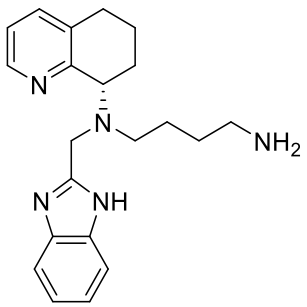
levels in the tumor microenvironment (TME). In clinical studies of a wide range of tumor types, including breast, ovarian, renal, lung, and melanoma, expression of CXCR4/CXCL12 has been associated with a poor prognosis and with an increased risk of metastasis to lymph nodes, lung, liver, and brain, which are sites of CXCL12 expression. CXCR4 is frequently expressed on melanoma cells, particularly the CD133+ population that is considered to represent melanoma stem cells; *in vitro* experiments and murine models have demonstrated that CXCL12 is chemotactic for such cells.

[0004] Furthermore, there is now evidence implicating the CXCL12/CXCR4 axis in contributing to the loss or lack of tumor responsiveness to angiogenesis inhibitors (also referred to as "angiogenic escape"). In animal cancer models, interference with CXCR4 function has been demonstrated to alter the TME and sensitize the tumor to immune attack by multiple mechanisms such as elimination of tumor re-vascularization and increasing the ratio of CD8+ T cells to Treg cells. These effects result in significantly decreased tumor burden and increased overall survival in xenograft, syngeneic, and transgenic cancer models. See Vanharanta et al. (2013) Nat Med 19: 50-56; Gale and McColl (1999) BioEssays 21: 17-28; Highfill et al. (2014) Sci Transl Med 6: ra67; Facciabene et al. (2011) Nature 475: 226-230.

[0005] These data underscore the significant, unmet need for CXCR4 inhibitors to treat the many diseases and conditions mediated by aberrant or undesired expression of the receptor, for example in cellular proliferative disorders.

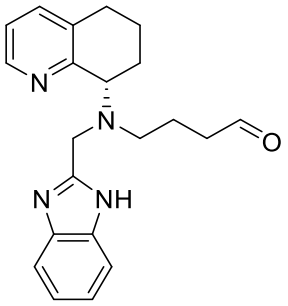
SUMMARY

[0005a] In an aspect of the present disclosure, there is provided a X4P-001 composition comprising a compound of formula **I**:



I

or a pharmaceutically acceptable salt thereof; and the following compound:



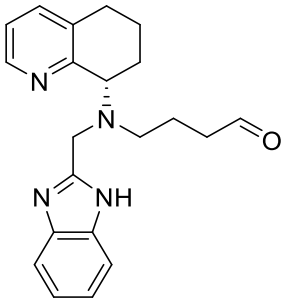
I-6

or a pharmaceutically acceptable salt thereof, in an amount from about 0.001 to about 0.5% w/w of the X4P-001 composition.

[0005b] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising the X4P-001 composition disclosed herein, and a pharmaceutically acceptable adjuvant, carrier, or vehicle.

[0005c] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising the X4P-001 composition disclosed herein, and a pharmaceutically acceptable adjuvant, carrier, or vehicle.

[0005d] In another aspect of the present disclosure, there is provided a compound of the following formula:



I-6

or a pharmaceutically acceptable salt thereof.

[0006] It has now been found that disclosed X4P-001 compositions of the present disclosure, and pharmaceutically acceptable compositions thereof, are effective as CXC receptor type 4 (CXCR4) inhibitors. In one example, the present disclosure provides an X4P-001 composition comprising a compound of formula **I**:

[0007] X4P-001 compositions of the present disclosure, and pharmaceutically acceptable compositions thereof, are useful for treating a variety of diseases, disorders, or conditions associated with CXCR4, such as hyperproliferative conditions including various cancers. Such diseases, disorders, or conditions include those described herein.

BRIEF DESCRIPTION OF THE FIGURES

[0008] FIG. 1 shows a detailed summary of the manufacturing process for capsules containing a solid drug product formulation (unit dosage form) of X4P-001.

[0009] FIG. 2 shows a scheme of the original synthesis process (Process version 2 or Process 2) used to prepare X4P-001 for clinical trials.

[0010] FIG. 3 shows a comparison of Process 3 (the current, improved synthesis) and Process 2 (the original process) for the preparation of X4P-001.

[0011] FIG. 4 shows a detailed comparison between Process version 2 and 3 for the consecutive downstream operations in the work-up and isolation of the API.

[0012] FIG. 5 shows HPLC and MS data for X4P-001, PTL/ST/0511, batch 3-1 (prepared using Process 2), 25ºC/60% RH, t=3 months. HPLC conditions 1 (described in detail below); 1 mg/mL in methanol, injection volume 100 µL.

[0013] FIG. 6 shows HPLC and MS data for X4P-001, PTL/ST/0511, batch 3-1 (prepared using Process 2), 25ºC/60% RH t = 3 months. HPLC conditions 2 (described in detail below); 1 mg/mL in methanol, injection volume 100 µL.

[0014] FIG. 7 shows HPLC and MS data for X4P-001, PTL/ST/0511, batch 3-1 (prepared using Process 2), 25ºC/60% RH t = 3 months. HPLC conditions 2 (described in detail below); sample concentration 10 mg/mL in methanol, 100 µL injection.

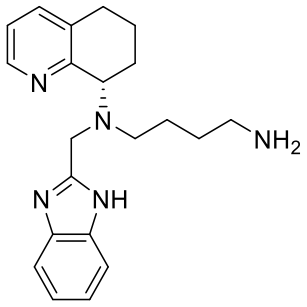
[0015] FIG. 8 shows HPLC and MS data for X4P-001, degradation sample 80ºC/80% RH t = 1 day. HPLC conditions 2 (described in detail below); sample concentration 10 mg/mL in methanol, 100 µL injection volume.

