it is now estimated to benefit less than 20% of cancer patients. Increasing the fraction of patients responding and the length of their response is an urgent unmet clinical need. Accordingly, there is a need to develop methods and combination therapies to initiate or enhance the effectiveness of the checkpoint inhibitors in both the nonresponding subject population and the responding subject population.

**[0011]** Anti-tumor T cells must circulate into tumors through blood vessels, bind the endothelium, and pass across the vessel wall and migrate through cancer-associated fibroblasts (CAFs) and extracellular matrix (ECM) before encountering cancer cells. However, because up to 80% of intratumoral blood vessels lack perfusion, the area of vessel wall for T cells to migrate across is limited.

**[0012]** Compressed blood vessels impair blood flow and oxygen delivery to tumors, resulting in increased hypoxia in the tumors and resistance to immunotherapy through numerous mechanisms. Strategies that decompress vessels potentiate the efficacy of ICB in ICB-resistant mouse models of metastatic breast cancer. If there was a way to decompress tumor vessels while also facilitating vessel adhesion and transmigration of T cells into the tumor parenchyma, the fraction of cancer patients that respond to ICB could increase.

**[0013]** All references cited herein, including patent applications, patent publications, and scientific literature, are herein incorporated by reference in their entirety, as if each individual reference were specifically and individually indicated to be incorporated by reference.

## SUMMARY

**[0013a]** In an aspect of the present disclosure, there is provided a use of a pharmaceutical composition comprising ketotifen, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a solid tumor in a subject in need thereof, wherein the pharmaceutical composition is to be administered in combination with a checkpoint inhibitor.

**[0013b]** In another aspect of the present disclosure, there is provided a use of a pharmaceutical composition comprising a checkpoint inhibitor, in the treatment of a solid tumor in a subject in need thereof, wherein the pharmaceutical composition is to be administered in combination with ketotifen, or a pharmaceutically acceptable salt thereof.

**[0013c]** In a further aspect of the present disclosure, there is provided a use of a pharmaceutical composition comprising a combination of ketotifen, or a pharmaceutically acceptable salt thereof, and a checkpoint inhibitor, in the manufacture of a medicament for

the treatment of a solid tumor in a subject in need thereof, wherein the pharmaceutical composition is to be administered to the subject in need thereof.

**[0013d]** In another aspect of the present disclosure, there is provided a use of a pharmaceutical composition comprising ketotifen, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for increasing blood flow of a solid tumor in a subject, wherein the pharmaceutical composition is to be administered in combination with a checkpoint inhibitor.

**[0013e]** In a further aspect of the present disclosure, there is provided a kit comprising:

(a) an effective amount of ketotifen, or a pharmaceutically acceptable salt thereof;

(b) an effective amount of a checkpoint inhibitor; and

(c) instructions for using the ketotifen, or a pharmaceutically acceptable salt thereof and the checkpoint inhibitor according to the use disclosed herein.

**[0014]** Provided herein are methods for treating a solid tumor in a subject in need thereof comprising administering to the subject an effective amount of ketotifen, or a pharmaceutically acceptable salt thereof, in combination with a checkpoint inhibitor. Also provided herein are methods for initiating, enhancing or prolonging the effects of a checkpoint inhibitor, or enabling a subject to respond to a checkpoint inhibitor in a subject in need thereof comprising administering to the subject an effective amount of ketotifen, or a pharmaceutically acceptable salt thereof, in combination with a checkpoint inhibitor, wherein the subject has a solid tumor. Also provided herein are methods for potentiating the effects of a checkpoint inhibitor in a subject in need thereof comprising administering to the subject an effective amount of ketotifen, or a pharmaceutically acceptable salt thereof, in combination with a checkpoint inhibitor, wherein the subject has a solid tumor. Also provided herein are methods for increasing blood flow of a solid tumor in a subject comprising administering to

