surfactant, such as a non-ionic surfactant or a zwitterionic surfactant, and/or a protectant.

[0005] In some of any examples, the cell surface molecule is HER1 (also known as epidermal growth factor receptor, ErbB-1, and EGFR) and/or the antibody is cetuximab. In some of any examples, the antibody binds to HER1 (EGFR) or a portion thereof. In some of any examples, the antibody is cetuximab or a biosimilar, interchangeable, or biobetter thereof. In some of any examples, the antibody is cetuximab. In some of any examples, the conjugate is cetuximab-IR700.

[0006] Also provided herein are pharmaceutical compositions that include (1) a conjugate comprising a cetuximab or a biosimilar, interchangeable, or biobetter thereof linked to IR700 and (2) one or more stabilizing agents in an amount effective to reduce or prevent aggregation of the conjugate, wherein the one or more stabilizing agents comprises a surfactant and/or a protectant. In one aspect, the present disclosure refers to a pharmaceutical composition comprising: (1) a conjugate comprising a cetuximab antibody linked to IR700, wherein the conjugate is present at a concentration of between 2 mg/mL and 10 mg/mL, and (2) one or more stabilizing agents in an amount effective to reduce or prevent aggregation of the conjugate, wherein the one or more stabilizing agents comprises a surfactant, wherein the surfactant is a non-ionic surfactant that is polysorbate 80, wherein the polysorbate 80 is present in the amount of between 0.01% and 0.1% by weight to volume (w/v), inclusive, and a protectant, wherein the protectant comprises trehalose, wherein the trehalose is present in the amount of between 5% and 9% by weight to volume (w/v), inclusive, wherein the composition is formulated in a pharmaceutically acceptable buffer that is between 5mM and 25 mM sodium phosphate, and has a pH of from pH 6.8 to pH 7.4, inclusive.

[0007] In some of any examples, the one or more stabilizing agents comprises a surfactant. In some of any examples, the one or more stabilizing agents include a surfactant, such as a non-ionic surfactant. In some of any examples, the non-ionic surfactant is a polysorbate, a lecithin, a polyethylene glycol (PEG), a polyoxyethylene glycol sorbitan alkyl ester, a polyethylene glycol octylphenyl ether, a block copolymer of polyethylene glycol and polypropylene glycol, a polyethylene glycol alkyl ether, or combinations thereof. In some of any examples, the non-ionic surfactant is selected from the group consisting of a polysorbate, a polyethylene glycol (PEG), a block copolymer of polyethylene glycol and polypropylene glycol or a polyethylene glycol octylphenyl ether, or a combination thereof.

[0008] In some of any examples, the surfactant is present at a percentage by weight to volume (w/v) of at least or at least about 0.01%. In some of any examples, the surfactant, e.g., non-ionic surfactant or a zwitterionic surfactant, is present at a percentage by volume (w/v) of at least or at least about 0.001%, 0.002%, 0.005%, 0.010%, 0.020%, 0.030%, 0.035%, 0.04%, 0.045%, 0.05%, 0.055%, 0.060%, 0.065%, 0.070%, 0.075%, 0.080%, 0.085%, 0.090%, 0.095%, or 0.100%. In some of any examples, , the surfactant, e.g., non-ionic surfactant or a zwitterionic surfactant, is present at a percentage by weight to volume (w/v) of between 0.001% and 0.10%, between 0.001% and 0.075%, between 0.001% and 0.05%, between 0.001% and 0.01%, between 0.001% and 0.005%, 0.005% and 0.10%, between 0.005% and 0.075%, between 0.005% and 0.05%, between 0.005% and 0.01%, between 0.01% and 0.10%, between 0.01% and 0.075%, between 0.01% and 0.05%, between 0.05% and 0.1%, between 0.05% and 0.075% and between 0.075% and 0.10%, each

of between 0.01% and 5%, between 0.025% and 2.5%, between 0.05% and 2.5%, between 0.05% and 1%, between 0.05% and 0.75%, between 0.05% and 0.5%, between 0.05% and 0.25%, between 0.1% and 5%, between 0.1% and 2.5%, between 0.1% and 1%, between 0.1% and 0.75%, between 0.1% and 0.5%, between 0.1% and 0.25%, between 0.5% and 5%, between 0.5% and 2.5%, between 0.5% and 1% and between 0.5% and 0.75%, each inclusive. In some of any examples, the CHAPS is present at a percentage by weight to volume (w/v) of at or about or at least or at least about 0.05%, 0.5% or 1%.

