.2	1.2	1.3	2.5
200	300 mM Meglumine and 300 mM Niacin	98.8	98.8	98.5	97.1	1.2	1.2	1.5	2.9
200	300 mM Lysine and 300 mM Niacin	98.7	98.7	98.4	97.2	1.3	1.3	1.6	2.8
200	140 mM Arginine·HCl and 300 mM Niacinamide	98.9	98.9	98.7	96.8	1.1	1.1	1.3	3.1
200	300 mM Histidine and 300 mM Niacinamide	98.6	98.6	98.3	96.6	1.4	1.4	1.7	3.4
200	300 mM Meglumine and 300 mM Niacinamide	98.6	98.6	98.5	97.1	1.4	1.4	1.4	2.8
200	140 mM Lysine·HCl and 300 mM Niacinamide	98.9	98.9	98.8	97.6	1.1	1.1	1.2	2.4
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	98.6	98.6	98.5	96.4	1.4	1.4	1.5	3.5
200	Water (blank), pH 7.0	98.5	98.5	98.3	95.8	1.5	1.5	1.7	4.0
100	300 mM Arginine and 300 mM Niacin	98.9	98.9	98.8	98.0	1.1	1.1	1.2	2.0
100	300 mM Histidine and 300 mM Niacin	98.8	98.8	98.6	97.5	1.2	1.2	1.4	2.4
100	300 mM Meglumine and 300 mM Niacin	99.0	99.0	98.9	98.2	1.0	1.0	1.0	1.8
100	300 mM Lysine and 300 mM Niacin	98.8	98.8	98.6	97.5	1.2	1.2	1.4	2.4
100	140 mM Arginine·HCl and 300 mM Niacinamide	98.8	98.8	98.7	97.7	1.2	1.2	1.2	2.2
100	300 mM Histidine and 300 mM Niacinamide	99.0	99.0	98.9	97.8	1.0	1.0	1.1	2.2
100	300 mM Meglumine and 300 mM Niacinamide	98.8	98.8	98.6	97.5	1.2	1.2	1.3	2.5
100	140 mM Lysine·HCl and 300 mM Niacinamide	98.9	98.9	98.7	97.7	1.1	1.1	1.3	2.3
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	98.7	98.7	98.6	97.0	1.3	1.3	1.4	2.9
100	Water (blank), pH 7.0	98.7	98.7	98.4	96.7	1.3	1.3	1.6	3.1

Table 167 SE-UPLC results of formulated Aflibercept in 5 mM Acetate buffer, pH 4.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	98.8	98.8	98.4	97.7	1.2	1.2	1.6	2.1
300	30 mM Histidine and 30 mM Niacin	98.7	98.7	98.4	97.5	1.3	1.3	1.6	2.3
300	30 mM Meglumine and 30 mM Niacin	98.8	98.8	98.4	97.3	1.2	1.2	1.5	2.5
300	30 mM Lysine and 30 mM Niacin	98.8	98.8	98.4	97.4	1.2	1.2	1.6	2.5
300	30 mM Arginine·HCl and 30 mM Niacinamide	98.7	98.7	98.3	97.2	1.3	1.3	1.7	2.7
300	30 mM Histidine and 30 mM Niacinamide	98.6	98.6	98.3	96.7	1.4	1.4	1.6	3.2
300	30 mM Meglumine and 30 mM Niacinamide	98.7	98.7	98.3	97.2	1.3	1.3	1.7	2.6
300	30 mM Lysine·HCl and 30 mM Niacinamide	98.8	98.8	98.5	97.0	1.2	1.2	1.5	2.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	98.4	98.3	97.2	95.0	1.6	1.7	2.7	4.8
300	Water (Blank), pH 4.5	98.5	98.5	98.3	95.8	1.4	1.4	1.7	3.9
200	30 mM Arginine and 30 mM Niacin	98.8	98.8	98.6	97.7	1.2	1.2	1.4	2.1
200	30 mM Histidine and 30 mM Niacin	99.0	99.0	98.7	98.3	1.0	1.0	1.3	1.5
200	30 mM Meglumine and 30 mM Niacin	98.9	98.9	98.8	97.9	1.1	1.1	1.2	1.9
200	30 mM Lysine and 30 mM Niacin	98.8	98.8	98.6	98.1	1.2	1.2	1.3	1.7
200	30 mM Arginine·HCl and 30 mM Niacinamide	98.8	98.8	98.7	98.0	1.2	1.2	1.2	1.8
200	30 mM Histidine and 30 mM Niacinamide	98.8	98.8	98.6	98.0	1.2	1.2	1.3	1.9
200	30 mM Meglumine and 30 mM Niacinamide	98.9	98.9	98.7	98.3	1.1	1.1	1.3	1.6
200	30 mM Lysine·HCl and 30 mM Niacinamide	99.0	99.0	98.7	98.0	1.0	1.0	1.3	1.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	98.5	98.3	97.8	96.4	1.5	1.7	2.1	3.5
200	Water (blank), pH 4.5	98.6	98.6	98.4	96.6	1.3	1.3	1.5	2.4
100	30 mM Arginine and 30 mM Niacin	99.1	99.1	99.0	98.0	0.9	0.9	1.0	1.8
100	30 mM Histidine and 30 mM Niacin	99.2	99.2	98.9	98.1	0.8	0.8	1.1	1.7
100	30 mM Meglumine and 30 mM Niacin	99.2	99.2	99.1	98.1	0.8	0.8	0.9	1.7
100	30 mM Lysine and 30 mM Niacin	99.1	99.1	98.8	98.2	0.9	0.9	1.2	1.6
100	30 mM Arginine·HCl and 30 mM Niacinamide	99.1	99.1	99.0	98.1	0.9	0.9	0.9	1.7
100	30 mM Histidine and 30 mM Niacinamide	99.1	99.1	99.0	98.2	0.9	0.9	0.9	1.6
100	30 mM Meglumine and 30 mM Niacinamide	99.1	99.1	98.8	98.0	0.9	0.9	1.1	1.8
100	30 mM Lysine·HCl and 30 mM Niacinamide	98.9	98.9	98.8	98.2	1.1	1.1	1.2	1.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	98.7	98.7	98.5	97.3	1.3	1.3	1.5	2.6
100	Water (blank), pH 4.5	98.8	98.8	98.7	97.7	1.2	1.2	1.3	2.1

Table 168 SE-UPLC results of formulated Aflibercept in 20 mM Acetate buffer, pH 5.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	98.8	98.8	98.4	97.1	1.2	1.2	1.6	2.7
300	140 mM Histidine and 140 mM Niacin	98.7	98.7	98.4	97.1	1.3	1.3	1.5	2.7
300	140 mM Meglumine and 140 mM Niacin	98.8	98.8	98.5	97.4	1.2	1.2	1.5	2.4
300	140 mM Lysine and 140 mM Niacin	98.9	98.9	98.5	97.3	1.1	1.1	1.4	2.5
300	70 mM Arginine·HCl and 140 mM Niacinamide	98.6	98.6	98.2	97.3	1.4	1.4	1.7	2.6
300	140 mM Histidine and 140 mM Niacinamide	98.8	98.8	98.3	97.2	1.2	1.2	1.6	2.7
300	140 mM Meglumine and 140 mM Niacinamide	98.7	98.7	98.3	97.5	1.3	1.3	1.6	2.4
300	70 mM Lysine·HCl and 140 mM Niacinamide	98.8	98.8	98.4	97.4	1.2	1.2	1.5	2.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	98.6	98.6	98.1	96.7	1.4	1.4	1.8	3.2
300	Water (Blank), pH 5.0	98.6	98.5	97.9	95.8	1.4	1.5	1.9	3.7
200	140 mM Arginine and 140 mM Niacin	99.0	99.0	98.7	98.1	1.0	1.0	1.3	1.8
200	140 mM Histidine and 140 mM Niacin	98.8	98.8	98.7	97.9	1.2	1.2	1.2	1.9
200	140 mM Meglumine and 140 mM Niacin	98.9	98.9	98.7	97.8	1.1	1.1	1.3	2.2
200	140 mM Lysine and 140 mM Niacin	99.1	99.1	98.9	98.4	0.9	0.9	1.1	1.5
200	70 mM Arginine·HCl and 140 mM Niacinamide	98.8	98.8	98.5	98.1	1.2	1.2	1.4	1.9
200	140 mM Histidine and 140 mM Niacinamide	98.8	98.8	98.7	97.9	1.2	1.2	1.2	2.0
200	140 mM Meglumine and 140 mM Niacinamide	98.9	98.9	98.6	97.9	1.1	1.1	1.4	2.0
200	70 mM Lysine·HCl and 140 mM Niacinamide	98.9	98.9	98.7	97.9	1.1	1.1	1.2	1.9
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.0	98.8	98.8	98.5	97.7	1.2	1.2	1.5	2.2
200	Water (Blank), pH 5.0	98.8	98.8	98.3	97.3	1.2	1.2	1.7	2.5
100	140 mM Arginine and 140 mM Niacin	99.0	99.0	98.9	97.6	1.0	1.0	1.0	2.3
100	140 mM Histidine and 140 mM Niacin	98.9	98.9	98.8	97.6	1.1	1.1	1.1	2.3
100	140 mM Meglumine and 140 mM Niacin	99.1	99.1	99.0	97.7	0.9	0.9	1.1	2.2
100	140 mM Lysine and 140 mM Niacin	99.0	99.0	98.9	97.8	1.0	1.0	1.1	2.2
100	70 mM Arginine·HCl and 140 mM Niacinamide	99.2	99.2	99.0	97.8	0.8	0.8	1.0	2.2
100	140 mM Histidine and 140 mM Niacinamide	99.1	99.1	99.0	98.0	0.9	0.9	0.9	2.0
100	140 mM Meglumine and 140 mM Niacinamide	99.1	99.1	98.9	97.7	0.9	0.9	1.2	2.2
100	70 mM Lysine·HCl and 140 mM Niacinamide	99.0	99.0	98.9	97.6	1.0	1.0	1.1	2.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	98.9	98.9	98.7	98.4	1.1	1.1	1.3	1.5
100	Water (Blank), pH 5.0	98.9	98.9	98.6	97.9	1.1	1.1	1.3	1.9