the subject an effective amount of ketotifen, or a pharmaceutically acceptable salt thereof, in combination with a checkpoint inhibitor, wherein increasing blood flow of the solid tumor enhances the effect of the checkpoint inhibitor. In some examples, blood flow is measured using ultrasound-based blood flow measurements or using histological techniques to measure hypoxia. Also provided herein are methods of improving the delivery or efficacy of a checkpoint inhibitor in a subject comprising administering an effective amount of ketotifen, or a pharmaceutically acceptable salt thereof, in combination with the checkpoint inhibitor, wherein the subject has a solid tumor, thereby improving the delivery or efficacy of the therapy in the subject. In some examples, administering ketotifen, or pharmaceutically acceptable salt thereof, increases the number of anti-tumor T cells that colocalize with the solid tumor. In some examples, administering ketotifen, or a pharmaceutically acceptable salt thereof, reduces the tissue stiffness of the solid tumor. In some examples, the tissue stiffness of the solid tumor is measured using ultrasound elastography. In some examples, administering ketotifen, or pharmaceutically acceptable salt thereof, decreases the levels of an extracellular matrix protein in the solid tumor. In some examples, the extracellular matrix protein is collagen I or hyaluronan binding protein (HABP). In some examples, administering ketotifen, or pharmaceutically acceptable salt thereof, reduces hypoxia in the solid tumor. In some examples, the checkpoint inhibitor inhibits a checkpoint protein selected from the group consisting of CTLA-4, PD-1, PD-L1, PD-L2, B7-H3, B7-H4, BMA, HVEM, TIM3, GAL9, LAG3, VISTA, KIR, 2B4, CD160, CGEN-15049, CHK1, CHK2, A2aR, and B-7 family ligands or a combination thereof. In some examples, the checkpoint inhibitor is a CTLA-4, PD-L1, PD-L2, or PD-1 inhibitor. In some examples, the checkpoint inhibitor is an anti-PD-1 antibody, anti-PD-L1 antibody, or anti-CTLA4 antibody. In some examples, the checkpoint inhibitor is selected from the group consisting of MEDI0680, AMP-224, nivolumab, pembrolizumab, pidilizumab, MEDI4736, atezolizumab, ipilimumab, tremelimumab, and BMS-936559. In some examples, the checkpoint inhibitor is a combination of an anti-PD-1 antibody and an anti-CTLA-4 antibody. In some examples, the ketotifen, or pharmaceutically acceptable salt thereof, is administered to the subject once per day. In some examples, the ketotifen, or pharmaceutically acceptable salt thereof, is administered to the subject twice per day. In some examples, the ketotifen, or pharmaceutically acceptable salt thereof, is administered to the subject at a dose from about 0.01 mg/kg to about 5 mg/kg. In some examples, the ketotifen, or pharmaceutically acceptable salt thereof, is administered to the subject at a dose from about 100 mg to about 1200 mg. In some examples, the

ketotifen, or pharmaceutically acceptable salt thereof, is administered to the subject at a dose from about 125 mg to about 500 mg. In some examples, the ketotifen, or pharmaceutically acceptable salt thereof, is administered to the subject at a dose of about 125 mg. In some examples, the ketotifen, or pharmaceutically acceptable salt thereof, is administered to the subject at a dose of about 500 mg. In some examples, the ketotifen, or pharmaceutically acceptable salt thereof, is administered to the subject prior to the subject being administered the checkpoint inhibitor. In some examples, the ketotifen, or pharmaceutically acceptable salt thereof, is administered to the subject beginning at least 1 day prior to the subject being administered the checkpoint inhibitor. In some examples, the ketotifen, or pharmaceutically acceptable salt thereof, is administered to the subject beginning at least 2 days prior to the subject being administered the checkpoint inhibitor. In some examples, the ketotifen, or pharmaceutically acceptable salt thereof, is administered to the subject beginning at least 3 days prior to the subject being administered the checkpoint inhibitor. In some examples, the ketotifen, or pharmaceutically acceptable salt thereof, is administered to the subject beginning at least 5 days prior to the subject being administered the checkpoint inhibitor. In some examples, the administration of ketotifen, or pharmaceutically acceptable salt thereof, to the subject is maintained for at least a portion of the time the subject is administered the checkpoint inhibitor. In some examples, the administration of ketotifen, or pharmaceutically acceptable salt thereof, to the subject is maintained for the entire period of time the subject is administered the checkpoint inhibitor. In some examples, one or more therapeutic effects in the subject is improved after administration of the ketotifen, or pharmaceutically acceptable salt thereof, and the checkpoint inhibitor relative to a baseline. In some examples, the one or more therapeutic effects is selected from the group consisting of: size of a tumor derived from the cancer, objective response rate, duration of response, time to response, progression free survival and overall survival. In some examples, the size of a tumor derived from the cancer is reduced by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80% relative to the size of the tumor derived from the cancer before administration of the ketotifen, or pharmaceutically acceptable salt thereof, and the checkpoint inhibitor. In some examples, the objective response rate is at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80%. In some examples, the subject exhibits progression-free

