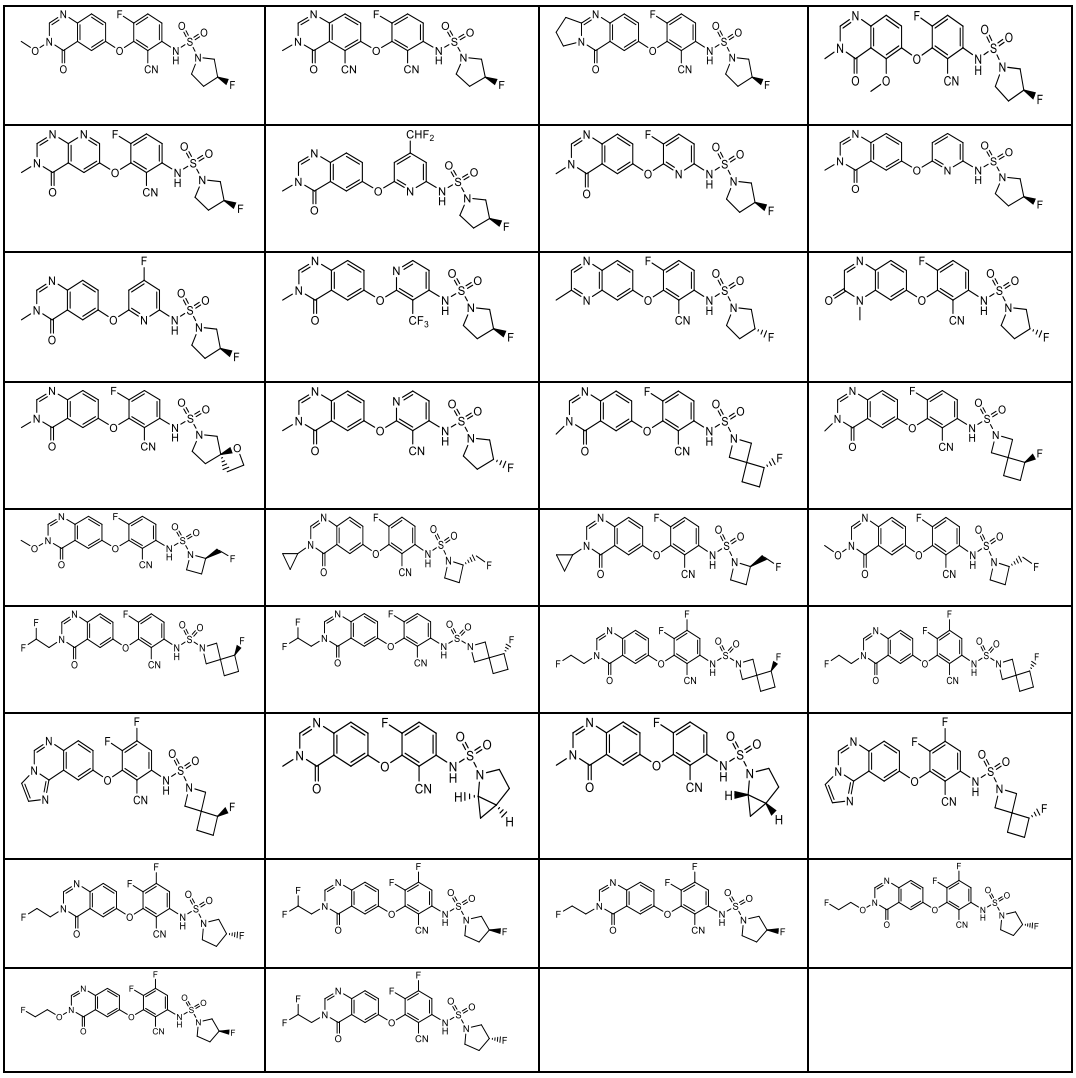


[0035] The present invention also provides a pharmaceutical composition or pharmaceutical preparation, which comprises the compound, and the stereoisomer, the deuterated product or the pharmaceutically acceptable salt thereof described in any one of the above solutions, and a pharmaceutically acceptable carrier and/or excipient. The pharmaceutical composition can be in a unit preparation form (the unit preparation is also referred to as "preparation specification").

