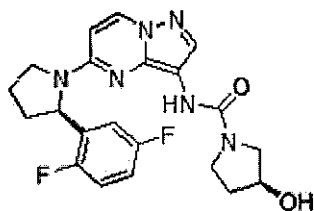


In some embodiments of the kits, the one or more probes are labeled with a detectable probe. In some embodiments of the kits, the one or more probes are covalently attached to a substrate (e.g., a film, a plate, or a bead).

Also provided herein are methods of treating a subject having a cancer that include: (a)

identifying a subject having a cancer cell that has: at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein including a mutation at one or more amino acid position(s) selected from the group of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750; at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein including a mutation at one or more amino acid position(s) selected from the group of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein including a mutation at one or more amino acid position(s) selected from the group of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810; and (b) administering to the identified subject a therapeutically effective amount of a Trk inhibitor.

In one aspect, provided herein is use of a Trk inhibitor, wherein the Trk inhibitor is the



compound of formula I: or a hydrogen sulfate salt thereof, in the manufacture of a medicament for treating a subject having a cancer, the use comprising:

identifying a subject having a cancer cell that has:

at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750;

at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or

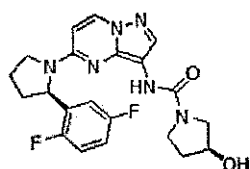
at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810;

wherein the medicament is to be administered to the identified subject.

Also provided herein are methods of treating a subject identified as having a cancer cell that has: at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein including a mutation at one or more amino acid position(s) selected from the group of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750; at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein including a mutation at one or more amino acid position(s) selected from the group of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein including a mutation at one or more amino acid position(s)

selected from the group of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810, the method comprising administering to the subject a therapeutically effective amount of a Trk inhibitor.

In one aspect, provided herein is use of a Trk inhibitor, wherein the Trk inhibitor is

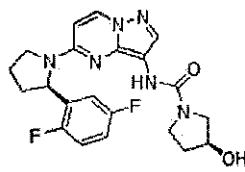


the compound of formula I:

or a hydrogen sulfate salt thereof, in the manufacture of a medicament for treating a subject identified as having a cancer cell that has: at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750; at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810.

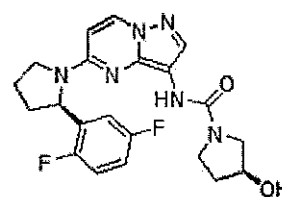
In one aspect, provided herein are methods of selecting a treatment for a cancer, the methods comprising: (a) identifying a cancer cell that has: at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750; at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539,

540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810; and (b) selecting a treatment comprising a
5 therapeutically effective amount of a Trk inhibitor for the identified cancer cell, wherein the



Trk inhibitor is the compound of formula I:
thereof.

In one aspect, provided herein are methods of selecting a treatment for a cancer, the methods comprising selecting a treatment comprising a therapeutically effective amount of a

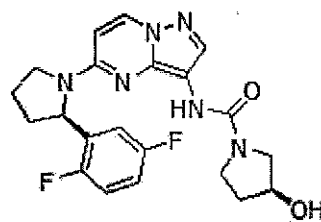


10 Trk inhibitor, wherein the Trk inhibitor is the compound of formula I:
or a hydrogen sulfate salt thereof, for a cancer cell identified as having: at least one point
mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a
mutation at one or more amino acid position(s) selected from the group of 241, 314, 318,
319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687,
15 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750; at least one point mutation in a
NTRK2

gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805;

5 and/or at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 10 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810.