[0015] In some of any examples, the one or more stabilizing agents include a protectant such as a tonicity agent. In some of any examples, the protectant is trehalose, sorbitol, sucrose, mannitol, xylitol or glycerol. In some examples, the protectant is trehalose. In some of any examples, the protectant is present at a percentage by weight to volume (w/v) of between 1% and 20%, between 1% and 5%, between 1% and 10%, and between 5% and 9%. In some of any examples, the protectant is present at a percentage by weight to volume (w/v) of at or at about or at least or at least about 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14% or 15% by weight to volume (w/v).

[0016] In some of any examples, the one or more stabilizing agents include a protectant and a surfactant, e.g., a non-ionic surfactant or a zwitterionic surfactant.

[0017] In some of any examples, the conjugate is formulated as a concentrate and the protectant is present at a percentage by weight to volume (w/v) at or at about 20%, 25%, 30%, 35%, 40% or 50%.

[0018] Also provided are pharmaceutical compositions that include (1) a conjugate comprising an anti-HER1 (EGFR) antibody linked to IR700, (2) polysorbate 80, and (3) trehalose.

[0019] In some of any examples, the conjugate is formulated to a concentration that is from or from about 1.0 to or to about 5.0 mg/mL, from or from about 2.0 to or to about 10.0 mg/mL, from or from about 5.0 to or to about 50 mg/mL, or from or from about 20 to or to about 50 mg/mL. In some of any examples, the conjugate is formulated to a concentration of between 2 mg/mL and 10 mg/mL, inclusive. In some of any examples, the conjugate is formulated to a concentration of, of about, or of least at or about 5 mg/mL.

[0020] In some of any examples, the polysorbate 80 is present at between 0.01% and 0.1%, between 0.1% and 0.5%, or between 0.02% and 0.04% by weight to volume (w/v), each inclusive. In some of any examples, the polysorbate 80 is present at or at about 0.02% by weight to volume (w/v).

[0048] In some of any examples of the provided methods, the composition comprises 5 mg/mL cetuximab-IR700 conjugate.

[0048a] In one aspect, the present disclosure refers to use of the pharmaceutical composition as disclosed herein in the manufacture of a medicament for the treatment of a tumor or cancer in a subject, wherein: (a) the pharmaceutical composition is to be administered to the subject in a therapeutically effective amount; and (b) after the pharmaceutical composition is to be administered, the cancer or tumor is to be irradiated at a wavelength to induce phototoxic activity of the conjugate.

[0048b] In one aspect, the present disclosure refers to use of a pharmaceutical composition comprising a cetuximab-IR700 conjugate in a formulation comprising 10 mM sodium phosphate, 0.02% (w/v) polysorbate 80 and 9% (w/v) trehalose at pH 7.1 in the manufacture of a medicament for the treatment of a tumor or cancer, wherein the conjugate is present at a concentration of between 2 mg/mL and 10 mg/mL, and wherein: (a) the pharmaceutical composition is to be intravenously administered in an amount that is or is about 640 mg/m^2; and (b) after the pharmaceutical composition is to be administered, the lesion is to be irradiated at 24 ± 4 hours at a wavelength of 690 ± 20 nm at a dose of at least or about 50 J cm^{-2} or 100 J/cm of fiber length.

Brief Description of the Drawings

[0049] **FIG. 1A** displays size-exclusion high performance liquid chromatography (SE-HPLC) profiles for cetuximab in the presence or absence of various concentrations of polysorbate 20. HMW corresponds to high molecular weight peaks. **FIG. 1B** displays SE-HPLC profiles for cetuximab-IR700 conjugate in the presence or absence of various concentrations of polysorbate 20. HMW corresponds to high molecular weight peaks. **FIG. 1C** displays SE-HPLC profiles for cetuximab in the presence or absence of various concentrations of polysorbate 80. HMW corresponds to high molecular weight peaks. **FIG. 1D** displays SE-HPLC profiles for cetuximab-IR700 in the presence or absence of various concentrations of polysorbate 80. HMW corresponds to high molecular weight peaks. **FIG. 1E** displays SE-HPLC profiles for cetuximab-IR700 in the presence or absence of higher concentrations of polysorbate 80 than those shown in FIG. 1D. HMW corresponds to high molecular weight peaks. The inset is an expanded view of the HMW peaks.

[0050] **FIG. 2** displays melting temperature profiles for the cetuximab-IR700 conjugate in various conditions and for the unconjugated cetuximab.