Table 169 SE-UPLC results of formulated Aflibercept in 50 mM Acetate buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	99.0	99.0	98.6	97.6	1.0	1.0	1.3	2.2
300	300 mM Histidine and 300 mM Niacin	98.7	98.7	98.4	97.2	1.3	1.3	1.6	2.7
300	300 mM Meglumine and 300 mM Niacin	98.8	98.8	98.5	97.2	1.2	1.2	1.5	2.7
300	300 mM Lysine and 300 mM Niacin	98.7	98.7	98.4	97.3	1.3	1.3	1.6	2.6
300	140 mM Arginine·HCl and 300 mM Niacinamide	98.8	98.8	98.5	97.7	1.2	1.2	1.4	2.2
300	300 mM Histidine and 300 mM Niacinamide	99.0	99.0	98.6	97.4	1.0	1.0	1.4	2.5
300	300 mM Meglumine and 300 mM Niacinamide	98.8	98.8	98.5	97.2	1.2	1.2	1.5	2.7
300	140 mM Lysine·HCl and 300 mM Niacinamide	98.9	98.9	98.6	97.0	1.1	1.1	1.4	2.8
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	98.7	98.7	98.2	96.9	1.3	1.3	1.8	2.9
300	Water (Blank), pH 6.0	98.5	98.5	98.0	95.6	1.5	1.5	1.8	4.0
200	300 mM Arginine and 300 mM Niacin	98.8	98.8	98.5	97.9	1.2	1.2	1.4	2.0
200	300 mM Histidine and 300 mM Niacin	98.8	98.8	98.7	98.0	1.2	1.2	1.2	1.8
200	300 mM Meglumine and 300 mM Niacin	99.0	99.0	98.9	98.0	1.0	1.0	1.1	1.8
200	300 mM Lysine and 300 mM Niacin	98.9	98.9	98.6	98.1	1.1	1.1	1.4	1.8
200	140 mM Arginine·HCl and 300 mM Niacinamide	99.0	99.0	98.7	97.9	1.0	1.0	1.2	2.0
200	300 mM Histidine and 300 mM Niacinamide	98.7	98.7	98.4	98.1	1.3	1.3	1.6	1.7
200	300 mM Meglumine and 300 mM Niacinamide	99.0	99.0	98.7	98.3	1.0	1.0	1.3	1.5
200	140 mM Lysine·HCl and 300 mM Niacinamide	98.7	98.7	98.5	98.0	1.3	1.3	1.5	1.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	98.7	98.7	98.5	97.5	1.3	1.3	1.4	2.4
200	Water (blank), pH 6.0	98.6	98.6	98.4	97.1	1.4	1.4	1.6	2.7
100	300 mM Arginine and 300 mM Niacin	99.0	99.0	98.8	97.9	1.0	1.0	1.3	2.0
100	300 mM Histidine and 300 mM Niacin	99.0	99.0	98.9	97.8	1.0	1.0	1.1	2.1
100	300 mM Meglumine and 300 mM Niacin	99.1	99.1	98.9	97.7	0.9	0.9	1.1	2.3
100	300 mM Lysine and 300 mM Niacin	98.9	98.9	98.8	97.7	1.1	1.1	1.3	2.3
100	140 mM Arginine·HCl and 300 mM Niacinamide	99.0	99.0	98.8	97.7	1.0	1.0	1.1	2.2
100	300 mM Histidine and 300 mM Niacinamide	99.0	99.0	98.8	97.6	1.0	1.0	1.2	2.4
100	300 mM Meglumine and 300 mM Niacinamide	98.8	98.8	98.7	97.6	1.2	1.2	1.2	2.3
100	140 mM Lysine·HCl and 300 mM Niacinamide	98.8	98.8	98.6	97.4	1.2	1.2	1.4	2.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	98.8	98.8	98.7	98.1	1.2	1.2	1.3	1.8
100	Water (blank), pH 6.0	98.8	98.8	98.6	97.8	1.2	1.2	1.4	2.0

Table 170 SE-UPLC results of formulated Aflibercept in 5 mM Citrate buffer, pH 4.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	98.7	98.7	98.4	97.0	1.3	1.3	1.6	2.8
300	30 mM Histidine and 30 mM Niacin	98.6	98.6	98.2	97.4	1.4	1.4	1.7	2.4
300	30 mM Meglumine and 30 mM Niacin	98.9	98.9	98.5	97.0	1.1	1.1	1.4	2.8
300	30 mM Lysine and 30 mM Niacin	98.8	98.8	98.3	97.7	1.2	1.2	1.7	2.2
300	30 mM Arginine-HCl and 30 mM Niacinamide	98.8	98.8	98.4	97.5	1.2	1.2	1.5	2.3
300	30 mM Histidine and 30 mM Niacinamide	98.6	98.6	98.1	97.0	1.4	1.4	1.8	2.8
300	30 mM Meglumine and 30 mM Niacinamide	98.9	98.9	98.6	97.0	1.1	1.1	1.4	2.9
300	30 mM Lysine-HCl and 30 mM Niacinamide	98.8	98.8	98.4	97.1	1.2	1.2	1.6	2.7
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	98.4	98.3	97.2	95.0	1.6	1.7	2.7	4.8
300	Water (Blank), pH 4.5	98.5	98.5	98.3	95.8	1.4	1.4	1.7	3.9
200	30 mM Arginine and 30 mM Niacin	99.0	99.0	98.9	98.0	1.0	1.0	1.0	1.9
200	30 mM Histidine and 30 mM Niacin	98.8	98.8	98.5	97.7	1.2	1.2	1.5	2.2
200	30 mM Meglumine and 30 mM Niacin	99.0	99.0	98.7	97.9	1.0	1.0	1.2	2.0
200	30 mM Lysine and 30 mM Niacin	98.9	98.9	98.6	98.0	1.1	1.1	1.4	1.8
200	30 mM Arginine-HCl and 30 mM Niacinamide	99.0	99.0	98.8	98.4	1.0	1.0	1.1	1.5
200	30 mM Histidine and 30 mM Niacinamide	98.9	98.9	98.8	98.0	1.1	1.1	1.2	1.9
200	30 mM Meglumine and 30 mM Niacinamide	99.0	99.0	98.7	98.3	1.0	1.0	1.3	1.5
200	30 mM Lysine-HCl and 30 mM Niacinamide	98.7	98.7	98.5	97.8	1.3	1.3	1.5	2.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	98.5	98.3	97.8	96.4	1.5	1.7	2.1	3.5
200	Water (blank), pH 4.5	98.6	98.6	98.4	96.6	1.3	1.3	1.5	2.4
100	30 mM Arginine and 30 mM Niacin	99.2	99.2	98.9	98.3	0.8	0.8	1.1	1.6
100	30 mM Histidine and 30 mM Niacin	98.9	98.9	98.8	98.2	1.1	1.1	1.2	1.6
100	30 mM Meglumine and 30 mM Niacin	98.9	98.9	98.6	98.1	1.1	1.1	1.3	1.7
100	30 mM Lysine and 30 mM Niacin	98.9	98.9	98.6	98.1	1.1	1.1	1.4	1.8
100	30 mM Arginine-HCl and 30 mM Niacinamide	99.0	99.0	98.9	98.2	1.0	1.0	1.1	1.7
100	30 mM Histidine and 30 mM Niacinamide	99.2	99.2	99.1	98.6	0.8	0.8	0.8	1.3
100	30 mM Meglumine and 30 mM Niacinamide	99.0	99.0	98.9	97.9	1.0	1.0	1.0	2.0
100	30 mM Lysine-HCl and 30 mM Niacinamide	99.1	99.1	98.8	98.3	0.9	0.9	1.1	1.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	98.7	98.7	98.5	97.3	1.3	1.3	1.5	2.6
100	Water (blank), pH 4.5	98.8	98.8	98.7	97.7	1.2	1.2	1.3	2.1