[0036] Further, the pharmaceutical composition or pharmaceutical preparation of the present invention comprises 1 mg-1500 mg of the compound, and the stereoisomer, the deuterated product or the pharmaceutically acceptable salt thereof described in any one of the above solutions, and a pharmaceutically acceptable carrier and/or excipient.

[0037] The present invention further provides the use of the compound, and the stereoisomer, the deuterated product or the pharmaceutically acceptable salt thereof described in any one of

mg, 50-900 mg, 50-800 mg, 50-700 mg, 50-600 mg, 50-500 mg, 50-400 mg, 50-300 mg, 50-250 mg, 50-200 mg, 50-150 mg, 50-125 mg, 50-100 mg; 100-1500 mg, 100-1000 mg, 100-900 mg, 100-800 mg, 100-700 mg, 100-600 mg, 100-500 mg, 100-400 mg, 100-300 mg, 100-250 mg, and 100-200 mg;

[0045] In some embodiments, the pharmaceutical composition or pharmaceutical preparation of the present invention comprises the above therapeutically effective amount of the compound, and the stereoisomer, the deuterated product or the pharmaceutically acceptable salt thereof of the present invention.

[0046] The present invention relates to a pharmaceutical composition or pharmaceutical preparation, which comprises a therapeutically effective amount of the compound, and the stereoisomer, the deuterated product or the pharmaceutically acceptable salt thereof of the present invention and a carrier and/or excipient.

[0047] The pharmaceutical composition can be in a unit preparation form (the amount of the active drug in the unit preparation is also referred to as the "preparation specification"). In some embodiments, the pharmaceutical composition comprises, but is not limited to, 1 mg, 1.25 mg, 2.5 mg, 5 mg, 10 mg, 12.5 mg, 15 mg, 20 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, 50 mg, 55 mg, 60 mg, 65 mg, 70 mg, 75 mg, 80 mg, 85 mg, 90 mg, 95 mg, 100 mg, 110 mg, 120 mg, 125 mg, 130 mg, 140 mg, 150 mg, 160 mg, 170 mg, 180 mg, 190 mg, 200 mg, 210 mg, 220 mg, 230 mg, 240 mg, 250 mg, 275 mg, 300 mg, 325 mg, 350 mg, 375 mg, 400 mg, 425 mg, 450 mg, 475 mg, 500 mg, 525 mg, 550 mg, 575 mg, 600 mg, 625 mg, 650 mg, 675 mg, 700 mg, 725 mg, 750 mg, 775 mg, 800 mg, 850 mg, 900 mg, 950 mg, 1000 mg, 1100 mg, 1200 mg, 1300 mg, 1400 mg, 1500 mg of the compound, and the stereoisomer, the deuterated product or the pharmaceutically acceptable salt thereof of the present invention.

[0048] A method for treating a disease in a mammal, the method comprises administering to a subject a therapeutically effective amount of the compound, and the stereoisomer, the deuterated product or the pharmaceutically acceptable salt thereof of the present invention, and a pharmaceutically acceptable carrier and/or excipient.

[0049] The therapeutically effective dose is preferably 1 mg-1500 mg.

[0050] The disease is preferably a tumor, especially a brain tumor.

[0051] A method for treating a disease in a mammal, the method comprises administering the compound, and the stereoisomer, the deuterated product or the pharmaceutically acceptable salt thereof of the present invention, and the pharmaceutically acceptable carrier and/or