In one aspect, provided herein are methods of determining the likelihood that a subject having a cancer will have a positive response to treatment with a Trk inhibitor,

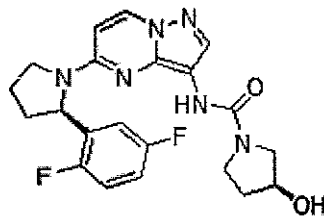


15 wherein the Trk inhibitor is the compound of formula I: hydrogen sulfate salt thereof, the methods comprising: (a) determining whether a cancer cell in a sample obtained from the subject has: at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 20 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750; at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 25 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 30 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810; and (b) determining that a subject having a cancer cell that has at least one point mutation in a NTRK1 gene, the at least one point mutation in a NTRK2 gene,

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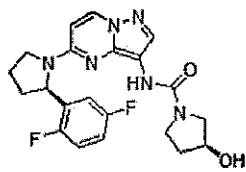
and/or at least one point mutation in a NTRK3 gene, has an increased likelihood of having a positive response to treatment with the Trk inhibitor.

In one aspect, provided herein are methods of determining the likelihood that a cancer will have a positive response to treatment with a Trk inhibitor, wherein the Trk



inhibitor is the compound of formula I:
thereof, the methods comprising: determining that a cancer cell that has: at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group of: 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750; at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810, has an increased likelihood of having a positive response to treatment with the Trk inhibitor.

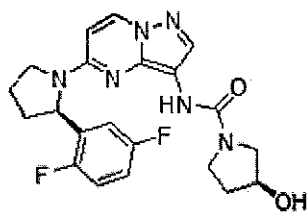
In one aspect, provided herein are methods of predicting the efficacy of a Trk inhibitor in a subject having cancer, wherein the Trk inhibitor is the compound of formula I:



or a hydrogen sulfate salt thereof, the methods comprising: (a) determining whether a cancer cell in a sample obtained from the subject has: at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750; at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino

acid position(s) selected from the group of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810; and (b) determining that the Trk inhibitor is more likely to be effective in a subject having a cancer cell in a sample obtained from the subject that has the at least one point mutation in a NTRK1 gene, the at least one point mutation in a NTRK2 gene, and/or the at least one point mutation in a NTRK3 gene.

In one aspect, provided are methods of predicting the efficacy of a Trk inhibitor in a subject having cancer, wherein the Trk inhibitor is the compound of formula I:



or a hydrogen sulfate salt thereof, the methods comprising:

determining that the Trk inhibitor is more likely to be effective in a subject having a cancer cell in a sample obtained from the subject that has: at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750; at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810.

In some embodiments of any of the use or methods described herein, the cancer is selected from the group of: adenocarcinoma, adrenal gland cortical carcinoma, adrenal gland neuroblastoma, anus squamous cell carcinoma, appendix adenocarcinoma, bladder urothelial carcinoma, bile duct adenocarcinoma, bladder carcinoma, bladder urothelial carcinoma, bone chordoma, bone marrow leukemia lymphocytic chronic, bone marrow leukemia non-

NTRK2 gene, and/or the at least one point mutation in a NTRK3 gene as having an increased likelihood of developing a cancer.

In one aspect, provided herein are methods of determining a cell's risk for developing a cancer, the methods comprising identifying a cell that has: at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750; at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group of: 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810, as having an increased likelihood of developing a cancer.

In one aspect, provided herein are methods of assisting in the diagnosis of a cancer in a subject, the methods comprising: (a) determining whether a cell in a sample obtained from the subject has: at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750; at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282,

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283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745,

5 746, 786, 787, 796, 801, 808, 809, and 810; and (b) determining that a subject having a cell that has the at least one point mutation in a NTRK1 gene, the at least one point mutation in a NTRK2 gene, and/or the at least one point mutation in a NTRK3 gene, has an increased likelihood of having a cancer.

In one aspect, provided are methods of assisting in the diagnosis of a cancer, the
10 methods comprising determining that a cell that has: at least one point mutation in a NTRK1

gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750; at least one point mutation in a NTRK2 gene that results in

15 the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or at least one point

mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a
20 mutation at one or more amino acid position(s) selected from the group of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707,

25 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810, has an increased likelihood of having a cancer.