Table 171 SE-UPLC results of formulated Aflibercept in 20 mM Citrate buffer, pH 5.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	98.6	98.6	98.3	97.4	1.4	1.4	1.6	2.4
300	140 mM Histidine and 140 mM Niacin	98.6	98.6	98.2	96.9	1.4	1.4	1.7	3.0
300	140 mM Meglumine and 140 mM Niacin	98.5	98.5	98.0	96.9	1.5	1.5	1.9	2.9
300	140 mM Lysine and 140 mM Niacin	98.7	98.7	98.3	97.4	1.3	1.3	1.7	2.5
300	70 mM Arginine·HCl and 140 mM Niacinamide	98.6	98.6	98.3	97.4	1.4	1.4	1.6	2.5
300	140 mM Histidine and 140 mM Niacinamide	98.5	98.5	98.0	97.4	1.5	1.5	2.0	2.4
300	140 mM Meglumine and 140 mM Niacinamide	98.7	98.7	98.4	97.5	1.3	1.3	1.5	2.4
300	70 mM Lysine·HCl and 140 mM Niacinamide	98.5	98.5	98.2	97.1	1.5	1.5	1.7	2.7
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	98.5	98.5	98.0	96.9	1.5	1.5	1.9	3.0
300	Water (Blank), pH 5.5	98.4	98.4	97.9	95.6	1.6	1.6	2.0	4.2
200	140 mM Arginine and 140 mM Niacin	98.8	98.8	98.5	98.2	1.2	1.2	1.4	1.6
200	140 mM Histidine and 140 mM Niacin	98.8	98.8	98.5	98.2	1.2	1.2	1.4	1.6
200	140 mM Meglumine and 140 mM Niacin	98.6	98.6	98.5	97.6	1.4	1.4	1.4	2.3
200	140 mM Lysine and 140 mM Niacin	98.7	98.7	98.4	97.6	1.3	1.3	1.5	2.2
200	70 mM Arginine·HCl and 140 mM Niacinamide	98.9	98.9	98.6	97.8	1.1	1.1	1.3	2.0
200	140 mM Histidine and 140 mM Niacinamide	98.9	98.9	98.8	98.3	1.1	1.1	1.1	1.6
200	140 mM Meglumine and 140 mM Niacinamide	98.7	98.7	98.5	97.9	1.3	1.3	1.4	2.0
200	70 mM Lysine·HCl and 140 mM Niacinamide	98.7	98.7	98.6	97.7	1.3	1.3	1.3	2.2
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	98.6	98.6	98.4	97.5	1.4	1.4	1.6	2.4
200	Water (blank), pH 5.5	98.4	98.4	98.1	96.8	1.6	1.6	1.9	3.0
100	140 mM Arginine and 140 mM Niacin	99.1	99.1	98.9	98.5	0.9	0.9	1.1	1.4
100	140 mM Histidine and 140 mM Niacin	99.1	99.1	98.8	98.5	0.9	0.9	1.2	1.4
100	140 mM Meglumine and 140 mM Niacin	99.0	99.0	98.9	98.1	1.0	1.0	1.0	1.7
100	140 mM Lysine and 140 mM Niacin	99.0	99.0	98.7	98.2	1.0	1.0	1.2	1.6
100	70 mM Arginine·HCl and 140 mM Niacinamide	98.9	98.9	98.6	98.2	1.1	1.1	1.4	1.6
100	140 mM Histidine and 140 mM Niacinamide	98.9	98.9	98.7	97.8	1.1	1.1	1.3	2.0
100	140 mM Meglumine and 140 mM Niacinamide	99.1	99.1	98.8	98.0	0.9	0.9	1.2	1.8
100	70 mM Lysine·HCl and 140 mM Niacinamide	99.1	99.1	99.0	98.5	0.9	0.9	0.9	1.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	98.8	98.8	98.6	98.0	1.2	1.2	1.4	1.9
100	Water (blank), pH 5.5	98.9	98.9	98.7	97.8	1.1	1.1	1.3	2.0

Table 172 SE-UPLC results of formulated Aflibercept in 50 mM Citrate buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	98.7	98.7	98.2	97.2	1.3	1.3	1.8	2.7
300	300 mM Histidine and 300 mM Niacin	99.0	99.0	98.6	97.1	1.0	1.0	1.3	2.7
300	300 mM Meglumine and 300 mM Niacin	98.7	98.7	98.4	97.0	1.3	1.3	1.5	2.8
300	300 mM Lysine and 300 mM Niacin	98.7	98.7	98.2	97.5	1.3	1.3	1.8	2.3
300	140 mM Arginine·HCl and 300 mM Niacinamide	98.7	98.7	98.3	97.0	1.3	1.3	1.7	2.9
300	300 mM Histidine and 300 mM Niacinamide	98.9	98.9	98.4	97.2	1.1	1.1	1.5	2.7
300	300 mM Meglumine and 300 mM Niacinamide	98.9	98.9	98.4	97.2	1.1	1.1	1.5	2.7
300	140 mM Lysine·HCl and 300 mM Niacinamide	98.8	98.8	98.3	97.4	1.2	1.2	1.6	2.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	98.7	98.7	98.2	96.9	1.3	1.3	1.8	2.9
300	Water (Blank), pH 6.0	98.5	98.5	98.0	95.6	1.5	1.5	1.8	4.0
200	300 mM Arginine and 300 mM Niacin	98.7	98.7	98.4	97.8	1.3	1.3	1.5	2.0
200	300 mM Histidine and 300 mM Niacin	98.8	98.8	98.5	98.1	1.2	1.2	1.5	1.8
200	300 mM Meglumine and 300 mM Niacin	98.7	98.7	98.6	97.8	1.3	1.3	1.3	2.1
200	300 mM Lysine and 300 mM Niacin	98.8	98.8	98.7	97.9	1.2	1.2	1.2	1.9
200	140 mM Arginine·HCl and 300 mM Niacinamide	98.9	98.9	98.8	98.3	1.1	1.1	1.2	1.5
200	300 mM Histidine and 300 mM Niacinamide	98.9	98.9	98.6	98.1	1.1	1.1	1.3	1.8
200	300 mM Meglumine and 300 mM Niacinamide	98.7	98.7	98.5	97.9	1.3	1.3	1.4	1.9
200	140 mM Lysine·HCl and 300 mM Niacinamide	98.9	98.9	98.7	98.0	1.1	1.1	1.2	1.8
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	98.7	98.7	98.5	97.5	1.3	1.3	1.4	2.4
200	Water (blank), pH 6.0	98.6	98.6	98.4	97.1	1.4	1.4	1.6	2.7
100	300 mM Arginine and 300 mM Niacin	98.9	98.9	98.8	97.6	1.1	1.1	1.2	2.3
100	300 mM Histidine and 300 mM Niacin	99.0	99.0	98.8	97.9	1.0	1.0	1.1	2.0
100	300 mM Meglumine and 300 mM Niacin	99.1	99.1	98.9	97.8	0.9	0.9	1.0	2.2
100	300 mM Lysine and 300 mM Niacin	98.8	98.8	98.6	97.6	1.2	1.2	1.4	2.4
100	140 mM Arginine·HCl and 300 mM Niacinamide	99.0	99.0	98.8	97.7	1.0	1.0	1.1	2.2
100	300 mM Histidine and 300 mM Niacinamide	99.1	99.1	98.9	98.0	0.9	0.9	1.1	1.9
100	300 mM Meglumine and 300 mM Niacinamide	98.9	98.9	98.8	97.8	1.1	1.1	1.1	2.2
100	140 mM Lysine·HCl and 300 mM Niacinamide	98.8	98.8	98.7	97.5	1.2	1.2	1.2	2.4
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	98.8	98.8	98.7	98.1	1.2	1.2	1.3	1.8
100	Water (blank), pH 6.0	98.8	98.8	98.6	97.8	1.2	1.2	1.4	2.0

