[0010] Citation or identification of any reference in Section 2 of this application is not to be construed as an admission that the reference is prior art to the present application.

3. SUMMARY

[0011] In one aspect, the present disclosure refers to use of 1-ethyl-7-(2-methyl-6-(1H-1,2,4-triazol-3-yl)pyridin-3-yl)-3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one or a pharmaceutically acceptable salt, clathrate, solvate, stereoisomer, tautomer or isotopologue thereof in the manufacture of a medicament for treating E-twenty six (ETS) overexpressing Ewings sarcoma in a patient, wherein the patient is having ETS overexpressing Ewings sarcoma.. Disclosed herein are methods for treating or preventing E-twenty six (ETS) overexpressing Ewings sarcoma comprising administering an effective amount of a TOR kinase inhibitor to a patient having ETS overexpressing Ewings sarcoma.

[0012] In another aspect, the disclosure refers to the use of 1-ethyl-7-(2-methyl-6-(1H-1,2,4-triazol-3-yl)pyridin-3-yl)-3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one or a pharmaceutically acceptable salt, clathrate, solvate, stereoisomer, tautomer or isotopologue thereof in the manufacture of a medicament for treating E-twenty six (ETS) overexpressing Ewings sarcoma in a patient by improving the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) of said patient.. In certain examples, disclosed herein are methods for improving the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) of a patient, comprising administering an effective amount of a TOR kinase inhibitor to a patient having ETS overexpressing Ewings sarcoma.

[0013]

[0014] In one aspect, the present disclosure refers to an *in vitro* method for measuring inhibition of phosphorylation of S6RP, 4E-BP1 or AKT in a patient having E-twenty six (ETS) overexpressing Ewings sarcoma, comprising measuring the amount of phosphorylated S6RP, 4E-BP1 or AKT in said patient who was administered an effective amount of 1-ethyl-7-(2-methyl-6-(1H-1,2,4-triazol-3-yl)pyridin-3-yl)-3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one or a pharmaceutically acceptable salt, clathrate, solvate, stereoisomer, tautomer or isotopologue thereof, and comparing said amount of phosphorylated S6RP, 4E-BP1 or AKT to that of said patient prior to administration of an effective amount of 1-ethyl-7-(2-methyl-6-(1H-1,2,4-triazol-3-yl)pyridin-3-yl)-3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one or a pharmaceutically acceptable salt, clathrate, solvate, stereoisomer, tautomer or isotopologue thereof. In another aspect, the present disclosure refers to an *in vitro* method for measuring inhibition of phosphorylation of DNA-PK S2056 in a skin sample of a patient having E-twenty six (ETS) overexpressing Ewings sarcoma, comprising measuring the amount of phosphorylated DNA-PK S2056 present in the skin sample of said patient who was administered an effective amount of 1-ethyl-7-(2-methyl-6-(1H-1,2,4-triazol-3-yl)pyridin-3-yl)-3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one or a pharmaceutically acceptable salt, clathrate, solvate, stereoisomer, tautomer or isotopologue thereof, and comparing said amount of phosphorylated DNA-PK S2056 to that in a skin sample from said patient prior to administration of an effective amount of 1-ethyl-7-(2-methyl-6-(1H-1,2,4-triazol-3-yl)pyridin-3-yl)-3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one or a pharmaceutically acceptable salt, clathrate, solvate, stereoisomer, tautomer or isotopologue thereof. In yet another aspect, the present disclosure refers to a kit comprising 1-ethyl-7-(2-methyl-6-(1H-1,2,4-triazol-3-yl)pyridin-3-yl)-3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one or a pharmaceutically acceptable salt, clathrate, solvate, stereoisomer, tautomer or isotopologue thereof and means for monitoring patient response to administration of 1-ethyl-7-(2-methyl-6-(1H-1,2,4-triazol-3-yl)pyridin-3-yl)-3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one or a pharmaceutically acceptable salt, clathrate, solvate, stereoisomer, tautomer or isotopologue thereof, wherein said patient has E-twenty six (ETS) overexpressing Ewings sarcoma.
The present examples can be understood more fully by reference to the detailed description and examples, which are intended to exemplify non-limiting examples.

4. DETAILED DESCRIPTION

4.1 DEFINITIONS

[0015] An "alkyl" group is a saturated, partially saturated, or unsaturated straight chain or branched non-cyclic hydrocarbon having from 1 to 10 carbon atoms, typically from 1 to 8 carbons or, in some examples, from 1 to 6, 1 to 4, or 2 to 6 or carbon atoms. Representative

alkyl groups include -methyl, -ethyl, -n-propyl, -n-butyl, -n-pentyl and -n-hexyl; while saturated branched alkyls include -isopropyl, -*sec*-butyl, -isobutyl, -*tert*-butyl, -isopentyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 2,3-dimethylbutyl and the like. Examples of unsaturared alkyl groups include, but are not limited to, vinyl, allyl, -CH=CH(CH_3), -CH=C(CH_3)$_2$, -C(CH_3)=CH_2, -C(CH_3)=CH(CH_3), -C(CH_2CH_3)=CH_2, -C≡CH, -C≡C(CH_3), -C≡C(CH_2CH_3), -CH_2C≡CH, -CH_2C≡C(CH_3) and -CH_2C≡C(CH_7CH_3), among others. An alkyl group can be substituted or unsubstituted. In