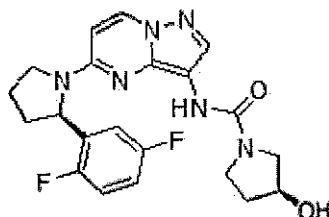
In some embodiments of any of the methods described herein, the subject is identified as having been exposed to a significant level of carcinogen(s). In some

embodiments of any of the methods described herein, the subject is suspected of having a

30 cancer. In some embodiments of any of the methods described herein, the subject has one or more symptoms of cancer. In some embodiments of any of the methods described herein, the cancer is selected from the group of: adenocarcinoma, adrenal gland cortical carcinoma, adrenal gland neuroblastoma, anus squamous cell carcinoma, appendix adenocarcinoma,

WHAT IS CLAIMED IS:

1. Use of a Trk inhibitor, wherein the Trk inhibitor is the compound of formula I:



or a hydrogen sulfate salt thereof, in the manufacture of a medicament for treating a subject having a cancer, the use comprising:

identifying a subject having a cancer cell that has:

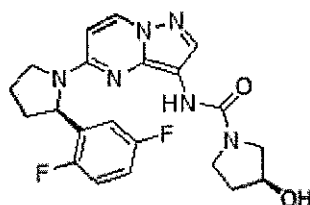
at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750;

at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or

at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810;

wherein the medicament is to be administered to the identified subject.

2. Use of a Trk inhibitor, wherein the Trk inhibitor is the compound of formula I:



or a hydrogen sulfate salt thereof, in the manufacture of a medicament for treating a subject identified as having a cancer cell that has: at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750; at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or at least one point mutation in a

NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810.

3. A method of selecting a treatment for a cancer, the method comprising:

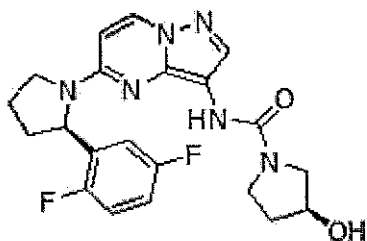
(a) identifying a cancer cell that has:

at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750;

at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or

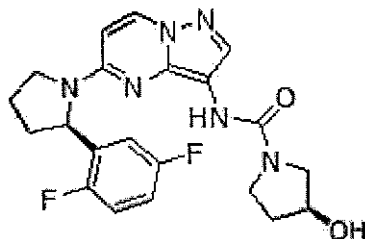
at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810; and

(b) selecting a treatment comprising a therapeutically effective amount of a Trk inhibitor for the identified cancer cell, wherein the Trk inhibitor is the compound of formula I:



or a hydrogen sulfate salt thereof.

4. A method of selecting a treatment for a cancer, the method comprising:
selecting a treatment comprising a therapeutically effective amount of a Trk inhibitor,
wherein the Trk inhibitor is the compound of formula I:



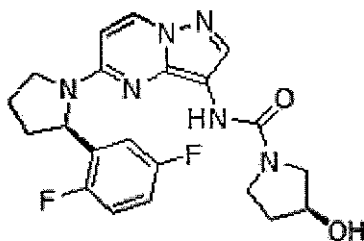
or a hydrogen sulfate salt thereof, for a cancer cell identified as having:

at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750;

at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or

at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810.

5. A method of determining the likelihood that a subject having a cancer will have a positive response to treatment with a Trk inhibitor, wherein the Trk inhibitor is the compound of formula I:



or a hydrogen sulfate salt thereof, the method comprising:

(a) determining whether a cancer cell in a sample obtained from the subject has:

at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750;

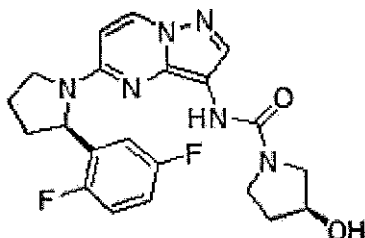
at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440,

598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or

at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810; and

(b) determining that a subject having a cancer cell that has at least one point mutation in a NTRK1 gene, the at least one point mutation in a NTRK2 gene, and/or at least one point mutation in a NTRK3 gene, has an increased likelihood of having a positive response to treatment with the Trk inhibitor.