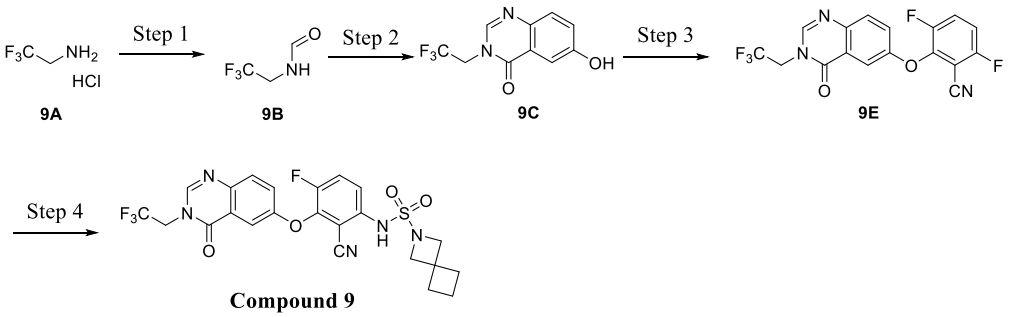
[0136] Step 1: 5B (0.27 g, 1.52 mmol) was dissolved in dry N,N-dimethylformamide (10 mL) in a 100 mL single-neck flask. Cesium carbonate (0.74 g, 2.28 mmol) was slowly added under an ice bath. After the addition, the obtained mixture was reacted under stirring at 50°C for 0.5 h. A solution of 4E (0.5 mg, 1.52 mmol) in N,N-dimethylformamide (5 mL) was slowly added dropwise under an ice bath. After the addition, the obtained mixture was reacted under stirring at 100°C for 2 h. After the reaction was completed, the reaction liquid was filtered. The filtrate was concentrated to obtain an oily liquid, which was separated and purified by preparative liquid chromatography (instrument: waters 2767 preparative liquid chromatographic instrument; chromatographic column: SunFire@ Prep C18 (19 mm × 150 mm); composition of mobile phase: mobile phase A: acetonitrile; mobile phase B: water (containing 0.1% trifluoroacetic acid); gradient: gradient elution using 20%-80% acetonitrile; cycle time: 15 min) to obtain compound 8 (0.3 g, yield: 42%).

[0137] LCMS m/z = 472.1 $[M+H]^+$;

[0138] ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.48 (s, 1H), 8.63 (s, 1H), 7.93 – 7.86 (t, 1H), 7.84 (d, 1H), 7.72 (dd, 1H), 7.60 (dd, 1H), 7.43 (d, 1H), 4.05 (s, 3H), 3.98 (s, 4H), 0.62 (s, 4H).

[0139] ^{19}F NMR (377 MHz, DMSO-d_6) δ -127.15 (s).

Example 9



[0140] Step 1: 9A (25 g, 184.46 mmol) and sodium formate (15.55 g, 21.51 mmol) were added into a 250 mL single-neck flask. The obtained mixture was reacted at 130°C for 2 hrs. After the reaction was completed, the obtained mixture was cooled to room temperature and filtered. The filtrate was concentrated to obtain 9B (22.0 g, yield 94%).

[0141] LCMS m/z = 128.2 $[M+H]^+$;

[0142] Step 2: 2-amino-5-hydroxybenzoic acid (1.0 g, 6.52 mmol) was added to 9B (6 mL, 36.2 mmol) in a 250 mL single-neck flask. The obtained mixture was reacted at 150°C for 21 hrs. After the reaction was completed, the obtained mixture was cooled to room temperature and

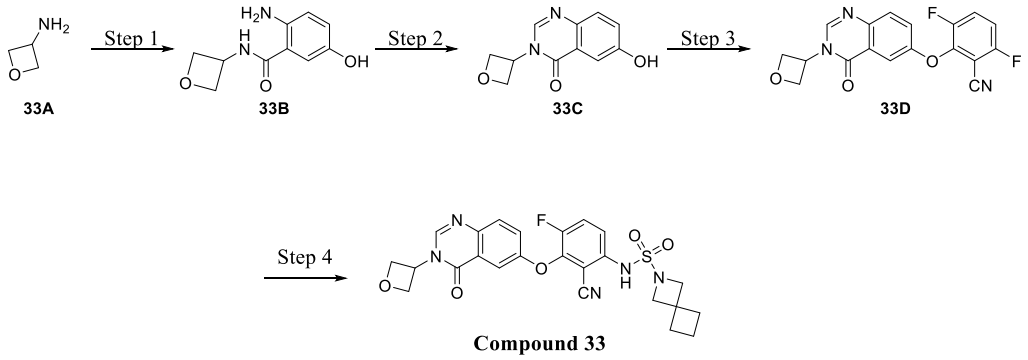
reaction liquid was extracted (ethyl acetate), washed, and concentrated to obtain a crude product. Column chromatography separation was performed (petroleum ether : ethyl acetate = 1 : 0-0 : 1) to obtain 32B (90 mg, yield 58.88%).