Table 173 SE-UPLC results of formulated Aflibercept in 5 mM Phosphate buffer, pH 6.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	98.8	98.8	98.4	96.5	1.2	1.2	1.5	3.4
300	30 mM Histidine and 30 mM Niacin	98.8	98.8	98.3	96.6	1.2	1.2	1.7	3.3
300	30 mM Meglumine and 30 mM Niacin	98.6	98.6	98.0	96.9	1.4	1.4	2.0	3.0
300	30 mM Lysine and 30 mM Niacin	98.8	98.8	98.3	97.0	1.2	1.2	1.6	3.0
300	30 mM Arginine-HCl and 30 mM Niacinamide	98.7	98.7	98.4	97.1	1.3	1.3	1.6	2.8
300	30 mM Histidine and 30 mM Niacinamide	98.7	98.7	98.2	96.2	1.3	1.3	1.7	3.8
300	30 mM Meglumine and 30 mM Niacinamide	98.7	98.7	98.2	96.6	1.3	1.3	1.8	3.4
300	30 mM Lysine-HCl and 30 mM Niacinamide	98.6	98.6	98.1	96.5	1.4	1.4	1.8	3.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	98.5	98.5	97.9	95.9	1.5	1.5	2.1	4.0
300	Water (Blank), pH 6.5	98.3	98.3	97.5	94.5	1.7	1.7	2.5	5.8
200	30 mM Arginine and 30 mM Niacin	98.6	98.6	98.5	96.6	1.4	1.4	1.4	3.4
200	30 mM Histidine and 30 mM Niacin	98.6	98.6	98.4	97.2	1.4	1.4	1.6	2.7
200	30 mM Meglumine and 30 mM Niacin	98.6	98.6	98.3	96.8	1.4	1.4	1.6	3.0
200	30 mM Lysine and 30 mM Niacin	98.9	98.9	98.8	97.0	1.1	1.1	1.1	2.8
200	30 mM Arginine-HCl and 30 mM Niacinamide	98.8	98.8	98.6	97.0	1.2	1.2	1.3	3.0
200	30 mM Histidine and 30 mM Niacinamide	98.8	98.8	98.7	96.6	1.2	1.2	1.3	3.2
200	30 mM Meglumine and 30 mM Niacinamide	98.6	98.6	98.5	96.9	1.4	1.4	1.4	2.9
200	30 mM Lysine-HCl and 30 mM Niacinamide	98.7	98.7	98.6	96.8	1.3	1.3	1.4	3.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	98.6	98.6	98.3	96.2	1.4	1.4	1.7	3.7
200	Water (blank), pH 6.5	98.4	98.4	98.0	95.3	1.6	1.6	1.9	4.6
100	30 mM Arginine and 30 mM Niacin	99.1	99.1	99.0	97.9	0.9	0.9	1.0	2.1
100	30 mM Histidine and 30 mM Niacin	99.0	99.0	98.8	97.4	1.0	1.0	1.2	2.5
100	30 mM Meglumine and 30 mM Niacin	99.1	99.1	99.0	97.6	0.9	0.9	1.1	2.3
100	30 mM Lysine and 30 mM Niacin	98.9	98.9	98.8	97.6	1.1	1.1	1.2	2.3
100	30 mM Arginine-HCl and 30 mM Niacinamide	98.8	98.8	98.6	97.7	1.2	1.2	1.5	2.3
100	30 mM Histidine and 30 mM Niacinamide	98.8	98.8	98.6	97.4	1.2	1.2	1.5	2.5
100	30 mM Meglumine and 30 mM Niacinamide	99.0	99.0	98.9	97.7	1.0	1.0	1.1	2.3
100	30 mM Lysine-HCl and 30 mM Niacinamide	99.0	99.0	98.9	97.4	1.0	1.0	1.2	2.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	98.8	98.8	98.6	97.2	1.2	1.2	1.4	2.7
100	Water (blank), pH 6.5	98.6	98.6	98.5	96.8	1.4	1.4	1.5	3.1

Table 174 SE-UPLC results of formulated Aflibercept in 20 mM Phosphate buffer, pH 7.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	98.6	98.6	98.0	96.9	1.4	1.4	2.0	2.9
300	140 mM Histidine and 140 mM Niacin	98.9	98.9	98.0	97.1	1.1	1.1	1.9	2.9
300	140 mM Meglumine and 140 mM Niacin	98.7	98.7	98.1	96.6	1.3	1.3	1.9	3.2
300	140 mM Lysine and 140 mM Niacin	98.7	98.7	97.7	97.1	1.3	1.3	2.3	2.8
300	70 mM Arginine·HCl and 140 mM Niacinamide	98.9	98.9	98.4	97.0	1.1	1.1	1.5	2.8
300	140 mM Histidine and 140 mM Niacinamide	98.8	98.8	98.0	96.6	1.2	1.2	1.9	3.3
300	140 mM Meglumine and 140 mM Niacinamide	98.6	98.6	97.6	96.9	1.4	1.4	2.4	3.1
300	70 mM Lysine·HCl and 140 mM Niacinamide	98.7	98.7	98.2	96.7	1.3	1.3	1.7	3.2
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	98.6	98.6	98.4	96.0	1.4	1.4	1.6	3.8
300	Water (Blank), pH 7.0	98.4	98.4	98.1	94.7	1.6	1.6	1.9	5.0
200	140 mM Arginine and 140 mM Niacin	98.6	98.6	98.3	96.9	1.4	1.4	1.7	3.1
200	140 mM Histidine and 140 mM Niacin	98.9	98.9	98.6	97.5	1.1	1.1	1.3	2.3
200	140 mM Meglumine and 140 mM Niacin	98.6	98.6	98.3	97.0	1.4	1.4	1.6	2.9
200	140 mM Lysine and 140 mM Niacin	98.8	98.8	98.5	97.0	1.2	1.2	1.5	2.9
200	70 mM Arginine·HCl and 140 mM Niacinamide	98.9	98.9	98.7	97.3	1.1	1.1	1.2	2.7
200	140 mM Histidine and 140 mM Niacinamide	98.8	98.8	98.5	97.4	1.2	1.2	1.4	2.5
200	140 mM Meglumine and 140 mM Niacinamide	98.6	98.6	98.5	96.8	1.4	1.4	1.4	3.0
200	70 mM Lysine·HCl and 140 mM Niacinamide	98.9	98.9	98.8	96.7	1.1	1.1	1.2	3.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	98.6	98.6	98.5	96.4	1.4	1.4	1.5	3.5
200	Water (blank), pH 7.0	98.5	98.5	98.3	95.8	1.5	1.5	1.7	4.0
100	140 mM Arginine and 140 mM Niacin	98.7	98.7	98.6	97.3	1.3	1.3	1.5	2.6
100	140 mM Histidine and 140 mM Niacin	98.9	98.9	98.7	97.2	1.1	1.1	1.4	2.8
100	140 mM Meglumine and 140 mM Niacin	98.7	98.7	98.6	97.3	1.3	1.3	1.4	2.7
100	140 mM Lysine and 140 mM Niacin	98.8	98.8	98.7	97.1	1.2	1.2	1.3	2.9
100	70 mM Arginine·HCl and 140 mM Niacinamide	99.0	99.0	98.8	97.5	1.0	1.0	1.1	2.5
100	140 mM Histidine and 140 mM Niacinamide	98.9	98.9	98.8	97.6	1.1	1.1	1.1	2.3
100	140 mM Meglumine and 140 mM Niacinamide	98.9	98.9	98.7	97.3	1.1	1.1	1.4	2.7
100	70 mM Lysine·HCl and 140 mM Niacinamide	98.8	98.8	98.6	97.1	1.2	1.2	1.4	2.8
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	98.7	98.7	98.6	97.0	1.3	1.3	1.4	2.9
100	Water (blank), pH 7.0	98.7	98.7	98.4	96.7	1.3	1.3	1.6	3.1

Table 175 SE-UPLC results of formulated Aflibercept in 50 mM Phosphate buffer, pH 7.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	98.3	98.3	97.5	95.5	1.7	1.7	2.4	4.3
300	300 mM Histidine and 300 mM Niacin	98.5	98.5	97.6	96.4	1.5	1.5	2.3	3.4
300	300 mM Meglumine and 300 mM Niacin	98.3	98.3	97.5	95.4	1.7	1.7	2.4	4.4
300	300 mM Lysine and 300 mM Niacin	98.5	98.5	97.7	95.6	1.5	1.5	2.2	4.3
300	140 mM Arginine·HCl and 300 mM Niacinamide	98.4	98.4	97.8	96.0	1.6	1.6	2.1	3.8
300	300 mM Histidine and 300 mM Niacinamide	98.3	98.3	97.6	95.9	1.7	1.7	2.3	4.0
300	300 mM Meglumine and 300 mM Niacinamide	98.2	98.2	97.4	95.4	1.8	1.8	2.6	4.6
300	140 mM Lysine·HCl and 300 mM Niacinamide	98.5	98.5	97.6	95.9	1.5	1.5	2.4	4.1
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	98.2	98.2	97.0	95.2	1.8	1.8	3.0	4.4
300	Water (Blank), pH 7.5	98.1	98.1	96.5	94.0	1.9	1.9	3.5	5.6
200	300 mM Arginine and 300 mM Niacin	98.6	98.6	98.2	96.6	1.4	1.4	1.8	3.2
200	300 mM Histidine and 300 mM Niacin	98.5	98.5	98.1	96.8	1.5	1.5	1.9	3.2
200	300 mM Meglumine and 300 mM Niacin	98.7	98.7	98.3	96.9	1.3	1.3	1.7	3.1
200	300 mM Lysine and 300 mM Niacin	98.6	98.6	98.1	96.2	1.4	1.4	1.9	3.8
200	140 mM Arginine·HCl and 300 mM Niacinamide	98.7	98.7	98.2	96.5	1.3	1.3	1.7	3.5
200	300 mM Histidine and 300 mM Niacinamide	98.5	98.5	97.9	96.8	1.5	1.5	2.0	3.0
200	300 mM Meglumine and 300 mM Niacinamide	98.6	98.6	98.2	96.4	1.4	1.4	1.7	3.6
200	140 mM Lysine·HCl and 300 mM Niacinamide	98.6	98.6	98.2	96.2	1.4	1.4	1.8	3.6
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	98.4	98.4	97.7	96.0	1.6	1.6	2.3	3.9
200	Water (blank), pH 7.5	98.3	98.3	97.0	95.1	1.7	1.7	3.0	4.7
100	300 mM Arginine and 300 mM Niacin	98.7	98.7	98.3	97.5	1.3	1.3	1.8	2.5
100	300 mM Histidine and 300 mM Niacin	98.6	98.6	98.2	97.5	1.4	1.4	1.7	2.4
100	300 mM Meglumine and 300 mM Niacin	98.5	98.5	98.1	96.8	1.5	1.5	2.0	3.2
100	300 mM Lysine and 300 mM Niacin	98.5	98.5	98.1	97.0	1.5	1.5	1.8	3.0
100	140 mM Arginine·HCl and 300 mM Niacinamide	98.8	98.8	98.6	97.4	1.2	1.2	1.4	2.5
100	300 mM Histidine and 300 mM Niacinamide	98.5	98.5	98.2	96.9	1.5	1.5	1.8	3.1
100	300 mM Meglumine and 300 mM Niacinamide	98.8	98.8	98.4	97.5	1.2	1.2	1.7	2.5
100	140 mM Lysine·HCl and 300 mM Niacinamide	98.5	98.5	98.3	97.4	1.5	1.5	1.8	2.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.5	98.5	98.5	98.0	96.8	1.5	1.5	2.0	3.1
100	Water (blank), pH 7.5	98.4	98.4	97.6	96.5	1.6	1.6	2.4	3.3