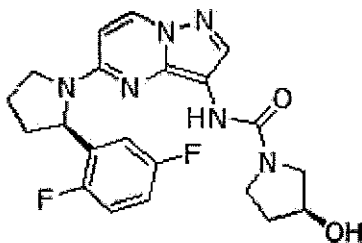
6. A method of determining the likelihood that a cancer will have a positive response to treatment with a Trk inhibitor, wherein the Trk inhibitor is the compound of formula I:



688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810,

has an increased likelihood of having a positive response to treatment with the Trk inhibitor.

7. A method of predicting the efficacy of a Trk inhibitor in a subject having cancer, wherein the Trk inhibitor is the compound of formula I:



or a hydrogen sulfate salt thereof, the method comprising:

(a) determining whether a cancer cell in a sample obtained from the subject has:

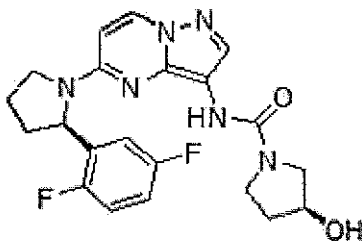
at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750;

at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or

at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810; and

(b) determining that the Trk inhibitor is more likely to be effective in a subject having a cancer cell in a sample obtained from the subject that has the at least one point mutation in a NTRK1 gene, the at least one point mutation in a NTRK2 gene, and/or the at least one point mutation in a NTRK3 gene.

8. A method of predicting the efficacy of a Trk inhibitor in a subject having cancer, wherein the Trk inhibitor is the compound of formula I:



or a hydrogen sulfate salt thereof, the method comprising:

determining that the Trk inhibitor is more likely to be effective in a subject having a cancer cell in a sample obtained from the subject that has:

at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750;

at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or

at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810.

9. The use of claim 1 or 2, or the method of any one of claims 3-8, wherein the cancer is selected from the group consisting of: adenocarcinoma, adrenal gland cortical carcinoma, adrenal gland neuroblastoma, anus squamous cell carcinoma, appendix adenocarcinoma, bladder urothelial carcinoma, bile duct adenocarcinoma, bladder carcinoma, bladder urothelial carcinoma, bone chordoma, bone marrow leukemia lymphocytic chronic, bone marrow leukemia non-lymphocytic acute myelocytic, bone marrow lymph proliferative disease, bone marrow multiple myeloma, bone sarcoma, brain astrocytoma, brain glioblastoma, brain medulloblastoma, brain meningioma, brain oligodendroglioma, breast adenoid cystic carcinoma, breast carcinoma, breast ductal carcinoma in situ, breast invasive ductal carcinoma, breast invasive lobular carcinoma, breast metaplastic carcinoma, cervix neuroendocrine carcinoma, cervix squamous cell carcinoma, colon adenocarcinoma, colon carcinoid tumor, duodenum adenocarcinoma, endometrioid tumor, esophagus adenocarcinoma, esophagus and stomach carcinoma, eye intraocular melanoma, eye

unknown primary melanoma, unknown primary sarcomatoid carcinoma, unknown primary squamous cell carcinoma, unknown undifferentiated neuroendocrine carcinoma, unknown primary undifferentiated small cell carcinoma, uterus carcinosarcoma, uterus endometrial adenocarcinoma, uterus endometrial adenocarcinoma endometrioid, uterus endometrial adenocarcinoma papillary serous, and uterus leiomyosarcoma.

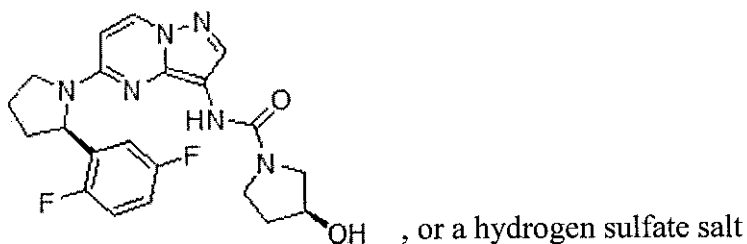
10. The use or method of any one of claims 1-9, wherein the subject is previously identified or diagnosed as having the cancer.

