

stability over months to years under conditions typical for storage of drugs for self-administration, *i.e.* at refrigerator temperature in a syringe, resulting in a long shelf-life for the corresponding drug product.

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SUMMARY

The present disclosure provides formulations of anti-LAG3 antibodies or antigen binding fragments. Applicants discovered certain excipients that mitigate the phase separation of anti-LAG3 in solution. The disclosure provides one or more of an excipient selected from the group consisting of histidine, aspartate, glutamine, glycine, proline, methionine, arginine or a pharmaceutically acceptable salt thereof, NaCl, KCl, LiCl, CaCl₂, MgCl₂, ZnCl₂, and FeCl₂, at a total concentration of 10-1000 mM, and a buffer at pH about 5-8. In one aspect, the present disclosure provides a formulation comprising: about 5-300 mg/mL of an anti-LAG3 antibody or antigen-binding fragment thereof, one or more of an excipient selected from the group consisting of histidine, aspartate, glutamine, glycine, proline, methionine, arginine or pharmaceutically acceptable salt thereof, NaCl, KCl, LiCl, CaCl₂, MgCl₂, ZnCl₂, and FeCl₂, at a total concentration of 10-1000 mM, and a buffer at pH about 5-8. The present disclosure provides a formulation comprising an anti-LAG3 antibody or antigen binding fragment thereof and a buffer at pH about 5-8, and one or more of arginine, histidine or a pharmaceutically acceptable salt thereof, or NaCl at a total concentration of 15-250 mM. In one example, the formulation comprises an anti-LAG3 antibody or antigen-binding fragment thereof, a sugar or polyol; a non-ionic surfactant, a buffer at pH about 5-8, 25-200 mM arginine or a pharmaceutically acceptable salt thereof. In a further example, the formulation comprises about 25 mg/mL anti-LAG3 antibody; about 50 mg/mL sucrose; about 0.2 mg/mL polysorbate 80; about 10 mM L-histidine buffer at about pH 5.8-6.0; about 70 mM L-Arginine-HCl thereof; and optionally about 10 mM L-methionine. The formulation optionally comprises an anti-PD-1 antibody.

The disclosure provides a co-formulation of anti-LAG3 antibodies or antigen binding fragments and anti-PD-1 antibodies or antigen binding fragments with arginine or a pharmaceutically acceptable salt thereof at a total concentration of 10-1000 mM, and a buffer at pH about 5-8, and optionally 3-100 mM of methionine. In one example, the formulation comprises about 25 mg/mL anti-LAG3 antibody and about 25 mg/ml anti-PD-1 antibody; about 50 mg/mL sucrose; about 0.2 mg/mL polysorbate 80; about 10 mM L-histidine buffer at pH about 5.8-6.0; about 70 mM L-Arginine-HCl thereof; and about 10 mM L-methionine. Surprisingly, the anti-LAG3/anti-PD-1 co-formulations shows better

stability than the individual antibody formulations. The formulations can be lyophilized for reconstitution or in liquid form.

5 In another aspect, the present disclosure provides a formulation comprising: an anti-LAG3 antibody or antigen-binding fragment thereof comprising a variable light chain region comprising CDRL1 of SEQ ID NO: 39, CDRL2 of SEQ ID NO: 40, CDRL3 of SEQ ID NO: 41, and a variable heavy chain region comprising CDRH1 of SEQ ID NO: 42, CDRH2 of SEQ ID NO: 59, CDRH3 of SEQ ID NO: 44, an anti-PD-1 antibody or antigen-binding fragment thereof comprising a variable light chain region comprising CDRL1 of SEQ ID NO: 1, CDRL2 of SEQ ID NO: 2, CDRL3 of SEQ ID NO: 3, and a variable heavy chain region comprising
10 CDRH1 of SEQ ID NO: 6, CDRH2 of SEQ ID NO: 7, and CDRH3 of SEQ ID NO: 8, L-arginine or a pharmaceutically acceptable salt thereof at a concentration of 25-250 mM, and a buffer at pH about 5-8.

The present disclosure also provides a method of treating cancer or infection, comprising administering the reconstituted or liquid formulation (solution formulation) to a
15 subject in need thereof. In further examples the formulation is used in treating chronic

infection. Also contemplated is the use of the solution or lyophilized formulation in the manufacture of a medicament for treating cancer or infection.

In another aspect, the present disclosure provides a vessel or injection device comprising the formulation as defined herein.

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BREIF DESCRIPTON OF THE DRAWINGS

Figure 1: Number of particles per container $\geq 10 \mu\text{m}$ as measured by mHIAC for anti-LAG3 drug product samples that were stored at -80°C , -20°C , 5°C , 25°C , and 40°C .

Figure 2: Number of particles per container $\geq 25 \mu\text{m}$ as measured by mHIAC for anti-LAG3 drug product samples that were stored at -80°C , -20°C , 5°C , 25°C , and 40°C .

Figure 3: Potency as measured by ELISA for anti-LAG3 drug product samples that were stored at -80°C , -20°C , 5°C , 25°C , and 40°C .

Figure 4: Monomer (%) by UP-SEC for anti-LAG3 drug product samples that were stored at -80°C , -20°C , 5°C , 25°C , and 40°C .

Figure 5: High molecular weight species (%) by UP-SEC for anti-LAG3 drug product samples that were stored at -80°C , -20°C , 5°C , 25°C , and 40°C .

Figure 6: Acidic Variants (%) by HP-IEX for anti-LAG3 drug product samples that were stored at -80°C , -20°C , 5°C , 25°C , and 40°C .

Figure 7: Total Main Peak (%) by HP-IEX for anti-LAG3 drug product samples that were stored at -80°C , -20°C , 5°C , 25°C , and 40°C .

Figure 8: Basic Variants (%) by HP-IEX for anti-LAG3 drug product samples that were stored at -80°C , -20°C , 5°C , 25°C , and 40°C .

Figure 9: Purity Heavy Chain + Light Chain (%) by CE-SDS Reducing for anti-LAG3 drug product samples that were stored at -80°C , -20°C , 5°C , 25°C , and 40°C .

Figure 10: Purity Intact IgG (%) by CE-SDS Non-Reducing for anti-LAG3 drug product samples that were stored at -80°C , -20°C , 5°C , 25°C , and 40°C .

Figure 11: Homology model of anti-LAG3 antibody Ab6 showing Tryptophan surface exposure. Trp102 is surface exposed as measured by accessible surface area ($85.25\text{\AA}^2$) calculated using a homology model.

Figure 12: Reduction of self-interaction (KD) and improvement of colloidal stability (OD350) and relative solubility (%PEGmid-point) of anti-LAG3 antibody in the presence of salt (50 mM NaCl) and in the presence of L-arginine hydrochloride (40 mM) in 10 mM histidine buffer pH 5.6.

Figure 13: Effect of L-arginine hydrochloride on the diffusion interaction parameter (KD) and turbidity (OD350 at 50 mg/mL) of the anti-LAG3 antibody in 10 mM histidine buffer at pH 5.8 and at pH 6.0.

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