survival of at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the ketotifen, or pharmaceutically acceptable salt thereof, and the checkpoint inhibitor. In some examples, the subject exhibits overall survival of at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the ketotifen, or pharmaceutically acceptable salt thereof, and the checkpoint inhibitor. In some examples, the duration of response to the antibody-drug conjugate is at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the ketotifen, or pharmaceutically acceptable salt thereof, and the checkpoint inhibitor. In some examples, the solid tumor is selected from the group consisting of mesothelioma, breast cancer, breast cancer lung metastases, sarcoma, pancreatic cancer, ovarian cancer, liver metastases, prostate cancer, brain cancer, melanoma, renal cell carcinoma, colorectal cancer, hepatocellular carcinoma, lung cancer, squamous cell carcinoma of the head and neck, urothelial carcinoma, esophageal squamous cell carcinoma, gastric cancer, esophageal cancer, cervical cancer, Merkel cell carcinoma, endometrial carcinoma, and cutaneous squamous cell carcinoma. In some examples, the solid tumor is a sarcoma. In some examples, the sarcoma is osteosarcoma or fibrosarcoma. In some examples, the subject is a human. In some examples of any of the preceding methods, the method further comprises administering an additional chemotherapeutic agent. In some examples, the additional chemotherapeutic agent is doxorubicin or an analogue or derivative thereof.

**[0015]** Also provided herein is a kit comprising: (a) an effective amount of ketotifen, or a pharmaceutically acceptable salt thereof; (b) an effective amount of a checkpoint inhibitor;

and (c) instructions for using the ketotifen, or a pharmaceutically acceptable salt thereof and the checkpoint inhibitor according to any of the methods described herein.

**[0016]** Also provided herein are methods of determining an effective amount of ketotifen in a subject with a solid tumor comprising: (a) measuring the blood flow and/or stiffness of the solid tumor; (b) administering to the subject an effective amount of ketotifen; and (c) measuring the blood flow and/or stiffness of the solid tumor after administering the ketotifen, wherein an increase in blood flow and/or a decrease in stiffness following administration of the ketotifen to the subject indicates that the amount administered was an effective amount. Also provided herein are methods for treating a solid tumor in a subject in need thereof comprising: (a) measuring the blood flow and/or stiffness of the solid tumor; (b) administering to the subject an effective amount of ketotifen; (c) measuring the blood flow and/or stiffness of the solid tumor after administering the ketotifen; and (d) administering a chemotherapeutic agent if the blood flow of the solid tumor is increased and/or the stiffness of the solid tumor is decreased after administering the ketotifen. Also provided herein are methods for treating a solid tumor in a subject in need thereof comprising: (a) measuring the blood flow and/or stiffness of the solid tumor; (b) administering to the subject an effective amount of ketotifen; (c) measuring the blood flow and/or stiffness of the solid tumor after administering the ketotifen; (d) determining that the subject is responsive to a chemotherapeutic agent based on an increase in the blood flow of the solid tumor or a decrease in the stiffness of the solid tumor after administering the ketotifen; and (e) administering the chemotherapeutic agent to the subject who has been determined to be responsive to the chemotherapeutic agent based on the increase in the blood flow of the solid tumor or the decrease in the stiffness of the solid tumor after administering the ketotifen. Also provided herein are methods for predicting response to treatment with a chemotherapeutic agent comprising: (a) measuring the blood flow and/or stiffness of the solid tumor; (b) administering to the subject an effective amount of ketotifen; (c) measuring the blood flow and/or stiffness of the solid tumor after administering the ketotifen, wherein an increase in the blood flow of the solid tumor or a decrease in the stiffness of the solid tumor after administering the ketotifen indicates that the subject is likely to respond to treatment with the chemotherapeutic agent. In some examples, the effective amount of ketotifen is determined by measuring the change in blood flow and/or stiffness of the solid tumor following administration of the ketotifen to the subject, wherein an increase in blood flow and/or a decrease in stiffness following administration of the ketotifen to the subject indicates that the amount administered was an effective amount. In some examples, the method

