

syndrome, where nearly all mutated forms of SHP2 demonstrate increased PTP activity. Thus, there is a need for SHP2 phosphatase inhibitor compounds and methods for treating cancer and other disorders with these compounds.

SUMMARY

wherein

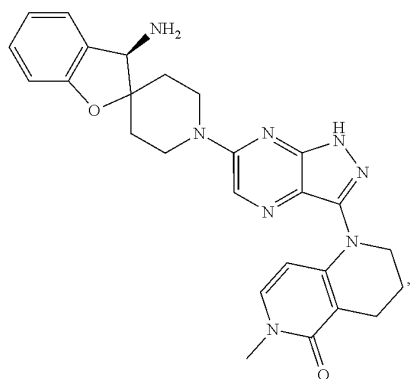
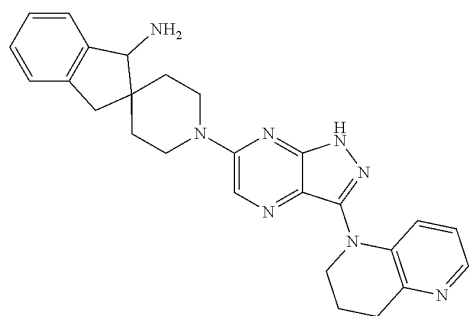
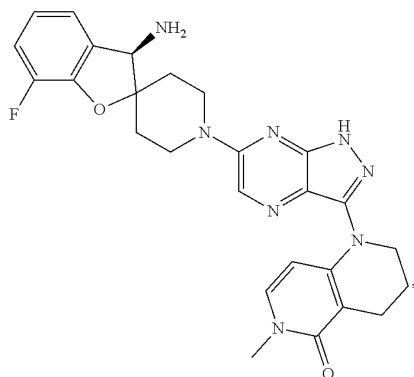
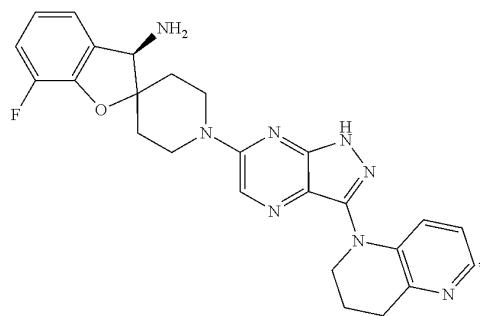
U is $\mathbb{C}$, $\mathbb{C}R^4$ or $\mathbb{N}$;

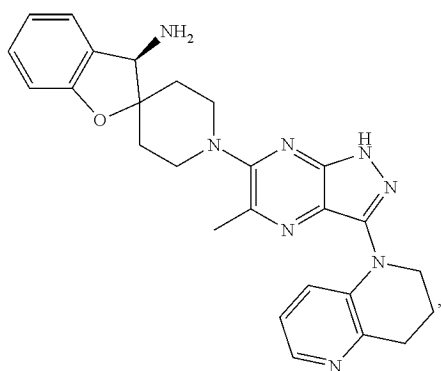
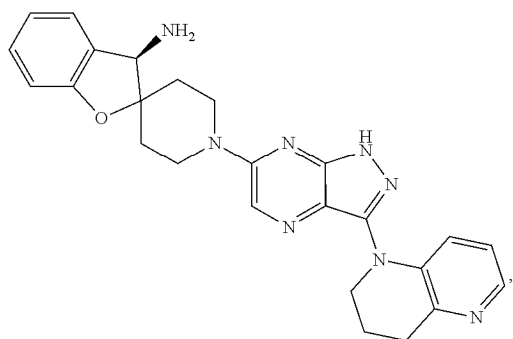
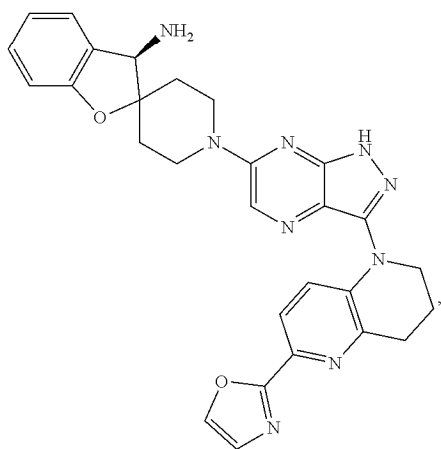
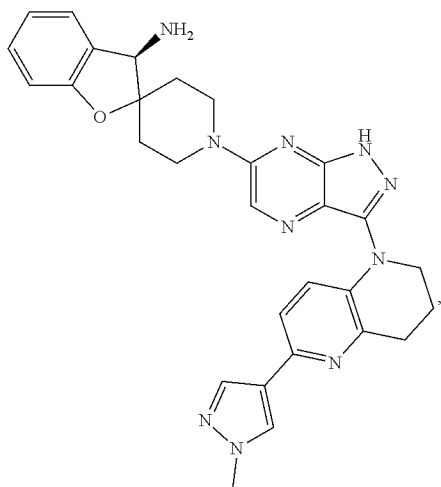
B is fused to D such that the two atoms shared by D and B are both carbon or one carbon and one nitrogen;

