typically bulky polar organic compounds, such as many of the GRAS (US Food and Drug Administration's list of compounds generally regarded as safe), inactive injectable ingredients and FDA-approved therapeutics.

In one aspect, the present disclosure refers to a liquid pharmaceutical formulation for injection comprising: (i) at least about 100 mg/ml of an antibody; (ii) thiamine or a pharmaceutically acceptable salt thereof; and (iii) a pharmaceutically acceptable solvent; wherein the liquid pharmaceutical formulation, when in a volume suitable for injection, has an absolute viscosity of from about 1 cP to about 100 cP at 25°C as measured using a cone and plate viscometer or a microfluidic viscometer; and the absolute viscosity of the liquid pharmaceutical formulation is less than the absolute viscosity of a control formulation comprising the antibody and the pharmaceutically acceptable solvent but without the thiamine or a pharmaceutically acceptable salt thereof; wherein the absolute viscosity is an extrapolated zero-shear viscosity.

The concentration of proteins is between about 10 mg/mL and about 5,000 mg/mL, more preferably from about 100 mg/mL to about 2,000 mg/mL. In some examples, the concentration of proteins is between about 100 mg/mL to about 500 mg/mL, more preferably from about 300 mg/mL to about 500 mg/mL. Formulations containing proteins and viscosity-lowering agents are stable when stored at a temperature of 4° C, for a period of at least one month, preferably at least two months, and most preferably at least three months. The viscosity of the formulation is less than about 75 cP, preferably below 50 cP, and most preferably below 20 cP at about 25° C. In some examples, the viscosity is less than about 15 cP or even less than or about 10 cP at about 25° C. In certain examples, the viscosity of the formulation is about 10 cP. Formulations containing proteins and viscosity-lowering agents typically are measured at shear rates from about 0.6 $s^{-1}$ to about 450 $s^{-1}$, and preferably from about 2 $s^{-1}$ to about 400 $s^{-1}$, when measured using a cone and plate viscometer. Formulations containing proteins and viscosity-lowering agents typically are measured at shear rates from about 3 $s^{-1}$ to about 55,000 $s^{-1}$, and preferably from about 20 $s^{-1}$ to about 2,000$s^{-1}$,when measured using a microfluidic viscometer.

The viscosity of the protein formulation is reduced by the presence of

some examples, a low-viscosity formulation is provided where the viscosity of the corresponding formulation without the viscosity-lowering agent is greater than about 200 cP, greater than about 500 cP, or even above about 1,000 cP. In a preferred example, the shear rate of the formulation is at least about 0.5 $s^{-1}$, when measured using a cone and plate viscometer or at least about 1.0 $s^{-1}$, when measured using a microfluidic viscometer.

For examples in which the protein is a "high-molecular-weight protein", the high molecular weight protein may have a molecular weight between about 100 kDa and about 1,000 kDa, preferably between about 120 kDa and about 500 kDa, and most preferably between about 120 kDa and about 250 kDa. The high-molecular-weight protein can be an antibody, such as a mAb, or a PEGylated, or otherwise a derivatized form thereof. Preferred mAbs include natalizumab (TYSABRI®), cetuximab (ERBITUX®), bevacizumab (AVASTIN®), trastuzumab (HERCEPTIN®), infliximab (REMICADE®), rituximab (RITUXAN®), panitumumab (VECTIBIX®), ofatumumab (ARZERRA®), and biosimilars thereof. The high-molecular-weight protein, optionally PEGylated, can be an enzyme. Other proteins and mixtures of proteins may also be formulated to reduce their viscosity.

In some examples, the protein and viscosity-lowering agent are provided in a lyophilized dosage unit, sized for reconstitution with a sterile aqueous pharmaceutically acceptable vehicle, to yield the concentrated low-viscosity liquid formulations. The presence of the viscosity-lowering agent(s) facilitates and/or accelerates the reconstitution of the lyophilized dosage unit compared to a lyophilized dosage unit not containing a viscosity-lowering agent.

Methods are provided herein for preparing concentrated, low-viscosity liquid formulations of high-molecular-weight proteins such as mAbs, as well as methods for storing the low-viscosity, high-concentration protein formulations, and for administration thereof to patients. In another example, the viscosity-lowering agent is added to facilitate processing (e.g., pumping, concentration, and/or filtration) by reducing the viscosity of the protein solutions.

In another aspect, the present disclosure refers to a method of preparing the liquid pharmaceutical formulation disclosed herein comprising the step of combining the antibody, the pharmaceutically acceptable solvent, and the thiamine or a pharmaceutically acceptable salt thereof.

In yet another aspect, the present disclosure refers to a lyophilized composition comprising: (i) an antibody; (ii) thiamine or a pharmaceutically acceptable salt thereof; and (iii) a pharmaceutically acceptable excipient.