comprises measuring the blood flow of the solid tumor and the blood flow of the solid tumor is increased after administering the ketotifen. In some examples, the method comprises measuring the stiffness of the solid tumor and the stiffness of the solid tumor is decreased after administering the ketotifen. In some examples, the ketotifen is administered for at least 1 day, at least 2 days, at least 3 days, at least 4 days, or at least 5 days prior to the administration of the chemotherapeutic agent. In some examples, the ketotifen is administered at a dose that increases the blood flow of the solid tumor and/or decreases the stiffness of the solid tumor. In some examples, blood flow and/or stiffness of the solid tumor is measured using ultrasound. In some examples, blood flow of the solid tumor is measured using histological techniques to measure hypoxia. In some examples, the chemotherapeutic agent is a checkpoint inhibitor. In some examples, the checkpoint inhibitor inhibits a checkpoint protein selected from the group consisting of CTLA-4, PD-1, PD-L1, PD-L2, B7-H3, B7-H4, BMA, HVEM, TIM3, GAL9, LAG3, VISTA, KIR, 2B4, CD160, CGEN-15049, CHK1, CHK2, A2aR, and B-7 family ligands or a combination thereof. In some examples, the checkpoint inhibitor is a CTLA-4, PD-L1, PD-L2, or PD-1 inhibitor. In some examples, the checkpoint inhibitor is an anti-PD-1 antibody, anti-PD-L1 antibody, or anti-CTLA4 antibody. In some examples, the checkpoint inhibitor is selected from the group consisting of MEDI0680, AMP-224, nivolumab, pembrolizumab, pidilizumab, MEDI4736, atezolizumab, ipilimumab, tremelimumab, and BMS-936559. In some examples, the checkpoint inhibitor is a combination of an anti-PD-1 antibody and an anti-CTLA-4 antibody. In some examples, the solid tumor is selected from the group consisting of breast cancer, breast cancer lung metastases, sarcoma, pancreatic cancer, ovarian cancer, liver metastases, prostate cancer, brain cancer, melanoma, renal cell carcinoma, colorectal cancer, hepatocellular carcinoma, lung cancer, squamous cell carcinoma of the head and neck, urothelial carcinoma, esophageal squamous cell carcinoma, gastric cancer, esophageal cancer, cervical cancer, Merkel cell carcinoma, endometrial carcinoma, and cutaneous squamous cell carcinoma. In some examples, the solid tumor is a sarcoma. In some examples, the sarcoma is osteosarcoma or fibrosarcoma. In some examples, the subject is a human. In some examples of the preceding methods, the chemotherapeutic agent is doxorubicin or an analogue or derivative thereof.

**[0017]** It is to be understood that one, some, or all of the properties of the various embodiments and/or examples described herein may be combined to form other embodiments and/or examples of the present disclosure. These and other aspects and/or examples of the disclosure will become apparent to one of skill in the

art. These and other embodiments and/or examples of the disclosure are further described by the detailed description that follows.

## BRIEF DESCRIPTION OF THE DRAWINGS

**[0018]** Representative embodiments of the invention are disclosed by reference to the following figures. It should be understood that the embodiments depicted are not limited to the precise details shown.