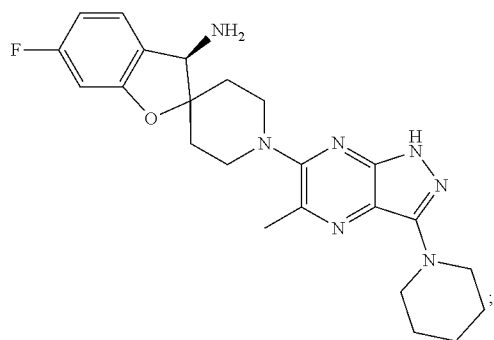
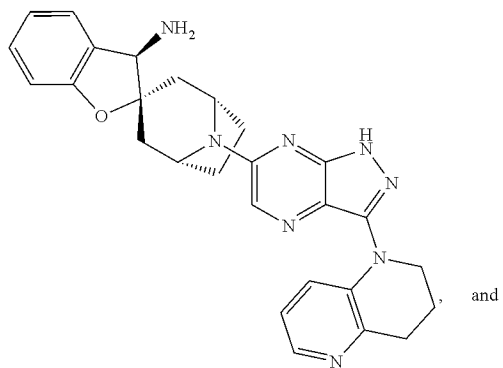
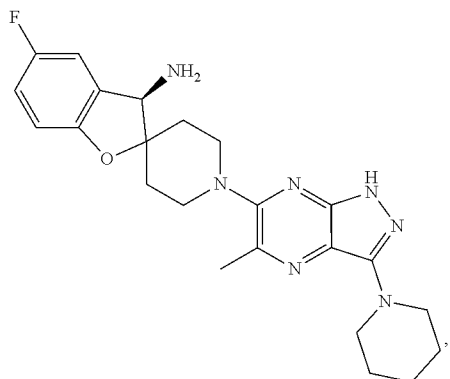
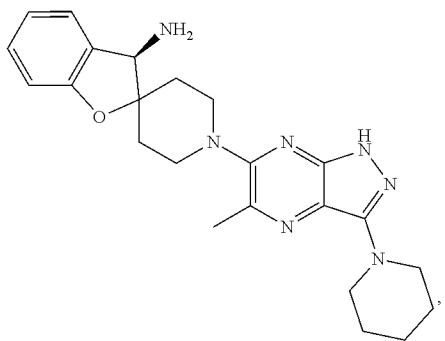
20 R⁶ is independently for each occurrence selected from the group consisting of H, -(C₁-C₆)alkyl, -C(O)OC₁₋₄alkyl, and phenyl;

R^{D1} is selected from the group consisting of hydroxyl, cyano, halogen, and $-N(R^6)_2$;