11. The use of claim 1 or the method of any one of claims 3, 5, and 7, wherein the step of identifying a cancer cell or a subject having a cancer cell that has the at least one point mutation in a NTRK1 gene, the at least one point mutation in a NTRK2 gene, and/or the at least one point mutation in a NTRK3 gene comprises performing an assay to determine the presence of the at least one point mutation in a NTRK1 gene, the at least one point mutation in a NTRK2 gene, and/or the at least one point mutation in a NTRK3 gene, in a cancer cell in a sample from the subject.

12. The use or method of claim 11, wherein the assay is selected from the group consisting of: denaturing gradient gel electrophoresis (DGGE), temperature gradient gel electrophoresis (TGGE), temperature gradient capillary electrophoresis, a single strand conformational polymorphism assay, a molecular beacon assay, a dynamic hybridization assay, a PCR-based assay, and denaturing high performance liquid chromatography.

13. The use or method of claim 11, wherein the assay comprises sequencing a segment of the NTRK1 gene comprising the at least one point mutation, a segment of the NTRK2 gene comprising the at least one point mutation, and/or a segment of the NTRK3 gene comprising the at least one point mutation.

14. The use or method of any one of claims 1-13, wherein the Trk inhibitor is a crystalline form of the compound of Formula I:



thereof.

15. The method of claim 3 or 4, wherein:

a therapeutically effective amount of the selected treatment is to be administered to the identified subject.

16. The method of claim 3, 4, and 15, further comprising:

recording the selected treatment in the identified subject's clinical record.

17. The method of claim 16, wherein the subject's clinical record is a computer readable medium.

18. The method of claim 5 or 6, wherein:

a therapeutically effective amount of the Trk inhibitor is to be administered to a subject or a cancer determined to have an increased likelihood of having a positive response to treatment with the Trk inhibitor.

19. A method of determining a subject's risk for developing a cancer, the method comprising:

(a) determining whether a cell in a sample obtained from the subject has:

at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750;

at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440,

598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or

at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810; and

(b) identifying a subject having a cell that has the at least one point mutation in a NTRK1 gene, the at least one point mutation in a NTRK2 gene, and/or the at least one point mutation in a NTRK3 gene as having an increased likelihood of developing a cancer.

20. A method of determining a cell's risk for developing a cancer, the method comprising:

identifying a cell that has:

at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750;

at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of: 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or

at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687,

688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810;

as having an increased likelihood of developing a cancer.

21. A method of assisting in the diagnosis of a cancer in a subject, the method comprising:

(a) determining whether a cell in a sample obtained from the subject has:

at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750;

at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or

at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810; and

(b) determining that a subject having a cell that has the at least one point mutation in a NTRK1 gene, the at least one point mutation in a NTRK2 gene, and/or the at least one point mutation in a NTRK3 gene, has an increased likelihood of having a cancer.

22. A method of assisting in the diagnosis of a cancer, the method comprising:

determining that a cell that has:

at least one point mutation in a NTRK1 gene that results in the expression of a TrkA protein comprising a mutation at one or more amino acid position(s) selected from the group

consisting of 241, 314, 318, 319, 320, 321, 510, 511, 512, 552, 553, 554, 636, 637, 638, 649, 654, 655, 679, 680, 687, 688, 689, 690, 692, 695, 696, 697, 747, 748, 749, and 750;

at least one point mutation in a NTRK2 gene that results in the expression of a TrkB protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 240, 241, 242, 251, 252, 256, 257, 258, 264, 314, 315, 401, 426, 427, 428, 440, 598, 599, 600, 602, 603, 664, 665, 666, 677, 678, 679, 680, 689, 691, 692, 746, 747, 748, 749, 784, 785, 786, 787, 788, 789, 804, and 805; and/or