[0290] Step 3: 32B (90 mg, 0.21 mmol), 1B (74 g, 0.42 mmol), potassium carbonate (35 mg, 0.25 mmol), Xantphos (24 mg, 0.04 mmol), and $Pd_2(dba)_3$ (19 mg, 0.02 mmol) and 1,4-dioxane (3 mL) were added in sequence into a 50 mL reaction flask. The obtained mixture was reacted under stirring at 120°C for 5 h. The reaction liquid was filtered, the filtrate was concentrated under reduced pressure, and the residue was separated and purified by preparative liquid chromatography (instrument: waters 2767 preparative liquid chromatographic instrument; chromatographic column: SunFire@ Prep C18 (19 mm × 150 mm); composition of mobile phase: mobile phase A: acetonitrile; mobile phase B: water (containing 0.1% trifluoroacetic acid); gradient: gradient elution using 20%-70% acetonitrile; cycle time: 15 min) to obtain compound 32 (18.28 mg, yield 16.74%).

[0291] LCMS m/z = 520.9 $[M+H]^+$;

[0292] ^1H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.84 (d, 1H), 7.66-7.59 (m, 3H), 4.17 (s, 3H), 3.99 (s, 4H), 2.20 (t, 4H), 1.89-1.81 (m, 2H).

Example 33



[0293] Step 1: 33A (2.92 g, 39.98 mmol) and water (40 mL) were added into a 250 mL single-neck flask. 4B (2.10 g, 11.76 mmol) was added at 0-5°C, The obtained mixture was reacted at room temperature for 4 hrs. After the reaction was completed, the reaction liquid was concentrated and purified by column chromatography (dichloromethane/methanol=10/1) to obtain 33B (2.2 g, yield 89%).

[0294] LCMS m/z = 209.1 $[M+H]^+$;

[0295] Step 2: 33B (2.0 g, 9.61 mmol) was added to trimethyl orthoformate (20 mL) in a 100 mL single-neck flask. The obtained mixture was reacted at 105°C overnight. After the reaction was

completed, the reaction liquid was cooled to room temperature, concentrated and purified by column chromatography (petroleum ether/ethyl acetate = 1/2) to obtain 33C (870 mg, yield 41%).

[0296] LCMS m/z = 219.1 $[M+H]^+$;

[0297] Step 3: 33C (0.87 g, 3.99 mmol) was dissolved in dry N,N-dimethylformamide (10 mL) in a 25 mL single-neck flask. Cesium carbonate (1.56 g, 4.79 mmol) was slowly added under an ice bath. After the addition, the obtained mixture was reacted under stirring at room temperature for 0.5 h. 2,3,6-trifluorobenzonitrile (0.66 g, 4.19 mmol) was slowly added dropwise under an ice bath. After the addition, the obtained mixture was reacted under stirring at room temperature overnight. After the reaction was completed, ethyl acetate (15 mL) was added to the reaction system to dilute the reaction. Then water (20 mL) was added to quench the reaction, and extraction was performed with ethyl acetate (20 mL × 2). The organic phase was washed with water (20 mL × 2). The organic phase was concentrated and then purified by column chromatography (petroleum ether/ethyl acetate = 1/1) to obtain 33D (0.71 g, yield 50%).

[0298] LCMS m/z =356.2 $[M+H]^+$;

[0299] ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.39 (s, 1H), 8.00 – 7.94(m, 1H), 7.82- 7.80(d, 1H), 7.76-7.73 (dd,1H), 7.61-7.55 (m, 2H), 5.55-4.47 (p, 1H), 4.97-4.93 (t, 2H), 4.89-4.85 (t, 2H).