Table 176 SE-UPLC results of formulated Aflibercept in 5 mM Tris buffer, pH 6.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	98.8	98.8	98.4	97.3	1.2	1.2	1.6	2.6
300	30 mM Histidine and 30 mM Niacin	98.6	98.6	98.2	97.3	1.4	1.4	1.7	2.5
300	30 mM Meglumine and 30 mM Niacin	98.7	98.7	98.3	97.3	1.3	1.3	1.6	2.5
300	30 mM Lysine and 30 mM Niacin	98.5	98.5	98.0	96.7	1.5	1.5	2.0	3.2
300	30 mM Arginine·HCl and 30 mM Niacinamide	98.6	98.6	98.2	96.8	1.4	1.4	1.7	3.1
300	30 mM Histidine and 30 mM Niacinamide	98.6	98.6	98.1	97.0	1.4	1.4	1.8	2.8
300	30 mM Meglumine and 30 mM Niacinamide	98.8	98.8	98.5	97.5	1.2	1.2	1.4	2.3
300	30 mM Lysine·HCl and 30 mM Niacinamide	98.6	98.6	98.1	97.3	1.4	1.4	1.9	2.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	98.5	98.5	97.9	95.9	1.5	1.5	2.1	4.0
300	Water (Blank), pH 6.5	98.3	98.3	97.5	94.5	1.7	1.7	2.5	5.8
200	30 mM Arginine and 30 mM Niacin	98.6	98.6	98.4	98.0	1.4	1.4	1.5	1.9
200	30 mM Histidine and 30 mM Niacin	98.9	98.9	98.6	97.8	1.1	1.1	1.3	2.1
200	30 mM Meglumine and 30 mM Niacin	98.9	98.9	98.6	98.1	1.1	1.1	1.4	1.7
200	30 mM Lysine and 30 mM Niacin	98.7	98.7	98.6	98.0	1.3	1.3	1.4	1.8
200	30 mM Arginine·HCl and 30 mM Niacinamide	98.6	98.6	98.4	97.9	1.4	1.4	1.6	1.9
200	30 mM Histidine and 30 mM Niacinamide	98.9	98.9	98.8	97.8	1.1	1.1	1.2	2.0
200	30 mM Meglumine and 30 mM Niacinamide	98.9	98.9	98.7	98.2	1.1	1.1	1.3	1.7
200	30 mM Lysine·HCl and 30 mM Niacinamide	98.9	98.9	98.7	97.9	1.1	1.1	1.2	2.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	98.6	98.6	98.3	96.2	1.4	1.4	1.7	3.7
200	Water (blank), pH 6.5	98.4	98.4	98.0	95.3	1.6	1.6	1.9	4.6
100	30 mM Arginine and 30 mM Niacin	99.0	99.0	98.7	98.1	1.0	1.0	1.2	1.7
100	30 mM Histidine and 30 mM Niacin	99.1	99.1	99.0	98.4	0.9	0.9	1.0	1.5
100	30 mM Meglumine and 30 mM Niacin	98.9	98.9	98.6	97.9	1.1	1.1	1.4	1.9
100	30 mM Lysine and 30 mM Niacin	99.0	99.0	98.8	98.1	1.0	1.0	1.1	1.7
100	30 mM Arginine·HCl and 30 mM Niacinamide	98.9	98.9	98.6	98.0	1.1	1.1	1.4	1.8
100	30 mM Histidine and 30 mM Niacinamide	98.8	98.8	98.7	97.9	1.2	1.2	1.3	1.9
100	30 mM Meglumine and 30 mM Niacinamide	98.9	98.9	98.6	98.1	1.1	1.1	1.3	1.8
100	30 mM Lysine·HCl and 30 mM Niacinamide	98.9	98.9	98.8	97.9	1.1	1.1	1.2	1.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.5	98.8	98.8	98.6	97.2	1.2	1.2	1.4	2.7
100	Water (blank), pH 6.5	98.6	98.6	98.5	96.8	1.4	1.4	1.5	3.1

Table 177 SE-UPLC results of formulated Aflibercept in 20 mM Tris buffer, pH 7.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	98.7	98.7	97.9	96.5	1.3	1.3	2.0	3.5
300	140 mM Histidine and 140 mM Niacin	98.9	98.9	98.3	96.4	1.1	1.1	1.7	3.4
300	140 mM Meglumine and 140 mM Niacin	98.9	98.9	97.9	96.3	1.1	1.1	2.0	3.5
300	140 mM Lysine and 140 mM Niacin	98.8	98.8	98.3	96.6	1.2	1.2	1.6	3.2
300	70 mM Arginine·HCl and 140 mM Niacinamide	98.7	98.7	98.0	96.9	1.3	1.3	1.9	3.1
300	140 mM Histidine and 140 mM Niacinamide	98.7	98.7	97.9	96.7	1.3	1.3	2.1	3.1
300	140 mM Meglumine and 140 mM Niacinamide	98.9	98.9	98.0	96.3	1.1	1.1	1.9	3.7
300	70 mM Lysine·HCl and 140 mM Niacinamide	98.6	98.6	97.6	96.7	1.4	1.4	2.4	3.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	98.6	98.6	98.4	96.0	1.4	1.4	1.6	3.8
300	Water (Blank), pH 7.0	98.4	98.4	98.1	94.7	1.6	1.6	1.9	4.0
200	140 mM Arginine and 140 mM Niacin	98.6	98.6	98.3	96.5	1.4	1.4	1.7	3.5
200	140 mM Histidine and 140 mM Niacin	98.7	98.7	98.6	96.7	1.3	1.3	1.4	3.1
200	140 mM Meglumine and 140 mM Niacin	98.6	98.6	98.5	97.2	1.4	1.4	1.4	2.8
200	140 mM Lysine and 140 mM Niacin	98.7	98.7	98.5	96.9	1.3	1.3	1.5	3.0
200	70 mM Arginine·HCl and 140 mM Niacinamide	98.7	98.7	98.4	97.3	1.3	1.3	1.5	2.7
200	140 mM Histidine and 140 mM Niacinamide	98.9	98.9	98.7	97.0	1.1	1.1	1.2	2.9
200	140 mM Meglumine and 140 mM Niacinamide	98.6	98.6	98.5	96.8	1.4	1.4	1.5	3.0
200	70 mM Lysine·HCl and 140 mM Niacinamide	98.7	98.7	98.4	96.6	1.3	1.3	1.6	3.4
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	98.6	98.6	98.5	96.4	1.4	1.4	1.5	3.5
200	Water (blank), pH 7.0	98.5	98.5	98.3	95.8	1.5	1.5	1.7	4.0
100	140 mM Arginine and 140 mM Niacin	98.7	98.7	98.6	97.6	1.3	1.3	1.5	2.4
100	140 mM Histidine and 140 mM Niacin	99.0	99.0	98.9	97.8	1.0	1.0	1.1	2.2
100	140 mM Meglumine and 140 mM Niacin	98.7	98.7	98.5	97.2	1.3	1.3	1.6	2.7
100	140 mM Lysine and 140 mM Niacin	99.0	99.0	98.8	97.7	1.0	1.0	1.3	2.2
100	70 mM Arginine·HCl and 140 mM Niacinamide	98.9	98.9	98.7	97.8	1.1	1.1	1.4	2.2
100	140 mM Histidine and 140 mM Niacinamide	98.9	98.9	98.7	97.3	1.1	1.1	1.4	2.6
100	140 mM Meglumine and 140 mM Niacinamide	99.0	99.0	98.8	97.3	1.0	1.0	1.3	2.7
100	70 mM Lysine·HCl and 140 mM Niacinamide	98.7	98.7	98.6	97.4	1.3	1.3	1.4	2.5
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 7.0	98.7	98.7	98.6	97.0	1.3	1.3	1.4	2.9
100	Water (blank), pH 7.0	98.7	98.7	98.4	96.7	1.3	1.3	1.6	3.1

