

CLAIMS:

1. Use of an anti-PD-1 therapeutic agent or an anti-PD-L1 therapeutic agent in the manufacture of a medicament for~~A method of~~ treating cancer in a patient, wherein the anti-PD-1 therapeutic agent or anti-PD-L1 therapeutic agent is to be administered with a device~~comprising:~~
~~placing a device~~ comprising a plurality of microneedles to be placed on the skin of the patient proximate to a first position under the skin of the patient, wherein the first position is proximate to lymph vessels and/or lymph capillaries in the patient's lymphatic system, and wherein the microneedles have a surface comprising nanotopography;
~~inserting wherein~~ the plurality of microneedles is to be inserted into the patient to a depth whereby at least the epidermis is penetrated and an end of at least one of the microneedles is proximate to the first position; and
wherein the anti-PD-1 therapeutic agent or anti-PD-L1 therapeutic agent is to be administered ~~administering~~ via the plurality of microneedles to the first position ~~an effective amount of an anti PD-1 therapeutic agent or an effective amount of an anti PD-L1 therapeutic agent to treat cancer in a patient.~~

2. Use of an anti-PD-1 therapeutic agent or an anti-PD-L1 therapeutic agent in the manufacture of a medicament for~~A method of~~ preventing or reducing cancer metastasis in a patient, wherein the anti-PD-1 therapeutic agent or anti-PD-L1 therapeutic agent is to be administered with a device comprising:
~~locating at least one lymph node in the patient that intervenes in the lymphatic system between a solid cancer tumor and a draining duct;~~
~~placing a device comprising~~ a plurality of microneedles to be placed on the skin of the patient proximate to a first position under the skin of the patient located between an ~~the~~ intervening lymph node and ~~the a~~ solid cancer tumor, wherein said intervening lymph node is at least one lymph node located in the patient that intervenes in the lymphatic system between a solid cancer tumor and a draining duct, wherein the first position is proximate to lymph vessels and/or lymph capillaries in the patient's

lymphatic system, and wherein the microneedles have a surface comprising nanotopography;

~~inserting wherein~~ the plurality of microneedles is to be inserted into the patient to a depth whereby at least the epidermis is penetrated and an end of at least one of the microneedles is proximate to the first position; and wherein the anti-PD-1 therapeutic agent or anti-PD-L1 therapeutic agent is to be administered~~administering~~ via the plurality of microneedles to the first position ~~a therapeutically effective amount of an anti-PD-1 therapeutic agent or an anti-PD-L1 therapeutic agent that is effective for preventing or reducing cancer metastasis in the patient.~~

3. Use of an anti-PD-1 therapeutic agent or an anti-PD-L1 therapeutic agent in the manufacture of a medicament for~~A method of~~ preventing or reducing cancer metastasis in a patient, wherein the anti-PD-1 therapeutic agent or anti-PD-L1 therapeutic agent is to be administered with a device comprising:

~~locating a solid cancer tumor in the patient;~~

~~locating at least one lymph node in the patient that intervenes in the lymphatic system between the solid cancer tumor and a draining duct;~~

~~placing a device that comprises~~ a plurality of microneedles to be placed on the skin of the patient at a first location on the skin of the patient that is proximate to lymph capillaries and/or lymph vessels that flow into the intervening lymph node, wherein said intervening lymph node is at least one lymph node located in the patient that intervenes in the lymphatic system between a solid cancer tumor located in the patient and a draining duct, wherein the microneedles have a surface comprising nanotopography;

~~inserting wherein~~ the plurality of microneedles is to be inserted into the patient to a depth whereby at least the epidermis is penetrated; and

wherein the anti-PD-1 therapeutic agent or anti-PD-L1 therapeutic agent is to be administered~~administering~~ via the plurality of microneedles to the lymph capillaries and/or lymph vessels that flow into the intervening lymph node ~~a therapeutically effective amount of an anti-PD-1~~

~~therapeutic agent or an anti-PD-L1 therapeutic agent that is effective in preventing or reducing cancer metastasis in the patient.~~