[0005a] In one aspect of the present disclosure, there is provided a compound selected from the group consisting of:

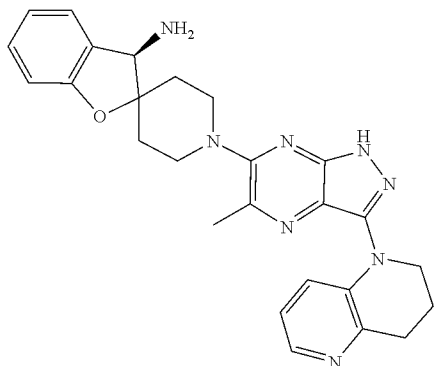






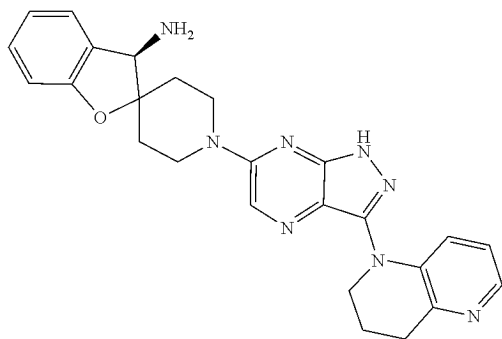
or a pharmaceutically acceptable salt thereof.

[0005b] In another aspect of the present disclosure, there is provided a compound represented by:



or a pharmaceutically acceptable salt thereof.

5 **[0005c]** In a further aspect of the present disclosure, there is provided a compound represented by:



or a pharmaceutically acceptable salt thereof.

10 **[0005d]** In another aspect of the present disclosure, there is provided a pharmaceutical composition disclosed herein and a pharmaceutically acceptable carrier.

[0005] The present disclosure also provides, for example, pharmaceutical compositions containing the compounds described herein. Further, the disclosure provides a method of inhibiting SHP2 phosphatase activity in a subject by administering a therapeutically effective amount of a compound or composition described herein, to a subject, *e.g.*, a human, in need.

5 **[0006]** The present disclosure further provides, for example, a method of treating a disorder in a subject by administering a therapeutically effective amount of a compound or composition described herein, to a subject in need thereof. Examples of disorders include Noonan syndrome, neutropenia, diabetes, neuroblastoma, melanoma, acute myeloid leukemia, juvenile leukemia, juvenile myelomonocytic leukemia, breast cancer, lung cancer,
10 and colorectal cancer. In addition to the compound or composition described herein, such method may include administration of a therapeutically effective amount of an antibody, an antibody-drug conjugate, an immunomodulator, or a histone deacetylase inhibitor.

[0007] The present disclosure is based, in part, on certain discoveries which are described more fully in the Examples section of the present application. For example, the present
15 disclosure is based, in part, on the discovery of compounds disclosed herein, and the SHP2 phosphatase inhibition exhibited by such compounds.

[0008] These and other examples of the disclosure are further described in the following sections of the application, including the Detailed Description, Examples, and Claims. Still other objects and advantages of the disclosure will become apparent by those of skill in the
20 art from the disclosure herein, which are simply illustrative and not restrictive. Thus, other examples will be recognized by the ordinarily skilled artisan without departing from the spirit and scope of the disclosure.