Table 178 SE-UPLC results of formulated Aflibercept in 50 mM Tris buffer, pH 7.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	98.5	98.5	97.7	96.2	1.5	1.5	2.2	3.6
300	300 mM Histidine and 300 mM Niacin	98.2	98.2	97.5	97.1	1.8	1.8	2.5	2.7
300	300 mM Meglumine and 300 mM Niacin	98.2	98.2	97.4	96.9	1.8	1.8	2.5	2.9
300	300 mM Lysine and 300 mM Niacin	98.2	98.2	97.6	96.2	1.8	1.8	2.4	3.8
300	140 mM Arginine·HCl and 300 mM Niacinamide	98.4	98.4	97.6	96.3	1.6	1.6	2.4	3.5
300	300 mM Histidine and 300 mM Niacinamide	98.4	98.4	97.5	96.4	1.6	1.6	2.5	3.4
300	300 mM Meglumine and 300 mM Niacinamide	98.2	98.2	97.3	95.3	1.8	1.8	2.6	4.5
300	140 mM Lysine·HCl and 300 mM Niacinamide	98.5	98.5	97.8	97.3	1.5	1.5	2.2	2.7
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	98.2	98.2	97.0	95.2	1.8	1.8	3.0	4.4
300	Water (Blank)	98.1	98.1	96.5	94.0	1.9	1.9	3.5	5.6
200	300 mM Arginine and 300 mM Niacin	98.4	98.4	98.0	97.0	1.6	1.6	2.0	2.8
200	300 mM Histidine and 300 mM Niacin	98.5	98.5	97.9	96.8	1.5	1.5	2.0	3.1
200	300 mM Meglumine and 300 mM Niacin	98.5	98.5	98.1	96.3	1.5	1.5	1.8	3.7
200	300 mM Lysine and 300 mM Niacin	98.5	98.5	98.1	96.7	1.5	1.5	1.9	3.2
200	140 mM Arginine·HCl and 300 mM Niacinamide	98.5	98.5	98.1	97.0	1.5	1.5	1.8	2.8
200	300 mM Histidine and 300 mM Niacinamide	98.7	98.7	98.1	96.3	1.3	1.3	1.8	3.7
200	300 mM Meglumine and 300 mM Niacinamide	98.7	98.7	98.1	96.4	1.3	1.3	1.8	3.6
200	140 mM Lysine·HCl and 300 mM Niacinamide	98.6	98.6	98.0	96.2	1.4	1.4	2.0	3.7
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	98.4	98.4	97.7	96.0	1.6	1.6	2.3	3.9
200	Water (blank)	98.3	98.3	97.0	95.1	1.7	1.7	3.0	4.7
100	300 mM Arginine and 300 mM Niacin	98.8	98.8	98.4	97.7	1.2	1.2	1.5	2.3
100	300 mM Histidine and 300 mM Niacin	98.7	98.7	98.3	97.1	1.3	1.3	1.6	2.9
100	300 mM Meglumine and 300 mM Niacin	98.7	98.7	98.4	97.6	1.3	1.3	1.7	2.4
100	300 mM Lysine and 300 mM Niacin	98.6	98.6	98.2	97.7	1.4	1.4	1.9	2.3
100	140 mM Arginine·HCl and 300 mM Niacinamide	98.6	98.6	98.2	97.7	1.4	1.4	1.8	2.2
100	300 mM Histidine and 300 mM Niacinamide	98.7	98.7	98.5	97.7	1.3	1.3	1.4	2.2
100	300 mM Meglumine and 300 mM Niacinamide	98.6	98.6	98.3	97.5	1.4	1.4	1.8	2.5
100	140 mM Lysine·HCl and 300 mM Niacinamide	98.8	98.8	98.4	97.2	1.2	1.2	1.6	2.7
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	98.5	98.5	98.0	96.8	1.5	1.5	2.0	3.1
100	Water (blank)	98.4	98.4	97.6	96.5	1.6	1.6	2.4	3.3

Table 179 SE-UPLC results of formulated Aflibercept in 5 mM Succinate buffer, pH 4.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	30 mM Arginine and 30 mM Niacin	98.9	98.9	98.4	97.5	1.1	1.1	1.5	2.4
300	30 mM Histidine and 30 mM Niacin	98.7	98.7	98.2	97.5	1.3	1.3	1.7	2.4
300	30 mM Meglumine and 30 mM Niacin	98.9	98.9	98.4	97.5	1.1	1.1	1.5	2.3
300	30 mM Lysine and 30 mM Niacin	98.7	98.7	98.3	97.1	1.3	1.3	1.6	2.7
300	30 mM Arginine-HCl and 30 mM Niacinamide	98.7	98.7	98.3	97.6	1.3	1.3	1.7	2.3
300	30 mM Histidine and 30 mM Niacinamide	98.8	98.8	98.3	97.5	1.2	1.2	1.6	2.3
300	30 mM Meglumine and 30 mM Niacinamide	98.7	98.7	98.2	96.8	1.3	1.3	1.7	3.1
300	30 mM Lysine-HCl and 30 mM Niacinamide	98.7	98.7	98.4	97.5	1.3	1.3	1.6	2.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	98.4	98.3	97.2	95.0	1.6	1.7	2.7	4.8
300	Water (Blank), pH 4.5	98.5	98.5	98.3	95.8	1.4	1.4	1.7	3.9
200	30 mM Arginine and 30 mM Niacin	98.8	98.8	98.5	97.8	1.2	1.2	1.5	2.0
200	30 mM Histidine and 30 mM Niacin	99.0	99.0	98.9	98.1	1.0	1.0	1.1	1.8
200	30 mM Meglumine and 30 mM Niacin	99.0	99.0	98.9	97.9	1.0	1.0	1.1	2.0
200	30 mM Lysine and 30 mM Niacin	99.0	99.0	98.7	98.2	1.0	1.0	1.3	1.7
200	30 mM Arginine-HCl and 30 mM Niacinamide	98.9	98.9	98.7	98.1	1.1	1.1	1.3	1.8
200	30 mM Histidine and 30 mM Niacinamide	98.8	98.8	98.5	98.0	1.2	1.2	1.5	1.8
200	30 mM Meglumine and 30 mM Niacinamide	98.8	98.8	98.6	97.9	1.2	1.2	1.3	1.9
200	30 mM Lysine-HCl and 30 mM Niacinamide	99.0	99.0	98.8	97.9	1.0	1.0	1.1	1.9
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	98.5	98.3	97.8	96.4	1.5	1.7	2.1	3.5
200	Water (blank), pH 4.5	98.6	98.6	98.4	96.6	1.3	1.3	1.5	2.4
100	30 mM Arginine and 30 mM Niacin	99.0	99.0	98.8	98.2	1.0	1.0	1.1	1.7
100	30 mM Histidine and 30 mM Niacin	99.0	99.0	98.7	97.9	1.0	1.0	1.3	1.9
100	30 mM Meglumine and 30 mM Niacin	98.9	98.9	98.7	97.9	1.1	1.1	1.2	2.0
100	30 mM Lysine and 30 mM Niacin	98.9	98.9	98.8	98.3	1.1	1.1	1.2	1.6
100	30 mM Arginine-HCl and 30 mM Niacinamide	99.1	99.1	98.8	98.4	0.9	0.9	1.2	1.5
100	30 mM Histidine and 30 mM Niacinamide	99.0	99.0	98.7	98.3	1.0	1.0	1.2	1.5
100	30 mM Meglumine and 30 mM Niacinamide	98.9	98.9	98.8	98.3	1.1	1.1	1.2	1.5
100	30 mM Lysine-HCl and 30 mM Niacinamide	99.1	99.1	99.0	98.3	0.9	0.9	0.9	1.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 4.5	98.7	98.7	98.5	97.3	1.3	1.3	1.5	2.6
100	Water (blank), pH 4.5	98.8	98.8	98.7	97.7	1.2	1.2	1.3	2.1