**[0019]** **FIG. 1A** shows representative immunofluorescence images of MCA205 tumor model paraffin sections stained for pimonidazole adducts following pimonidazole hydrochloride injection; scale bar=0.2 mm (top two rows DAPI stain; bottom two rows corresponding hypoxia stains). **FIGs. 1B-1C** show the quantification of hypoxia area fraction normalized to DAPI stain of MCA205 (**FIG. 1B**) and K7M2wt (**FIG. 1C**) tumors (n=5 mice per group, N=3-5 image fields per mouse). All data are expressed as mean ± standard error of the mean. Statistical analyses were performed by comparing the treated groups with the control *, and the 10 mg/kg with all other treatment groups **, with $p \leq 0.05$. **FIG. 1D** shows the quantification of mRNA expression levels of IFN-γ and VEGF in untreated and ketotifen (10 mg/kg) treated MCA205 tumors using the $2^{\wedge-\Delta\Delta CT}$ method (3 biological x 3 technical replicates were used). All data are expressed as mean ± standard error of the mean. Statistical analyses were performed by comparing the treated groups with the control *, and the 10 mg/kg with all other treatment groups **, with $p \leq 0.05$. **FIG. 1E** shows IFP levels in untreated and daily ketotifen treated mice for 7 days (n=7 mice per treatment group). All data are expressed as mean ± standard error of the mean. Statistical analyses were performed by comparing the treated groups with the control *, and the 10 mg/kg with all other treatment groups **, with $p \leq 0.05$.

**[0020]** **FIG. 2A** shows growth curves of MCA205 tumors after administration of daily ketotifen at various doses (1, 5, 10 and 25 mg/kg) compared to control. **FIG. 2B** shows growth curves of K7M2wt tumors after administration of daily ketotifen at 10 mg/kg dose compared to control. **FIGs. 2C-2D** show measurements of MCA205 (**FIG. 2C**) and K7M2wt (**FIG. 2D**) tumor mass following completion of treatment protocol. All data are expressed as mean ± standard error of the mean (n=5-7 mice per treatment group). **FIG. 2E** shows exemplary Western blot against the CD117 protein, with β-actin as a loading control (n=4 mice per group).

## CLAIMS

What is claimed is:

1. Use of a pharmaceutical composition comprising ketotifen, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a solid tumor in a subject in need thereof, wherein the pharmaceutical composition is to be administered in combination with a checkpoint inhibitor.

2. Use of a pharmaceutical composition comprising a checkpoint inhibitor, in the treatment of a solid tumor in a subject in need thereof, wherein the pharmaceutical composition is to be administered in combination with ketotifen, or a pharmaceutically acceptable salt thereof.

3. Use of a pharmaceutical composition comprising a combination of ketotifen, or a pharmaceutically acceptable salt thereof, and a checkpoint inhibitor, in the manufacture of a medicament for the treatment of a solid tumor in a subject in need thereof, wherein the pharmaceutical composition is to be administered to the subject in need thereof.

4. Use of a pharmaceutical composition comprising ketotifen, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for increasing blood flow of a solid tumor in a subject, wherein the pharmaceutical composition is to be administered in combination with a checkpoint inhibitor.

5. The use of claim 4, wherein blood flow is measured using ultrasound-based blood flow measurements or using histological techniques to measure hypoxia.

6. The use of any one of claims 1-5, wherein the ketotifen, or pharmaceutically acceptable salt thereof, increases the number of anti-tumor T cells that colocalize with the solid tumor.

7. The use of any one of claims 1-6, wherein the ketotifen, or pharmaceutically acceptable salt thereof, reduces the tissue stiffness of the solid tumor.

8. The use of claim 7, wherein the tissue stiffness of the solid tumor is measured using ultrasound elastography.

9. The use of any one of claims 1-8, wherein the ketotifen, or pharmaceutically acceptable salt thereof, decreases the levels of an extracellular matrix protein in the solid tumor.

10. The use of claim 9, wherein the extracellular matrix protein is collagen I or hyaluronan binding protein (HABP).

11. The use of any one of claims 1-10, wherein administering ketotifen, or pharmaceutically acceptable salt thereof, reduces hypoxia in the solid tumor.

12. The use of any one of claims 1-11, wherein the checkpoint inhibitor inhibits a checkpoint protein selected from the group consisting of CTLA-4, PD-1, PD-L1, PD-L2, B7-H3, B7-H4, BMA, HVEM, TIM3, GAL9, LAG3, VISTA, KIR, 2B4, CD160, CGEN-15049, CHK1, CHK2, A2aR, and B-7 family ligands or a combination thereof.