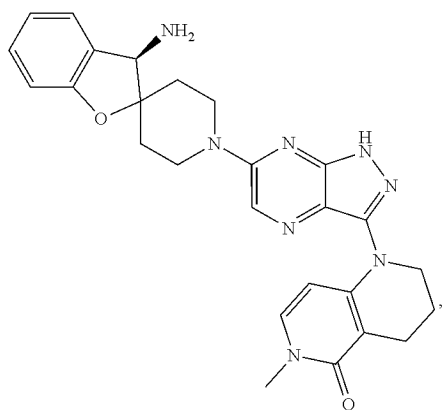
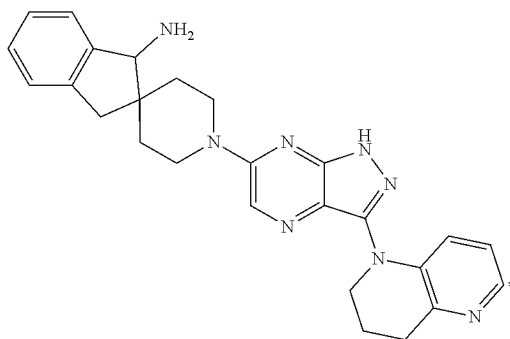
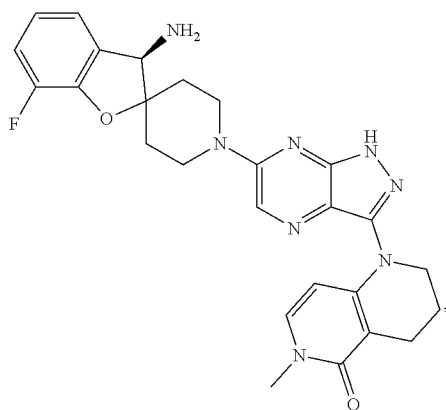
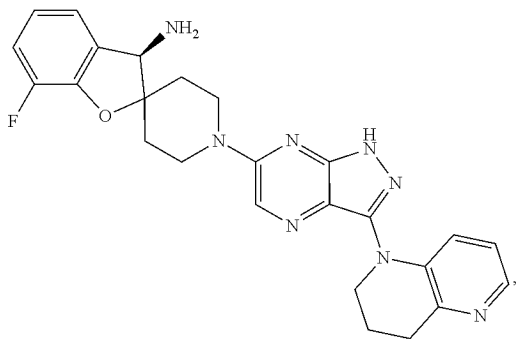
BRIEF DESCRIPTION OF THE DRAWINGS

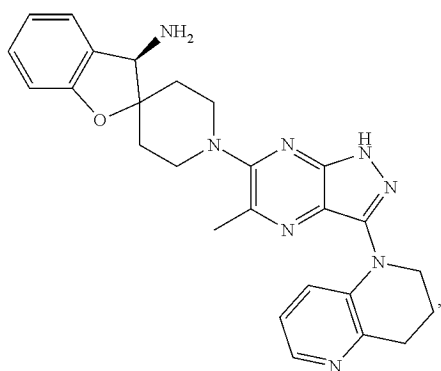
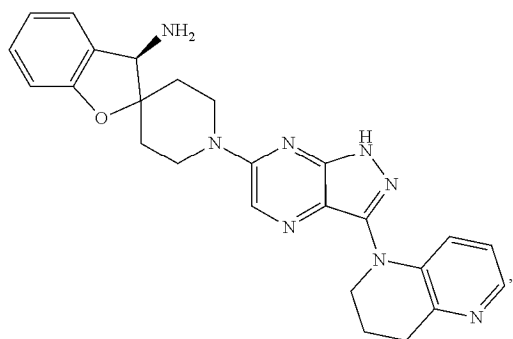
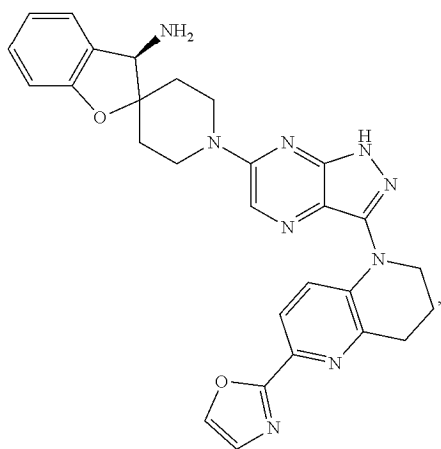
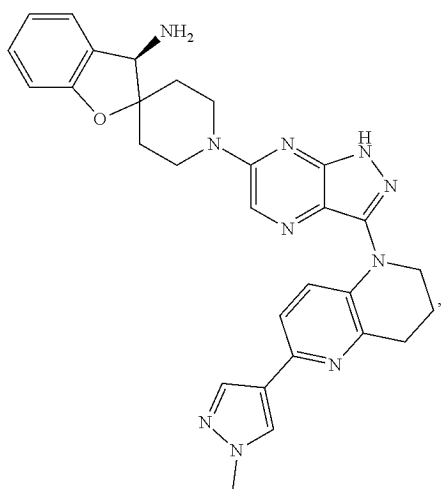
FIG. 1A depicts an isobologram illustrating synergistic growth inhibition of KYSE520
25 (squamous-cell carcinoma of the head and neck cells) using erlotinib (EGFR inhibitor) and a SHP2 inhibitor of the instant disclosure.

