

incidence of 3 years after primary diagnosis. The pattern of recurrence more often involves visceral organs and less common bones compared to other breast cancer subtypes [Foulkes, 2010].

Compared with the hormone receptor–positive breast cancers, TNBC has a worse prognosis, with an aggressive natural history [Lebert 2018]. At diagnosis, TNBC tumors are more likely to be T2 or T3, to be positive for lymphovascular invasion, and to have already metastasized to lymph nodes [Dent 2007]. Metastatic TNBC (mTNBC) accounts for a disproportionately high percentage of metastases, particularly distant recurrence, and death among patients with breast cancer. Currently, no treatments exist that are directed specifically to the metastatic process.

Chemotherapy is still the main treatment option for TNBC patients, and standard treatment is surgery with adjuvant therapy, such as chemotherapy and radiotherapy. Although TNBC responds to chemotherapeutic agents such as taxanes and anthracyclines better than other subtypes of breast cancer, prognosis still remains poor. As a variation, neoadjuvant chemotherapy is frequently used for triple-negative breast cancers [Hudis 2011]. This allows for a higher rate of breast-conserving surgeries and, from evaluating the response to the chemotherapy, gives important clues about the individual responsiveness of the particular cancer to chemotherapy.

Due to the loss of target receptors such as ER, PGR, and HER-2, patients with TNBC do not benefit from hormonal or trastuzumab-based therapy. Hence, surgery and chemotherapy, individually or in combination, appear to be the only available modalities. To date there are multiple approaches attempting to improve care of triple negative breast cancer patients, including DNA damaging agents like platinum, targeted EGFR and VEGF inhibitors, and, PARP inhibitors; however, none have been as clinically successful as anticipated and more targeted therapies need to be developed and explored [Aysola 2013]. Thus, metastatic TNBC is a complex disease with an unmet need and an unproven treatment regimen in clinics.

SUMMARY

In one aspect, the present disclosure relates to a use of a CCR5 binding agent in the manufacture of a medicament for treating or preventing cancer in a subject.

5 In another aspect, the present disclosure relates to a use of the monoclonal antibody PA14, leronlimab, or CCR5mAb004, or a binding fragment thereof in the manufacture of a medicament for reducing tumor burden in a subject having a CCR5+ cancer, comprising: selecting a cancer patient suitable for treatment with a CCR5 binding agent before treatment, comprising establishing that the patient has a cancer type typically known to be characterized by an elevated CCR5+ expression level or
10 measuring a tumor biopsy from said patient for CCR5+ expression.

In yet another aspect, the present disclosure relates to a use of a composition comprising the monoclonal antibody PA14, leronlimab, or CCR5mAb004, or a binding fragment thereof in the manufacture of a medicament for treating CCR5+ cancer.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

15 **Fig. 1A, Fig. 1B, Fig. 1C, Fig. 1D, Fig. 1E, and Fig. 1F** show maraviroc inhibition of lung metastasis in a mouse model. Fig. 1A shows timecourse images of

CLAIMS

1. Use of a CCR5 binding agent in the manufacture of a medicament for~~A method of~~ treating or preventing cancer ~~in a subject comprising administering to a subject in need thereof an effective amount of a CCR5 binding agent.~~
2. The ~~method~~use according to claim 1, wherein the cancer comprises CCR5-positive metastatic breast cancer.
3. The ~~use~~method according to claim 1, wherein the cancer comprises CCR5-positive melanoma, brain cancer, glioblastoma, throat cancer, lung cancer, stomach cancer, colon cancer, colon carcinoma, breast cancer, testicular cancer, ovarian cancer, uterine cancer, pancreatic cancer, bladder cancer, esophageal cancer, appendix cancer, or prostate cancer.
4. The ~~use~~method according to any one of the preceding claims, wherein the CCR5 binding agent competes with CCL5 for binding to the CCR5 cell receptor.
5. The ~~use~~method according to any one of the preceding claims, wherein the CCR5 binding agent comprises the monoclonal antibody PA14, leronlimab, or CCR5mAb004, or a binding fragment thereof.
6. The ~~use~~method according to any one of the preceding claims, wherein the CCR5 binding agent is to be administered in combination with another cancer therapy.
7. The ~~use~~method of claim 1, wherein the CCR5 binding agent comprises an antibody comprising:
 - (a) a heavy chain variable region (VH) comprising a heavy chain complementary determining region 1 (HCDR1) of SEQ ID NO:12, a heavy chain

complementary determining region 2 (HCDR2) of SEQ ID NO:13, and a heavy chain complementary determining region 3 (HCDR3) of SEQ ID NO:14; and

(b) a light chain variable region (VL) comprising a light chain complementary determining region 1 (LCDR1) of SEQ ID NO:9, a light chain complementary determining region 2 (LCDR2) of SEQ ID NO:10, and a light chain complementary determining region 3 (LCDR3) of SEQ ID NO:11.