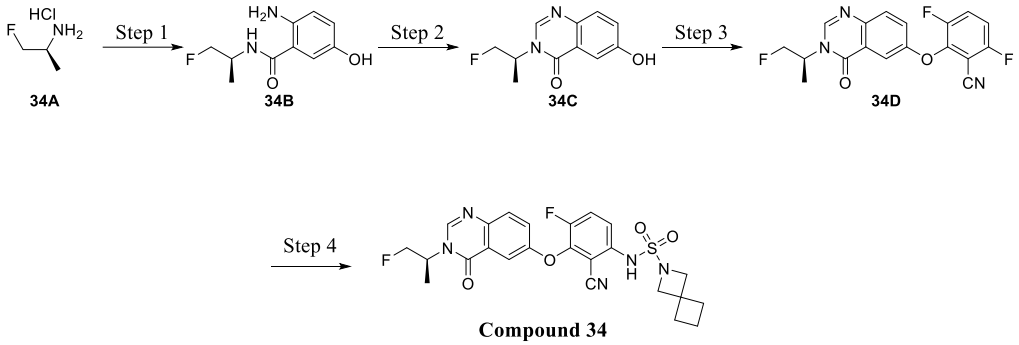
[0300] Step 4: 1B (0.22 g, 1.24 mmol) and cesium carbonate (0.44 g, 1.36 mmol) were added to dry N,N-dimethylformamide (10 mL) in a 25 mL single-neck flask. The obtained mixture was reacted at 50°C for 30 min. A solution of 33D (0.40 g, 1.13 mmol) in N,N-dimethylformamide (2 mL) was added dropwise at 50°C. After the addition, the obtained mixture was reacted under stirring at 80°C for 4 hrs. After the reaction was completed, the reaction was filtered, and the filtrate was separated and purified by preparative liquid chromatography (instrument: waters 2767 preparative liquid chromatographic instrument; chromatographic column: SunFire@ Prep C18 (19 mm × 150 mm); composition of mobile phase: mobile phase A: acetonitrile; mobile phase B: water (containing 0.1% trifluoroacetic acid); gradient: gradient elution using 20%-70% acetonitrile; cycle time: 15 min) to obtain 220 mg of solid, which was purified by column chromatography (petroleum ether/ethyl acetate = 1/1) to obtain compound 33 (160 mg, yield 27%).

[0301] LCMS m/z = 512.6 $[M+H]^+$;

[0302] ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.37 (s, 1H), 8.38 (s, 1H), 7.89 – 7.80 (m, 2H), 7.72-7.69 (dd,1H), 7.55-7.52 (dd, 1H), 7.37-7.36 (d,1H), 5.53-5.45 (p, 1H), 4.96-4.92 (t, 2H), 4.88-4.84 (t, 2H), 3.83 (s, 4H), 2.12-2.08 (t, 4H), 1.78 – 1.70 (m, 2H).

[0303] ^{19}F NMR (377 MHz, DMSO-d_6) δ -127.30 (s).

Example 34



[0304] Step 1: 34A (2.00 g, 17.57 mmol) and water (20 mL) were added into a 250 mL single-neck flask. A solution of sodium hydroxide (0.62 g, 15.62 mmol) in water (20 mL) was slowly added dropwise at 0-5°C. The obtained mixture was reacted at 0-5°C for 10 min. Then 4B (0.87 g, 4.88 mmol) was added at 0-5°C and the obtained mixture was reacted at room temperature for 4 hrs. After the reaction was completed, the reaction liquid was concentrated and then purified by column chromatography (dichloromethane/methanol = 10/1) to obtain 34B (0.83 g, yield 80%).

[0305] LCMS m/z = 213.1 $[M+H]^+$;

[0306] Step 2: 34B (0.72 g, 3.39 mmol) was added to trimethyl orthoformate (10 mL) in a 100 mL single-neck flask. The obtained mixture was reacted at 105°C overnight. After the reaction was completed, the reaction liquid was cooled to room temperature, concentrated and purified by column chromatography (petroleum ether/ethyl acetate = 1/2) to obtain 34C (280 mg, yield 37%).

[0307] LCMS m/z = 223.2 $[M+H]^+$;

[0308] Step 3: 34C (0.28 g, 1.26 mmol) was dissolved in dry N,N-dimethylformamide (4 mL) in a 25 mL single-neck flask. Cesium carbonate (0.49 g, 1.51 mmol) was slowly added under an ice bath. After the addition, the obtained mixture was reacted under stirring at room temperature for 0.5 h. 2,3,6-trifluorobenzonitrile (0.22 g, 1.39 mmol) was slowly added dropwise under an ice bath. After the addition, the obtained mixture was reacted under stirring at room temperature overnight. After the reaction was completed, ethyl acetate (10 mL) was added to the reaction system to dilute the reaction. Then water (10 mL) was added to quench the reaction, and extraction was performed with ethyl acetate (10 mL × 2). The organic phase was washed with water (10 mL × 2). The organic phase was concentrated and then purified by column chromatography (petroleum ether/ethyl acetate = 3/1) to obtain 34D (0.25 g, yield 55%).

g, 6.18 mmol) was added at 0-5°C and the obtained mixture was reacted at room temperature for 4 hrs. After the reaction was completed, the reaction liquid was concentrated and then purified by column chromatography (dichloromethane/methanol = 10/1) to obtain 35B (0.65 g, yield 49%).