at least one point mutation in a NTRK3 gene that results in the expression of a TrkC protein comprising a mutation at one or more amino acid position(s) selected from the group consisting of 221, 222, 223, 242, 243, 244, 269, 270, 271, 276, 277, 281, 282, 283, 296, 297, 325, 326, 328, 329, 344, 345, 346, 349, 350, 351, 353, 354, 537, 538, 539, 540, 545, 550, 551, 560, 562, 575, 576, 577, 582, 583, 584, 601, 602, 603, 604, 607, 608, 609, 610, 612, 624, 625, 626, 627, 628, 629, 634, 635, 636, 637, 650, 651, 652, 653, 677, 678, 679, 687, 688, 689, 705, 706, 707, 708, 715, 716, 717, 730, 731, 732, 738, 744, 745, 746, 786, 787, 796, 801, 808, 809, and 810,

has an increased likelihood of having a cancer.

23. The method of any one of claims 19-22, wherein the subject or cell is identified as having been exposed to a significant level of carcinogen(s).

24. The method of any one of claims 19-22, wherein the subject or cell is suspected of having a cancer.

25. The methods of any one of claims 19-22, wherein the subject or cell has one or more symptoms of cancer.

26. The method of any one of claims 19-25, wherein the cancer is selected from the group consisting of: adenocarcinoma, adrenal gland cortical carcinoma, adrenal gland neuroblastoma, anus squamous cell carcinoma, appendix adenocarcinoma, bladder urothelial carcinoma, bile duct adenocarcinoma, bladder carcinoma, bladder urothelial carcinoma, bone chordoma, bone marrow leukemia lymphocytic chronic, bone marrow leukemia non-lymphocytic acute myelocytic, bone marrow lymph proliferative disease, bone marrow multiple myeloma, bone sarcoma, brain astrocytoma, brain glioblastoma, brain

neuroblastoma, soft tissue paraganglioma, soft tissue perivascular epithelioid cell tumor, soft tissue sarcoma, soft tissue synovial sarcoma, stomach adenocarcinoma, stomach adenocarcinoma diffuse-type, stomach adenocarcinoma intestinal type, stomach adenocarcinoma intestinal type, stomach leiomyosarcoma, thymus carcinoma, thymus thymoma lymphocytic, thyroid papillary carcinoma, unknown primary adenocarcinoma, unknown primary carcinoma, unknown primary malignant neoplasm, lymphoid neoplasm, unknown primary melanoma, unknown primary sarcomatoid carcinoma, unknown primary squamous cell carcinoma, unknown undifferentiated neuroendocrine carcinoma, unknown primary undifferentiated small cell carcinoma, uterus carcinosarcoma, uterus endometrial adenocarcinoma, uterus endometrial adenocarcinoma endometrioid, uterus endometrial adenocarcinoma papillary serous, and uterus leiomyosarcoma.

27. The method of claim 21 or 23, wherein the step of determining whether a cell in a sample obtained from the subject has the at least one point mutation in a NTRK1 gene, the at least one point mutation in a NTRK2 gene, and/or the at least one point mutation in a NTRK3 gene, comprises performing an assay to determine the presence of the at least one point mutation in a NTRK1 gene, the presence of the at least one point mutation in a NTRK2 gene, and/or the presence of the at least one point mutation in a NTRK3 gene, in a cell in the sample.

28. The method of claim 27, wherein the assay is selected from the group consisting of: denaturing gradient gel electrophoresis (DGGE), temperature gradient gel electrophoresis (TGGE), temperature gradient capillary electrophoresis, a single strand conformational polymorphism assay, a molecular beacon assay, a dynamic hybridization assay, a PCR-based assay, denaturing high performance liquid chromatography.

29. The method of claim 27, wherein the assay comprises sequencing a segment of the NTRK1 gene comprising the at least one point mutation, a segment of the NTRK2 gene comprising the at least one point mutation, and/or a segment of the NTRK3 gene comprising the at least one point mutation.

30. The method of claim 22, further comprising confirming the diagnosis of a cancer in a subject or cell determined to have an increased likelihood of having a cancer.