4. The ~~method~~-use of any one of claims 1-3, wherein the cancer comprises a tumor.
5. The ~~method~~-use of any one of claims 1-3, wherein the lymph node is a tumor draining lymph node.
6. The ~~method~~-use of any one of claims 1-3, wherein the cancer is a cancer susceptible to treatment with an anti-PD-1 therapeutic agent or anti-PD-L1 therapeutic agent.
7. The ~~method~~-use of any one of claims 1-3, wherein bioavailability of the anti-PD-1 therapeutic agent or the anti-PD-L1 therapeutic agent is up to 10%, 15% 20%, 25%, 30%, 35%, 40%, 45%, or 50%.
8. The ~~method~~-use of any one of claims 1-3, wherein a serum Tmax of the anti-PD-1 therapeutic agent or the anti-PD-L1 therapeutic agent is from 10 to 100 hours.
9. The ~~method~~-use of any one of claims 1-3, wherein a serum Cmax of the anti-PD-1 therapeutic agent or the anti-PD-L1 therapeutic agent is decreased up to 1.5-fold, 2-fold, 2.5-fold, 3-fold, 3.5-fold, or 4-fold, as compared to a serum Cmax following a therapeutically equivalent amount of the anti-PD-1 therapeutic agent or the anti-PD-L1 therapeutic agent administered by an intravenous delivery route.
10. The use~~method~~ of any one of claims 1-3, wherein a serum AUC_{0-t} of the anti-PD-1 therapeutic agent or the anti-PD-L1 therapeutic agent is decreased up to 1.5-fold, 2-fold, 2.5-fold, 3-fold, 3.5-fold, or 4-fold as compared to a serum AUC_{0-t} following a therapeutically equivalent amount of the anti-PD-1 therapeutic agent or the anti-PD-L1 therapeutic agent administered by an intravenous delivery route.
11. The ~~method~~-use of any one of claims 1-3, wherein delivery of the anti-PD-1 therapeutic agent or the anti-PD-L1 therapeutic agent to one or more lymph nodes is increased up to 1.5-fold, 2-fold, 2.5-fold, 3-fold, 3.5-fold, or 4-fold as compared to delivery to one or more lymph nodes of a therapeutically equivalent amount of the anti-PD-1

therapeutic agent or the anti-PD-L1 therapeutic agent administered by an intravenous delivery route.

12. The ~~method~~-use of any one of claims 1-3, wherein levels of the anti-PD-1 therapeutic agent or anti-PD-L1 therapeutic agent in one or more systemic organs is decreased 10-75% over a period of time as compared to levels in one or more systemic organs following a therapeutically equivalent amount of the anti-PD-1 therapeutic agent or the anti-PD-L1 therapeutic agent administered by an intravenous delivery route over a same period of time.
13. The ~~method~~-use of claim 12, wherein the organ is a liver or a kidney.
14. The ~~method~~-use of claim 12, wherein the period of time is up to 12 hours, 24 hours, 36 hours, 48 hours, 60 hours, or 72 hours.
15. The use~~method~~ of any one of claims 1-3, wherein the anti-PD-1 therapeutic agent or the anti-PD-L1 therapeutic agent is at least 90%, 95%, 99%, or 99.9% cleared from the patient's serum by 28 days after administration.
16. The ~~method~~-use of any one of claims 1-3, wherein the ~~administering~~-administration results in an undetectable primary tumor and/or an undetectable secondary tumor.
17. The ~~method~~-use of claim 16, wherein an incidence or probability of an undetectable primary tumor and/or an undetectable secondary tumor is at least 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or 99%.
18. The ~~method~~-use of any one of claims 1-3, wherein exposure of the anti-PD-1 therapeutic agent or the anti-PD-L1 therapeutic agent to T-cells in the patient's lymphatic system is increased up to 1.5-fold, 2-fold, or 2.5-fold, as compared to exposure to T-cells in the patient's lymphatic system following a therapeutically equivalent amount of the anti-PD-1 therapeutic agent or the anti-PD-L1 therapeutic agent administered by an intravenous delivery route.
19. The ~~method~~-use of any one of claims 1-3, wherein exposure of the anti-PD-1 therapeutic agent or the anti-PD-L1 therapeutic agent to one or more solid cancer tumors in the patient's lymphatic system is increased up to 1.5-fold, 2-fold, or 2.5-fold, as compared

to exposure to one or more solid cancer tumors in the patient's lymphatic system following a therapeutically equivalent amount of the anti-PD-1 therapeutic agent or the anti-PD-L1 therapeutic agent administered by an intravenous delivery route.

- 20. The ~~method~~-use of any one of claims 1-3, wherein tumor-infiltrating lymphocytes are increased up to 1.5-fold, 2-fold, or 2.5-fold as compared to tumor-infiltrating lymphocytes following a therapeutically equivalent amount of the anti-PD-1 therapeutic agent or the anti-PD-L1 therapeutic agent administered by an intravenous delivery route.
- 21. The ~~method~~-use of any one of claims 1-3, wherein incidence or severity of one or more immune-related Adverse Events is reduced as compared to one or more immune-related Adverse Events following a therapeutically equivalent amount of the anti-PD-1 therapeutic agent or the anti-PD-L1 therapeutic agent administered by an intravenous delivery route.