[0316] LCMS m/z = 213.1 $[M+H]^+$;

[0317] Step 2: 35B (0.72 g, 3.39 mmol) was added to triethyl orthoformate (10 mL) in a 100 mL single-neck flask. The obtained mixture was reacted under microwave at 180°C for 2.5 hrs. After the reaction was completed, the reaction liquid was cooled to room temperature, and concentrated to obtain crude product 35C, which was directly used in the next reaction.

[0318] LCMS m/z =223.2 $[M+H]^+$;

[0319] Step 3: Crude product 35C was dissolved in dry N,N-dimethylformamide (10 mL) in a 25 mL single-neck flask. Cesium carbonate (1.1 g, 3.41 mmol) was slowly added under an ice bath. After the addition, the obtained mixture was reacted under stirring at room temperature for 0.5 h. 2,3,6-trifluorobenzonitrile (0.49 g, 3.12 mmol) was slowly added dropwise under an ice bath. After the addition, the obtained mixture was reacted under stirring at room temperature overnight. After the reaction was completed, ethyl acetate (20 mL) was added to the reaction system to dilute the reaction. Then water (20 mL) was added to quench the reaction, and extraction was performed with ethyl acetate (20 mL × 2). The organic phase was washed with water (20 mL × 2). The organic phase was concentrated and then purified by column chromatography (petroleum ether/ethyl acetate = 3/1) to obtain 35D (0.16 g, yield 15%).

[0320] LCMS m/z = 360.1 $[M+H]^+$;

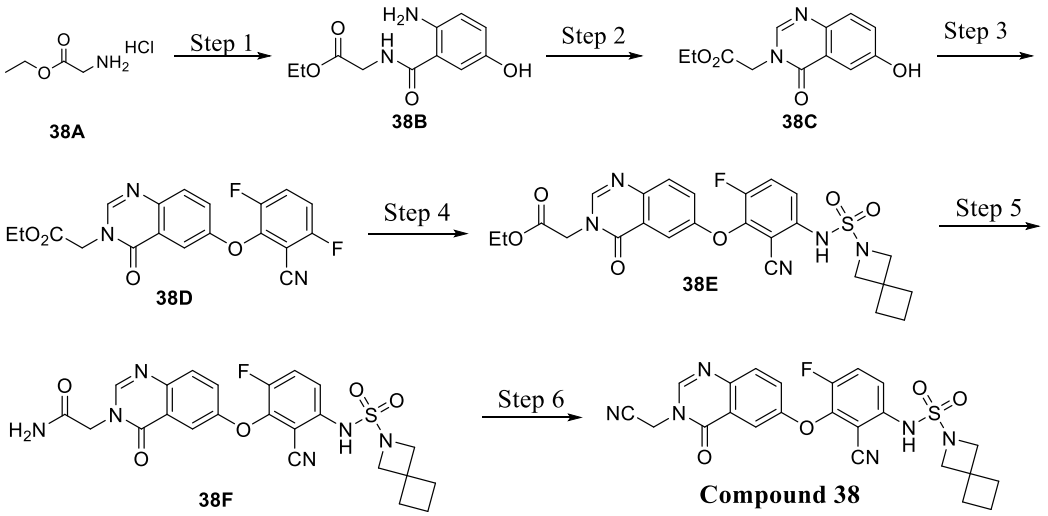
[0321] Step 4: 1B (83.27 mg, 0.47 mmol) and cesium carbonate (0.17 g, 0.54 mmol) were added to dry N,N-dimethylformamide (4 mL) in a 25 mL single-neck flask. The obtained mixture was reacted at 50°C for 30 min. A solution of 35D (0.16 g, 0.45 mmol) in N,N-dimethylformamide (1 mL) was added dropwise at 50°C. After the addition, the obtained mixture was reacted under stirring at 80°C for 3 hrs. After the reaction was completed, the reaction was filtered, and the filtrate was separated and purified by preparative liquid chromatography (instrument: waters 2767 preparative liquid chromatographic instrument; chromatographic column: SunFire@ Prep C18 (19 mm × 150 mm); composition of mobile phase: mobile phase A: acetonitrile; mobile phase B: water (containing 0.1% trifluoroacetic acid); gradient: gradient elution using 20%-70% acetonitrile; cycle time: 15 min) to obtain compound 35 (105 mg, yield 45%).