Table 180 SE-UPLC results of formulated Aflibercept in 20 mM Succinate buffer, pH 5.5 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	140 mM Arginine and 140 mM Niacin	98.5	98.5	98.1	97.1	1.5	1.5	1.8	2.7
300	140 mM Histidine and 140 mM Niacin	98.7	98.7	98.4	97.5	1.3	1.3	1.6	2.4
300	140 mM Meglumine and 140 mM Niacin	98.8	98.8	98.3	97.0	1.2	1.2	1.7	2.9
300	140 mM Lysine and 140 mM Niacin	98.7	98.7	98.2	97.3	1.3	1.3	1.7	2.5
300	70 mM Arginine·HCl and 140 mM Niacinamide	98.7	98.7	98.3	96.9	1.3	1.3	1.7	3.0
300	140 mM Histidine and 140 mM Niacinamide	98.6	98.6	98.3	97.1	1.4	1.4	1.6	2.7
300	140 mM Meglumine and 140 mM Niacinamide	98.8	98.8	98.4	97.4	1.2	1.2	1.5	2.5
300	70 mM Lysine·HCl and 140 mM Niacinamide	98.7	98.7	98.2	97.4	1.3	1.3	1.8	2.5
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	98.5	98.5	98.0	96.9	1.5	1.5	1.9	3.0
300	Water (Blank), pH 5.5	98.4	98.4	97.9	95.6	1.6	1.6	2.0	4.2
200	140 mM Arginine and 140 mM Niacin	98.9	98.9	98.8	98.2	1.1	1.1	1.1	1.7
200	140 mM Histidine and 140 mM Niacin	98.6	98.6	98.5	98.0	1.4	1.4	1.5	1.9
200	140 mM Meglumine and 140 mM Niacin	98.9	98.9	98.6	98.0	1.1	1.1	1.3	1.9
200	140 mM Lysine and 140 mM Niacin	98.9	98.9	98.7	97.8	1.1	1.1	1.2	2.1
200	70 mM Arginine·HCl and 140 mM Niacinamide	98.8	98.8	98.5	98.1	1.2	1.2	1.4	1.7
200	140 mM Histidine and 140 mM Niacinamide	98.6	98.6	98.5	97.5	1.4	1.4	1.4	2.4
200	140 mM Meglumine and 140 mM Niacinamide	98.9	98.9	98.6	98.3	1.1	1.1	1.4	1.5
200	70 mM Lysine·HCl and 140 mM Niacinamide	98.7	98.7	98.6	97.7	1.3	1.3	1.3	2.1
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	98.6	98.6	98.4	97.5	1.4	1.4	1.6	2.4
200	Water (blank), pH 5.5	98.4	98.4	98.1	96.8	1.6	1.6	1.9	3.0
100	140 mM Arginine and 140 mM Niacin	98.8	98.8	98.7	98.0	1.2	1.2	1.3	1.8
100	140 mM Histidine and 140 mM Niacin	98.8	98.8	98.7	98.0	1.2	1.2	1.3	1.9
100	140 mM Meglumine and 140 mM Niacin	98.8	98.8	98.6	97.9	1.2	1.2	1.3	2.0
100	140 mM Lysine and 140 mM Niacin	99.0	99.0	98.9	98.1	1.0	1.0	1.0	1.8
100	70 mM Arginine·HCl and 140 mM Niacinamide	99.0	99.0	98.7	98.1	1.0	1.0	1.2	1.8
100	140 mM Histidine and 140 mM Niacinamide	99.1	99.1	99.0	98.4	0.9	0.9	1.0	1.5
100	140 mM Meglumine and 140 mM Niacinamide	99.0	99.0	98.7	98.2	1.0	1.0	1.2	1.7
100	70 mM Lysine·HCl and 140 mM Niacinamide	98.8	98.8	98.7	98.2	1.2	1.2	1.3	1.6
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 5.5	98.8	98.8	98.6	98.0	1.2	1.2	1.4	1.9
100	Water (blank), pH 5.5	98.9	98.9	98.7	97.8	1.1	1.1	1.3	2.0

Table 181 SE-UPLC results of formulated Aflibercept in 50 mM Succinate buffer, pH 6.0 stored at 5°C, 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%				Aggregation%			
		T0	5°C	25°C	40°C	T0	5°C	25°C	40°C
300	300 mM Arginine and 300 mM Niacin	98.9	98.9	98.5	97.2	1.1	1.1	1.4	2.7
300	300 mM Histidine and 300 mM Niacin	98.9	98.9	98.6	97.1	1.1	1.1	1.3	2.8
300	300 mM Meglumine and 300 mM Niacin	98.9	98.9	98.6	97.7	1.1	1.1	1.4	2.1
300	300 mM Lysine and 300 mM Niacin	99.0	99.0	98.7	97.8	1.0	1.0	1.2	2.0
300	140 mM Arginine·HCl and 300 mM Niacinamide	98.9	98.9	98.5	97.7	1.1	1.1	1.5	2.2
300	300 mM Histidine and 300 mM Niacinamide	98.9	98.9	98.6	97.7	1.1	1.1	1.4	2.2
300	300 mM Meglumine and 300 mM Niacinamide	98.7	98.7	98.3	97.6	1.3	1.3	1.7	2.2
300	140 mM Lysine·HCl and 300 mM Niacinamide	98.9	98.9	98.5	97.6	1.1	1.1	1.5	2.3
300	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	98.7	98.7	98.2	96.9	1.3	1.3	1.8	2.9
300	Water (Blank), pH 6.0	98.5	98.5	98.0	95.6	1.5	1.5	1.8	4.0
200	300 mM Arginine and 300 mM Niacin	98.9	98.9	98.8	98.1	1.1	1.1	1.2	1.7
200	300 mM Histidine and 300 mM Niacin	98.8	98.8	98.5	98.0	1.2	1.2	1.4	1.8
200	300 mM Meglumine and 300 mM Niacin	98.7	98.7	98.6	97.9	1.3	1.3	1.3	1.9
200	300 mM Lysine and 300 mM Niacin	98.9	98.9	98.7	97.9	1.1	1.1	1.2	2.0
200	140 mM Arginine·HCl and 300 mM Niacinamide	98.9	98.9	98.7	98.0	1.1	1.1	1.2	1.9
200	300 mM Histidine and 300 mM Niacinamide	98.9	98.9	98.7	97.8	1.1	1.1	1.2	2.1
200	300 mM Meglumine and 300 mM Niacinamide	98.8	98.8	98.5	98.0	1.2	1.2	1.4	1.9
200	140 mM Lysine·HCl and 300 mM Niacinamide	98.9	98.9	98.6	97.9	1.1	1.1	1.3	2.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	98.7	98.7	98.5	97.5	1.3	1.3	1.4	2.4
200	Water (blank), pH 6.0	98.6	98.6	98.4	97.1	1.4	1.4	1.6	2.7
100	300 mM Arginine and 300 mM Niacin	99.0	99.0	98.7	98.4	1.0	1.0	1.2	1.4
100	300 mM Histidine and 300 mM Niacin	98.8	98.8	98.7	97.7	1.2	1.2	1.3	2.2
100	300 mM Meglumine and 300 mM Niacin	98.8	98.8	98.5	98.1	1.2	1.2	1.5	1.8
100	300 mM Lysine and 300 mM Niacin	98.7	98.7	98.5	97.8	1.3	1.3	1.5	2.0
100	140 mM Arginine·HCl and 300 mM Niacinamide	98.9	98.9	98.7	97.9	1.1	1.1	1.2	2.0
100	300 mM Histidine and 300 mM Niacinamide	98.7	98.7	98.6	97.9	1.3	1.3	1.3	1.9
100	300 mM Meglumine and 300 mM Niacinamide	98.7	98.7	98.5	97.9	1.3	1.3	1.5	2.0
100	140 mM Lysine·HCl and 300 mM Niacinamide	99.0	99.0	98.9	98.0	1.0	1.0	1.1	1.9
100	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	98.8	98.8	98.7	98.1	1.2	1.2	1.3	1.8
100	Water (blank), pH 6.0	98.8	98.8	98.6	97.8	1.2	1.2	1.4	2.0

Example 12: Effect of viscosity-reducing and stabilizing formulations on Rituximab stability in 20 mM histidine buffer, pH 6.0 at various temperatures.

[00117] This example tested the effect of viscosity-reducing and stabilizing formulations on Rituximab stability and compared it with the lead formulation (25 mM Phosphate, 81.2 mM of
5 Nicotinic acid and 29.4 mM Tryptophan) in WO2018211517.

[00118] Materials and Methods

[00119] Rituximab was produced by WuXi Biologics as described in Example 6, and formulated as indicated in Table 182. Through buffer exchange, Rituximab was transferred into ten test groups, encompassing eight with a 20 mM histidine pH 6.0 buffer, incorporating one of
10 the viscosity-reducing and stabilizing formulations, respectively, in Table 182. Furthermore, there was a control group comprising 25 mM phosphate buffer at pH 6.0, with 81.2 mM Nicotinic acid and 29.4 mM Tryptophan (matching the lead formulation 25 mM phosphate buffer at pH 6.0 along with 10 mg/mL Nicotinic acid (acid form) and 6 mg/mL Tryptophan from Examples 14 and 16-21 in WO2018211517). An additional control group solely consisted of a 20 mM histidine buffer
15 pH 6.0 and the protein (as blank control). The formulation containing Rituximab was subsequently concentrated to around 200 mg/mL (200 ± 5 mg/mL) using an Eppendorf centrifuge. To ascertain Rituximab's concentration in the groups, absorbance at 280 nm combined with SE-UPLC was gauged against a histidine buffer containing a viscosity-reducing and stabilizing agent for excipient-containing samples, and absorbance at 280 nm was measured for the protein solution
20 without a viscosity-reducing and stabilizing formulation. For Rituximab without excipients, the buffer alone (i.e., devoid of excipients) served as a blank for protein concentration calculation. The extinction coefficient was measured at $1.65 \text{ (mg/mL)}^{-1} \cdot \text{cm}^{-1}$.

[00120] Protein stability assessment, conducted over a 4-week period using SE-UPLC, utilized samples prepared as outlined previously. The data as shown in Table 182 demonstrated that
25 Rituximab at a concentration of 200 ± 5 mg/mL, formulated with the tested viscosity-reducing and stabilizing formulations, exhibited a monomer content higher than 93%, when stored even at 40°C for 4 weeks, comparable to or superior to the lead formulation in WO2018211517, indicating superior stabilization capacity of the tested viscosity-reducing and stabilizing formulations to prevent protein aggregation during sample preparation and storage.

Table 182 SE-UPLC results of formulated Rituximab in 20 mM Histidine buffer, pH 6.0 stored at 25°C and 40°C for 4 weeks. (25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0, the lead formulation from WO2018211517, is used as control.)