[0016] FIG. 9 shows HPLC and MS data for X4P-001, degradation sample 80ºC/80% RH t = 7 days. HPLC conditions 2 (described in detail below); sample concentration 10 mg/mL in methanol, 100 µL injection volume.

CLAIMS

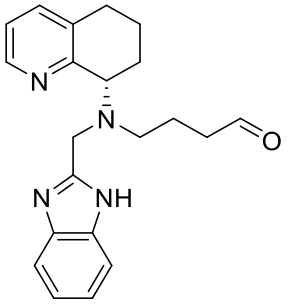
We claim:

1. An X4P-001 composition comprising a compound of formula **I**:



I

or a pharmaceutically acceptable salt thereof; and the following compound:



I-6

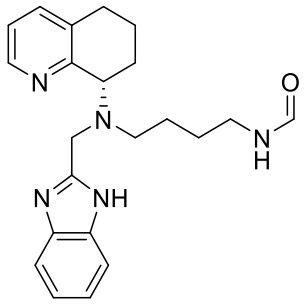
or a pharmaceutically acceptable salt thereof, in an amount from about 0.001 to about 0.5% w/w of the X4P-001 composition.

2. The X4P-001 composition of claim 1, wherein the amount of **I-6**, or a pharmaceutically acceptable salt thereof, is from about 0.01 to about 0.4% w/w of the X4P-001 composition.

3. The X4P-001 composition of claim 1, wherein the amount of **I-6**, or a pharmaceutically acceptable salt thereof, is from about 0.01 to about 0.3% w/w of the X4P-001 composition.

4. The X4P-001 composition of claim 1, wherein the amount of **I-6** is from 0.01 to 0.2% w/w of the X4P-001 composition.

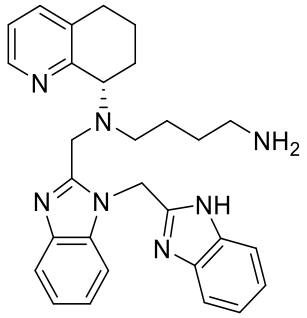
5. The X4P-001 composition of claim 2, wherein the composition comprises at least a detectable amount of the following compound:



I-2

or a pharmaceutically acceptable salt thereof.

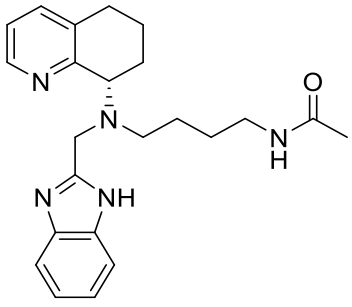
6. The X4P-001 composition of claim 2, wherein the composition comprises at least a detectable amount of the following compound:



I-3

or a pharmaceutically acceptable salt thereof.

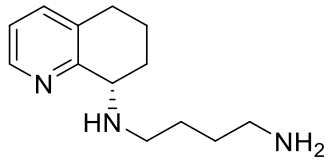
7. The X4P-001 composition of claim 6, wherein the composition comprises at least a detectable amount of the following compound:



I-5

or a pharmaceutically acceptable salt thereof.

8. The X4P-001 composition of claim 6, wherein the composition comprises at least a detectable amount of the following compound:



I-7

or a pharmaceutically acceptable salt thereof.

9. The X4P-001 composition of claim 5, wherein the amount of **I-2**, or a pharmaceutically acceptable salt thereof, is from about 0.01 to about 0.3% w/w of the X4P-001 composition.

10. The X4P-001 composition of claim 6, wherein the amount of **I-3**, or a pharmaceutically acceptable salt thereof, is from about 0.01 to about 0.4% w/w of the X4P-001 composition.

11. The X4P-001 composition of claim 8, wherein the amount of **I-3**, or a pharmaceutically acceptable salt thereof, is from about 0.01 to about 0.4% w/w of the X4P-001 composition.

12. The X4P-001 composition of claim 7, wherein the amount of **I-5**, or a pharmaceutically acceptable salt thereof, is from about 0.01 to about 0.4% w/w of the X4P-001 composition.

13. The X4P-001 composition of claim 11, wherein the amount of **I-7**, or a pharmaceutically acceptable salt thereof, is from about 0.01 to about 0.25% w/w of the X4P-001 composition.

14. The X4P-001 composition of claim 13, wherein the compound of formula **I** is present in the X4P-001 composition as a free base.

15. The X4P-001 composition of claim 14, wherein the composition comprises no more than 3.0% of total impurities.

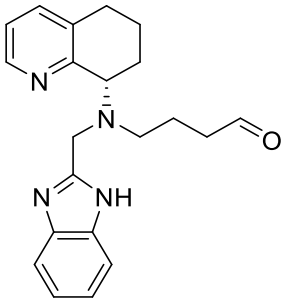
16. The X4P-001 composition of claim 15, wherein the R-enantiomeric excess (%ee) of the compound of formula **I** is no less than 97.0%.

17. The X4P-001 composition of claim 15, wherein the total weight of **I-6** and any additional impurities that are present comprise no more than about 0.8% w/w of the X4P-001 composition.

18. A pharmaceutical composition comprising the X4P-001 composition according to claim 1, and a pharmaceutically acceptable adjuvant, carrier, or vehicle.

19. A pharmaceutical composition comprising the X4P-001 composition according to claim 14, and a pharmaceutically acceptable adjuvant, carrier, or vehicle.

20. A compound of the following formula:



I-6

or a pharmaceutically acceptable salt thereof.