[0051] **FIG. 3** displays size exclusion high performance liquid chromatography (SE-HPLC) for the cetuximab-IR700 conjugate in formulations with various concentrations of non-ionic surfactant.

[0052] **FIG. 4** displays the effect of concentration of the cetuximab-IR700 conjugates in the formulation on the stability of the conjugates.

[0053] **FIGS. 5A-5C** displays DSC profiles cetuximab-IR680 (**FIG. 5A**), cetuximab-IR700 (**FIG. 5B**) and cetuximab-IR800 (**FIG. 5C**), formulated in PBS or in trehalose and Polysorbate 80 formulation.

[0054] **FIGS. 6A-6C** display HPLC-SEC of cetuximab-IR680 (**FIG. 6A**), cetuximab-IR700 (**FIG. 6B**) and cetuximab-IR800 (**FIG. 6C**), formulated in PBS or in trehalose and Polysorbate 80 formulation, after incubation at 40°C or 5°C for 1 month.

[0055] **FIG. 7A-7C** display HPLC-SEC results from PBS and Polysorbate 80 formulations for cetuximab-IR680 (**FIG. 7A**), cetuximab-IR700 (**FIG. 7B**), and cetuximab-IR800 (**FIG. 7C**) conjugates after agitation.

Claims

1. A pharmaceutical composition comprising: (1) a conjugate comprising a cetuximab antibody linked to IR700, wherein the conjugate is present at a concentration of between 2 mg/mL and 10 mg/mL, and (2) one or more stabilizing agents in an amount effective to reduce or prevent aggregation of the conjugate, wherein the one or more stabilizing agents comprises a surfactant, wherein the surfactant is a non-ionic surfactant that is polysorbate 80, wherein the polysorbate 80 is present in the amount of between 0.01% and 0.1% by weight to volume (w/v), inclusive, and a protectant, wherein the protectant comprises trehalose, wherein the trehalose is present in the amount of between 5% and 9% by weight to volume (w/v), inclusive, wherein the composition is formulated in a pharmaceutically acceptable buffer that is between 5mM and 25 mM sodium phosphate, and has a pH of from pH 6.8 to pH 7.4, inclusive.

2. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition comprises 5 mg/mL cetuximab-IR700 conjugate in a formulation comprising 10 mM sodium phosphate, 0.02% (w/v) polysorbate 80 and 9% (w/v) trehalose at a pH of or of about pH 7.1.

3. The pharmaceutical composition of claim 1 or claim 2, wherein the conjugate is present in at least 85% monomeric form.

4. The pharmaceutical composition of any one of claims 1-3, wherein the composition is lyophilized or is formulated for lyophilization or is reconstituted from a lyophilized composition.

5. A container comprising the pharmaceutical composition of any of claims 1-4, wherein the container is green, blue, amber, translucent, opaque, or is covered by a material with light transmission of less than 30%.

6. Use of the pharmaceutical composition of any of claims 1-5 in the manufacture of a medicament for the treatment of a tumor or cancer in a subject, wherein:

(a) the pharmaceutical composition is to be administered to the subject in a therapeutically effective amount; and

(b) after the pharmaceutical composition is to be administered, the cancer or tumor is to be irradiated at a wavelength to induce phototoxic activity of the conjugate.

7. The use of claim 6, wherein:

(a) the pharmaceutical composition is to be administered in an amount that is or is about 640 mg/m^2; and

(b) after the pharmaceutical composition is to be administered, the lesion is to be irradiated at 24 ± 4 hours at a wavelength of 690 ± 20 nm at a dose of at least or about 50 J cm^{-2} or 100 J/cm of fiber length, thereby treating the tumor or cancer in the subject.

8. Use of a pharmaceutical composition comprising a cetuximab-IR700 conjugate in a formulation comprising 10 mM sodium phosphate, 0.02% (w/v) polysorbate 80 and 9% (w/v) trehalose at pH 7.1 in the manufacture of a medicament for the treatment of a tumor or cancer, wherein the conjugate is present at a concentration of between 2 mg/mL and 10 mg/mL, and wherein:

(a) the pharmaceutical composition is to be intravenously administered in an amount that is or is about 640 mg/m^2; and

(b) after the pharmaceutical composition is to be administered, the lesion is to be irradiated at 24 ± 4 hours at a wavelength of 690 ± 20 nm at a dose of at least or about 50 J cm^{-2} or 100 J/cm of fiber length.

9. The use of any of claims 6-8 wherein the cancer is a head or neck cancer.