Protein Conc. (mg/mL)	Viscosity-reducing and stabilizing formulation	Monomer%			Aggregation%		
		T0	25°C	40°C	T0	25°C	40°C
200	140 mM Arginine and 140 mM Niacin	96.3	95.7	94.4	3.6	4.1	4.3
200	140 mM Histidine and 140 mM Niacin	96.3	96.0	94.3	3.6	3.8	4.2
200	140 mM Meglumine and 140 mM Niacin	96.2	95.3	93.4	3.8	4.5	5.3
200	140 mM Lysine and 140 mM Niacin	96.2	95.0	93.9	3.7	4.3	4.3
200	70 mM Arginine-HCl and 140 mM Niacinamide	96.2	95.2	94.3	3.8	4.5	4.4
200	140 mM Histidine and 140 mM Niacinamide	96.4	95.7	94.5	3.5	4.0	4.4
200	140 mM Meglumine and 140 mM Niacinamide	96.2	95.0	93.7	3.7	4.7	4.4
200	70 mM Lysine-HCl and 140 mM Niacinamide	96.2	95.0	93.8	3.7	4.8	5.0
200	25 mM phosphate buffer, 81.2 mM Nicotinic acid (acid form), 29.4 mM Tryptophan, pH 6.0	95.9	95.2	93.7	4.1	4.5	5.2
200	Buffer only (blank)	95.3	94.5	91.7	4.6	5.3	7.3

5

[00121] Those skilled in the art will further appreciate that the present invention may be embodied in other specific forms without departing from the spirit or central attributes thereof. In that the foregoing description of the present invention discloses only exemplary embodiments thereof, it is to be understood that other variations are contemplated as being within the scope of the present invention. Accordingly, the present invention is not limited to the particular embodiments that have been described in detail herein. Rather, reference should be made to the appended claims as indicative of the scope and content of the invention.

10

What is claimed

1. A viscosity-reducing and stabilizing liquid formulation, selected from:

- (a) 30-300 mM Arginine and 30-300 mM Niacin; or
- (b) 30-300 mM Histidine and 30-300 mM Niacin; or
- (c) 30-300 mM Meglumine and 30-300 mM Niacin; or
- (d) 30-300 mM Lysine and 30-300 mM Niacin; or
- (e) 30-300 mM Arginine-HCl and 30-300 mM Niacinamide; or
- (f) 30-300 mM Histidine and 30-300 mM Niacinamide; or
- (g) 30-300 mM Meglumine and 30-300 mM Niacinamide; or
- (h) 30-300 mM Lysine-HCl and 30-300 mM Niacinamide.

2. A pharmaceutically acceptable protein agent formulation, comprising:

- (i) one or more protein agents;
- (ii) a suitable buffer system;
- (iii) a viscosity-reducing and stabilizing formulation selected from:
 - (a) 30-300 mM Arginine and 30-300 mM Niacin; or
 - (b) 30-300 mM Histidine and 30-300 mM Niacin; or
 - (c) 30-300 mM Meglumine and 30-300 mM Niacin; or
 - (d) 30-300 mM Lysine and 30-300 mM Niacin; or
 - (e) 30-300 mM Arginine-HCl and 30-300 mM Niacinamide; or
 - (f) 30-300 mM Histidine and 30-300 mM Niacinamide; or
 - (g) 30-300 mM Meglumine and 30-300 mM Niacinamide; or
 - (h) 30-300 mM Lysine-HCl and 30-300 mM Niacinamide;

wherein the pharmaceutically acceptable protein agent formulation has a pH between about 4.5 and 7.5, increased stability, and a viscosity less than 100 cP as measured at 20 °C.

3. The protein agent formulation of claim 2, wherein the protein agents have a molecular weight from about 50 kDa to about 250 kDa and at a concentration from about 10 mg/mL to about 300 mg/mL, preferably from about 100 mg/mL to about 300 mg/mL.

4. The protein agent formulation of claim 2, wherein the protein agent is a therapeutic protein, including peptide or polypeptide, preferably an immunoglobulin, an antibody or antigen binding fragment thereof, or fusion protein, or antibody-drug conjugate (ADC), more preferably a monoclonal antibody or antigen binding fragment thereof, for example, Pembrolizumab, Adalimumab, Trastuzumab, Aflibercept, or Rituximab.

5. The protein agent formulation of claim 2, wherein the buffer system is selected from histidine buffer, acetate buffer, citrate buffer, phosphate buffer, tris buffer, succinate buffer, or any combination thereof.

6. The protein agent formulation of claim 5, wherein the buffer system is selected from:

- (1) histidine buffer at a concentration from about 5 mM to about 50 mM and at a pH 5.0 to 7.0;
- (2) acetate buffer at a concentration from about 5 mM to about 50 mM and at a pH 4.5 to 6.0;
- (3) citrate buffer at a concentration from about 5 mM to about 50 mM and at a pH 4.5 to 6.0;
- (4) phosphate buffer at a concentration from about 5 mM to about 50 mM and at a pH 6.5 to 7.5;
- (5) tris buffer at a concentration from about 5 mM to about 50 mM and at a pH 6.5 to 7.5; or
- (6) Succinate buffer at a concentration from about 5 mM to about 50 mM and at a pH 4.5 to 6.0.

7. The protein agent formulation of claim 2, wherein the pharmaceutically acceptable protein agent formulation further comprises other excipients or additives, for example, selected from: aggregation-reducing agents, sugars or sugar alcohols, polysaccharides, stabilizers, hyaluronidase, buffering agents, preservatives, carriers, antioxidants, chelating agents, natural or synthetic polymers, cryoprotectants, lyoprotectants, surfactants, bulking agents, acidifying agents, ingredients to reduce injection site discomfort, antifoaming agents, alkalizing agents, vehicles, solubilizing agents, tonicity modifiers, or stabilizing agents and combinations thereof.

8. The protein agent formulation of claim 2, wherein the protein agent formulation is administrated by parenteral administration, for example, subcutaneous, intramuscular, or intravenous administration.

9. The protein agent formulation of claim 2, wherein the protein agent formulation is a liquid formulation, for example, in aqueous liquid form or a non-aqueous liquid form, or the protein agent formulation is in a lyophilized form.

10. A method for reducing viscosity and increasing the stability of a formulation comprising a protein agent, comprising: adding a viscosity-reducing amount of any one of the viscosity-reducing and stabilizing formulation according to claim 1 to the formulation comprising a protein agent,

wherein the final formulation comprising a protein agent has a viscosity less than 100 cP as measured at 20 °C.

11. A method for preparing a liquid formulation comprising a protein agent with high concentration of a protein agent, high stability and low viscosity, comprising:

(i) dissolving the protein agent in a buffer; and

(ii) adding any one of the viscosity-reducing and stabilizing formulation according to claim 1;

wherein the liquid formulation has a viscosity less than 100 cP as measured at 20 °C.

12. The method of claim 11, wherein the buffer is selected from histidine buffer, acetate buffer, citrate buffer, phosphate buffer, tris buffer, succinate buffer, or any combination thereof.

13. The method of claim 12, wherein the buffer is selected from:

(1) histidine buffer at a concentration from about 5 mM to about 50 mM and at a pH 5.0 to 7.0;

(2) acetate buffer at a concentration from about 5 mM to about 50 mM and at a pH 4.5 to 6.0;

(3) citrate buffer at a concentration from about 5 mM to about 50 mM and at a pH 4.5 to 6.0;

(4) phosphate buffer at a concentration from about 5 mM to about 50 mM and at a pH 6.5 to 7.5;

(5) tris buffer at a concentration from about 5 mM to about 50 mM and at a pH 6.5 to 7.5; or

(6) Succinate buffer at a concentration from about 5 mM to about 50 mM and at a pH 4.5 to 6.0.

14. The method of claim 10 or claim 11, wherein the protein agent is a therapeutic protein, including peptide or polypeptide, preferably an immunoglobulin, an antibody or antigen binding fragment thereof, or a fusion protein, or antibody-drug conjugate (ADC), more preferably a monoclonal antibody or antigen binding fragment thereof, for example, Adalimumab, Trastuzumab, Aflibercept, or Rituximab.

15. The method of claim 10 or claim 11, wherein the protein agent is at a concentration from about 10 mg/mL to about 300 mg/mL, preferably from about 100 mg/mL to about 300 mg/mL.

16. The method of claim 10 or claim 11, wherein the formulation comprising a protein agent is administered by parenteral administration, for example, subcutaneous, intramuscular, or intravenous administration.

17. The method of claim 10 or claim 11, wherein the formulation comprising a protein agent is in aqueous liquid form or a non-aqueous liquid form.

18. The method of claim 10 or claim 11, wherein the formulation comprising a protein agent can be lyophilized.

19. The method of claim 10 or claim 11, wherein the formulation comprising a protein agent further comprises other excipients or additives, for example, selected from: aggregation-reducing agents, sugars or sugar alcohols, polysaccharides, stabilizers, hyaluronidase, buffering agents, preservatives, carriers, antioxidants, chelating agents, natural or synthetic polymers, cryoprotectants, lyoprotectants, surfactants, bulking agents, acidifying agents, ingredients to reduce injection site discomfort, antifoaming agents, alkalizing agents, vehicles, solubilizing agents, tonicity modifiers, or stabilizing agents and combinations thereof.

20. The method of claim 10 or claim 11, wherein the formulation comprising a protein agent has reduced protein aggregation during preparation and storage.