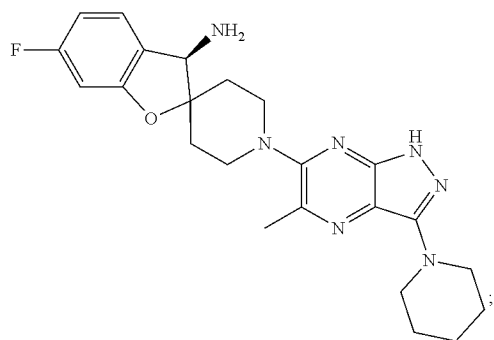
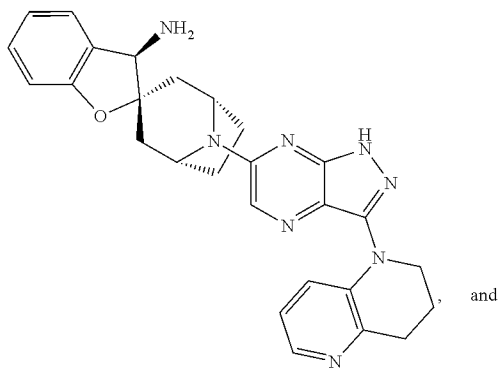
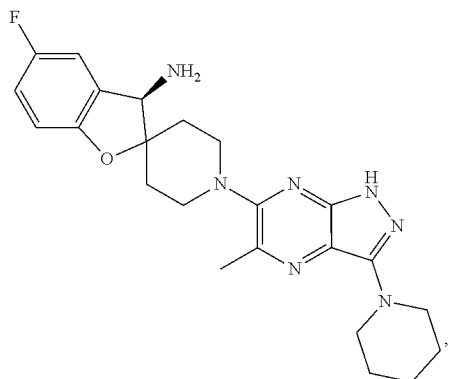
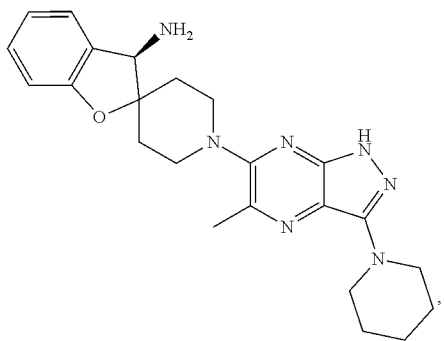
FIG. 1B. depicts an isobologram illustrating synergistic growth inhibition of NCI-H3122 (non-small cell lung cancer cells) using crizotinib (ALK inhibitor) and a SHP2 inhibitor of the instant disclosure.

