CLAIMS

What is claimed is:

1. Use of a first dose of a first Src homology region 2 (SH2)-containing protein tyrosine phosphatase 2 (SHP2) inhibitor in the manufacture of a medicament for treating cancer, by co-administration with a second dose of a second SHP2 inhibitor, wherein the first dose and the second dose are to be administered on an intermittent schedule, and wherein the first SHP2 inhibitor and the second SHP2 inhibitor are identical.

2. The use of claim 1, wherein the first dose is to be administered on a first day (D1) of the intermittent schedule and the second dose is to be administered on a fourth day (D4) of the intermittent schedule.

3. The use of claim 1, wherein the first dose is to be administered on a first day (D1) of the intermittent schedule and the second dose is to be administered on a second day (D2) of the intermittent schedule.

4. The use of any one of claims 1-3, wherein an iteration of the intermittent schedule is 7 days.

5. The use of claim 4, wherein a subsequent dose is to be administered on an eighth day (D8).

6. The use of claim 4, wherein a first iteration comprises the first dose and the second dose and wherein a subsequent dose is the first dose of a second or subsequent iteration.

7. The use of any one of claims 1-6, wherein a second therapeutic agent is to be further administered.

8. The use of claim 7, wherein the second therapeutic agent comprises a rat sarcoma (RAS) inhibitor.

9. The use of claim 7 or 8, wherein the first SHP2 inhibitor or the first dose of a SHP2 inhibitor and the second therapeutic agent are to be administered simultaneously.

10. The use of any one of claims 7-9, wherein the second dose of a SHP2 inhibitor and the second therapeutic agent are to be administered simultaneously.

11. The use of claim 7, wherein the second therapeutic agent is to be administered before the second dose of a SHP2 inhibitor.

12. The use of claim 7, wherein the second therapeutic agent is to be administered before the subsequent SHP2 inhibitor or the subsequent dose of a SHP2 inhibitor.

13. The use of any one of claims 7-12, wherein the first dose of the first SHP2 inhibitor and a first dose of the second therapeutic agent are to be administered on D1 of the intermittent schedule and wherein the second dose of the second SHP2 inhibitor and a second dose of the second therapeutic agent are to be administered on different days of the intermittent schedule.

14. The use of any one of claims 7-13, wherein an iteration of the intermittent schedule is 7 days.

15. The use of any one of claims 1-14, wherein the SHP2 inhibitor is an allosteric SHP2 inhibitor.

16. The use of any one of claims 1-15, wherein the SHP2 inhibitor comprises

(i) SHP099;

(ii) an allosteric SHP2 inhibitor compound of any one of Formula I, of Formula II, of Formula III, of Formula 1- VI, of Formula I-V2, of Formula I-W, of Formula i-X, of Formula I-Y, of Formula I-Z, of Formula IV, of Formula V, of Formula VI, of Formula IV-X, of Formula IV- Y, of Formula 1V-Z, of Formula VII, of Formula VIII, of Formula IX, and of Formula X;

(iii) TNO155;

(iv) JAB-3068;

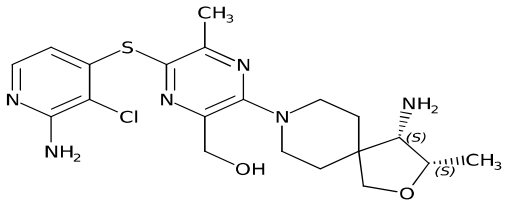
(v) a compound from Table 1, disclosed herein;

(vi) a compound from Table 2, disclosed herein;

(vii) RLY-1971; or

(viii) a combination thereof.

17. The use of any one of claims 1-16, wherein the SHP2 inhibitor comprises



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18. The use of any one of claims 1-17, wherein the subject further comprises a mutation in a component of a rat sarcoma (RAS) signaling pathway.

19. The use of claim 18, wherein the mutation in the component of the RAS signaling pathway occurs in KRAS, neurofibromin 1 (NF1), or serine/threonine-protein kinase B-raf (BRAF).

20. The use of claim 18 or 19, wherein the mutation in the component of the RAS signaling pathway comprises:

i) a substitution of a cysteine (C) for a glycine (G) at position 12 of KRAS ($KRAS^{G12C}$);
ii) a KRAS amplification ($KRAS^{amp}$);
iii) a loss of function (LOF) mutation of NF1 ($NF1^{LOF}$); or
iv) a class 3 mutant of BRAF ($BRAF^{class3}$).

21. The use of any one of claims 18-20, wherein the cancer:

(i) is non-small cell lung cancer;
(ii) presents a brain metastasis in the subject;
(iii) has a primary presentation in a pancreas of the subject;
(iv) has a secondary presentation in a pancreas of the subject;
(v) has a primary presentation in one or more of a large intestine, a small intestine, a stomach, a bladder, a kidney, a colon or a rectum of the subject;
(vi) has a secondary presentation in one or more of a large intestine, a small intestine, a stomach, a bladder, a kidney, a colon or a rectum of the subject;

(vii) has a primary presentation as a sarcoma in the subject; or

(viii) has a secondary presentation as a sarcoma in the subject.