13. The use of claim 12, wherein the checkpoint inhibitor is an anti-PD-1 antibody, anti-PD-L1 antibody, anti-CTLA4 antibody, or a combination thereof.

14. The use of any one of claims 1-13, wherein the ketotifen, or pharmaceutically acceptable salt thereof, is to be administered to the subject once per day.

15. The use of any one of claims 1-14, wherein the ketotifen, or pharmaceutically acceptable salt thereof, is to be administered to the subject at a dose from about 0.01 mg/kg to about 5 mg/kg.

16. The use of any one of claims 1-15, wherein the ketotifen, or pharmaceutically acceptable salt thereof, is to be administered to the subject at a dose from about 100 mg to about 1200 mg.

17. The use of any one of claims 1-16, wherein the ketotifen, or pharmaceutically acceptable salt thereof, is to be administered to the subject prior to the subject being administered the checkpoint inhibitor.

18. The use of any one of claims 1-17, wherein the administration of ketotifen, or pharmaceutically acceptable salt thereof, to the subject is maintained for at least a portion of the time the subject is to be administered the checkpoint inhibitor.

19. The use of any one of claims 1-18, wherein one or more therapeutic effects in the subject is improved after administration of the ketotifen, or pharmaceutically acceptable salt thereof, and the checkpoint inhibitor relative to a baseline, wherein the one or more therapeutic effects is selected from the group consisting of: size of a tumor derived from the cancer, objective response rate, duration of response, time to response, progression free survival and overall survival.

20. The use of any one of claims 1-19, wherein the size of a tumor derived from the cancer is reduced by at least about 10% relative to the size of the tumor derived from the cancer

before administration of the ketotifen, or pharmaceutically acceptable salt thereof, and the checkpoint inhibitor.

21. The use of any one of claims 1-20, wherein the objective response rate is at least about 20%.

22. The use of any one of claims 1-21, wherein the subject exhibits progression-free survival of at least about 1 month after administration of the ketotifen, or pharmaceutically acceptable salt thereof, and the checkpoint inhibitor.

23. The use of any one of claims 1-22, wherein the subject exhibits overall survival of at least about 1 month after administration of the ketotifen, or pharmaceutically acceptable salt thereof, and the checkpoint inhibitor.

24. The use of any one of claims 1-23, wherein the duration of response to the antibody-drug conjugate is at least about 1 month after administration of the ketotifen, or pharmaceutically acceptable salt thereof, and the checkpoint inhibitor.

25. The use of any one of claims 1-24, wherein the solid tumor is selected from the group consisting of mesothelioma, breast cancer, breast cancer lung metastases, sarcoma, pancreatic cancer, ovarian cancer, liver metastases, prostate cancer, brain cancer, melanoma, renal cell carcinoma, colorectal cancer, hepatocellular carcinoma, lung cancer, squamous cell carcinoma of the head and neck, urothelial carcinoma, esophageal squamous cell carcinoma, gastric cancer, esophageal cancer, cervical cancer, Merkel cell carcinoma, endometrial carcinoma, and cutaneous squamous cell carcinoma.

26. The use of any one of claims 1-25, wherein the subject is a human.

27. The use of any one of claims 1-26, wherein an additional chemotherapeutic agent is to be further administered.

28. The use of claim 27, wherein the additional chemotherapeutic agent is doxorubicin or an analogue or derivative thereof.

29. A kit comprising:

(a) an effective amount of ketotifen, or a pharmaceutically acceptable salt thereof;

(b) an effective amount of a checkpoint inhibitor; and

(c) instructions for using the ketotifen, or a pharmaceutically acceptable salt thereof and the checkpoint inhibitor according to the use of any one of claims 1-28.

30. The use of any one of claims 1-28 or the kit of claim 29, wherein the subject is selected for the treatment based on increased blood flow and/or decreased stiffness of the solid tumor in response to ketotifen, or a pharmaceutically acceptable salt thereof.