8. The usemethod according to any one of the preceding claims, wherein the CCR5 binding agent comprises leronlimab.

9. The usemethod according to any one of the preceding claims, wherein the metastatic breast cancer is metastatic triple negative metastatic breast cancer.

10. The usemethod according to any one of claims 1-8, wherein the cancer is metastatic HER2-positive breast cancer.

11. The usemethod according to any one of the preceding claims, wherein preventing the cancer comprises slowing the growth of the cancer.

12. The usemethod according to any one of the preceding claims, wherein preventing the cancer comprises preventing the formation of a tumor.

13. The usemethod according to any one of the preceding claims, wherein preventing the cancer comprises preventing the formation of tumor metastases.

14. The usemethod according to any one of the preceding claims, wherein preventing the cancer comprises limiting or reducing the size of a tumor.

15. The usemethod according to claim 14, wherein preventing the cancer comprises limiting or reducing the size of a metastatic tumor.

16. The ~~usemethod~~ according to claim 15, wherein limiting or reducing the size of a metastatic tumor comprises at least a 50% reduction in tumor volume.

17. The ~~usemethod~~ according to any one of the preceding claims, wherein preventing the cancer comprises reducing the number of circulating tumor cells in the subject.

18. The ~~usemethod~~ according to any one of the preceding claims, wherein preventing the cancer comprises reducing the number of epithelial mesenchymal transition cells in the subject.

19. The ~~usemethod~~ according to any one of the preceding claims, wherein preventing the cancer comprises reducing the number of cancer associated macrophage-like cells in the subject.

20. The ~~usemethod~~ according to any one of the preceding claims, wherein treating comprises causing the cancer progression to become stable.

21. The ~~usemethod~~ according to any one of the preceding claims, further comprising ~~administering to the subject~~that a cellular therapy, a chemotherapeutic agent, a small molecule, or an inhibitor of CCR5/CCL5 signaling is to be administered to the subject.

22. The ~~usemethod~~ according to claim 21, wherein the chemotherapeutic agent comprises carboplatin.

23. The ~~usemethod~~ according to claim 21, wherein the chemotherapeutic agent comprises one or more of taxotere, herceptin, and pertuzumab.

24. The ~~use~~method according to claim 21, wherein the inhibitor of CCR5/CCL5 signaling comprises maraviroc, vicriviroc, aplaviroc, SCH-C, TAK-779, PA14 antibody, 2D7 antibody, RoAb13 antibody, RoAb14 antibody, or 45523 antibody.

25. Use of the monoclonal antibody PA14, leronlimab, or CCR5mAb004, or a binding fragment thereof in the manufacture of a medicament ~~A method~~ for reducing tumor burden in a subject having a CCR5+ cancer, comprising:

selecting a cancer patient suitable for treatment with a CCR5 binding agent before treatment, comprising establishing that the patient has a cancer type typically known to be characterized by an elevated CCR5+ expression level or measuring a tumor biopsy from said patient for CCR5+ expression; ~~and~~

~~administering the monoclonal antibody PA14, leronlimab, or CCR5mAb004, or a binding fragment thereof.~~

26. The ~~method~~use of claim 25, wherein the monoclonal antibody PA14, leronlimab, or CCR5mAb004, or a binding fragment thereof, is to be administered in weekly injections of 700 mg.

27. The ~~use~~method of claim 25 or claim 26, further comprising ~~eliminating that~~ detectable brain metastasis is to be eliminated.

28. The ~~use~~method of any of claims 25-27, further comprising ~~reducing that~~ a number of brain lesions detectable by MRI are to be reduced.

29. The ~~use~~method of any of claims 25-28, further comprising ~~reducing that~~ the tumor volume of at least one brain tumor is to be reduced by greater than 50%.

30. The ~~use~~method of any of claims 25-29, further comprising, ~~reducing that~~ the subjects CTC or EMT counts are to be reduced to zero.

31. Use of Aa composition ~~for treating CCR5+ cancer~~ comprising the monoclonal antibody PA14, leronlimab, or CCR5mAb004, or a binding fragment thereof in the manufacture of a medicament for treating CCR5+ cancer.