CLAIMS

1. A compound selected from the group consisting of:



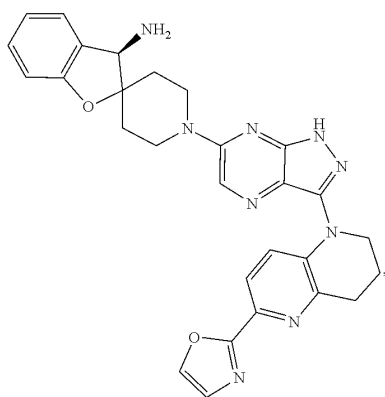
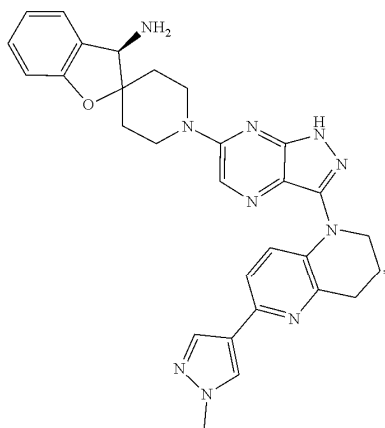
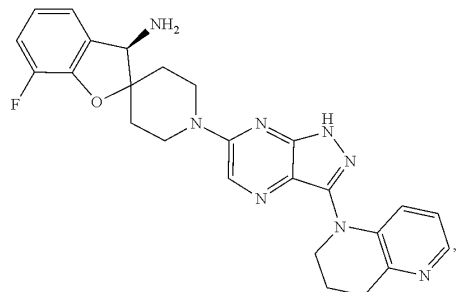


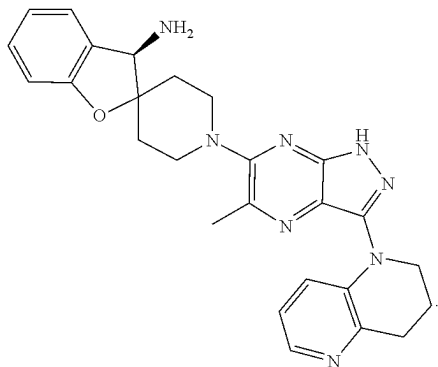
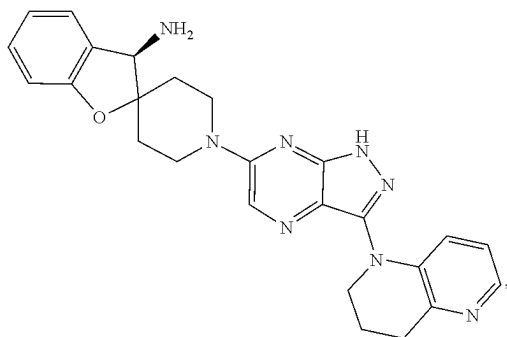


or a pharmaceutically acceptable salt thereof.

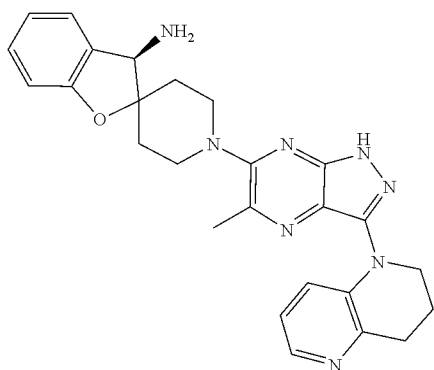
2. A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

3. The compound of claim 1, wherein the compound is selected from the group consisting of:





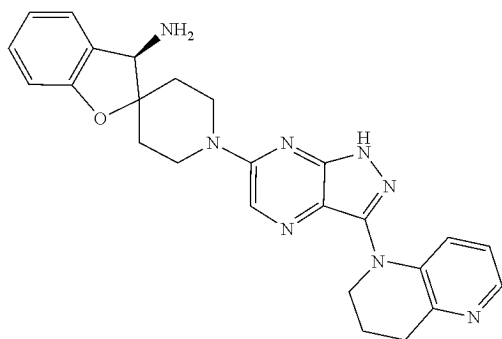
4. A compound represented by:



or a pharmaceutically acceptable salt thereof.

5. A pharmaceutical composition comprising a compound of claim 4 and a pharmaceutically acceptable carrier.

6. A compound represented by:



or a pharmaceutically acceptable salt thereof.

7. A pharmaceutical composition comprising a compound of claim 6 and a pharmaceutically acceptable carrier.