[0322] LCMS m/z = 516.6 $[M+H]^+$;

[0330] ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.42 (s, 1H), 8.36 (s, 1H), 7.85 (t, 1H), 7.78 (d, 1H), 7.68 (dd, 1H), 7.62 (dd, 1H), 7.38 (d, 1H), 3.47 (s, 3H), 3.37 (s, 1H), 3.17 (s, 1H), 2.93 (dd, 1H), 2.09 – 2.00 (m, 1H), 1.98 (d, 1H), 1.60 (s, 1H), 0.78 (s, 1H), 0.50 (d, 1H).

[0331] ^{19}F NMR (377 MHz, DMSO-d_6) δ -128.22 (s).

Example 38



[0332] Step 1: 38A (16.66 g, 119.37 mmol) and water (120 mL) were added into a 1000 mL single-neck flask. A solution of sodium hydroxide (4.29 g, 107.30 mmol) in water (120 mL) was slowly added dropwise at 0-5°C. The obtained mixture was reacted at 0-5°C for 10 min. Then 6-hydroxy-2H-benzo[d][1,3]oxazine-2,4(1H)-dione (6.00 g, 33.53 mmol) was added at 0-5°C, The obtained mixture was reacted at room temperature for 4 hrs. After the reaction was completed, the reaction liquid was concentrated and then purified by column chromatography (dichloromethane/methanol = 10/1) to obtain 38B (3.0 g, yield 37.56%).

[0333] LCMS m/z = 239.1 $[M+H]^+$;

[0334] Step 2: 38B (2.7 g, 11.33 mmol) was added to dry N,N-dimethylformamide (30 mL) in a 100 mL single-neck flask. Triethyl orthoformate (30 mL) was added at room temperature. The obtained mixture was reacted at 150°C for 4 hrs. After the reaction was completed, the reaction liquid was cooled to room temperature, and concentrated to obtain crude product 38C, which was directly used in the next reaction.

[0335] LCMS m/z = 249.1 $[M+H]^+$;

[0336] Step 3: 38C was dissolved in dry N,N-dimethylformamide (30 mL) in a 25 mL single-neck flask. Cesium carbonate (4.11 g, 13.54 mmol) was slowly added under an ice bath. After the addition, the obtained mixture was reacted under stirring at room temperature for 0.5 h. 2,3,6-

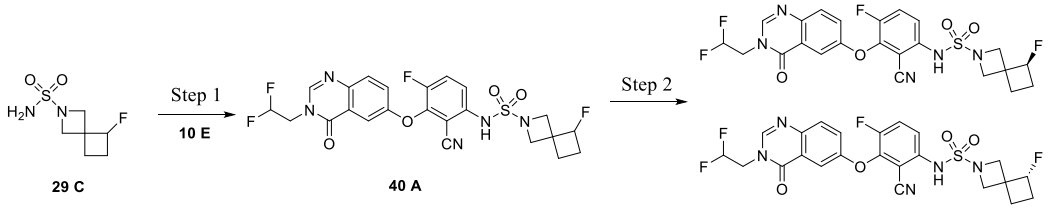
the reaction liquid was filtered and the filtrate was concentrated. The resulting oily liquid was purified by column chromatography (DCM : EA = 1 : 2) to obtain a crude compound. The crude compound was separated and purified by preparative liquid chromatography (instrument: waters 2767 preparative liquid chromatographic instrument; chromatographic column: SunFire@ Prep C18 (19 mm × 150 mm); composition of mobile phase: mobile phase A: acetonitrile; mobile phase B: water (containing 0.1% trifluoroacetic acid); gradient: gradient elution using 30%-70% acetonitrile; cycle time: 15 min) to obtain compound 39 (210 mg, yield: 31%).

[0349] LCMS m/z = 520.50 $[M+H]^+$;

[0350] ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.34 (s, 1H), 7.80 (d, 1H), 7.75 (dd, 1H), 7.59 (d, 1H), 7.53 (dd, 1H), 4.72 (dt, 2H), 4.32 (dt, 2H), 3.85 (s, 4H), 2.10 (t, 4H), 1.79 – 1.68 (m, 2H).

[0351] ^{19}F NMR (376 MHz, DMSO-d_6) δ -121.46 (s), -150.87 (s), -222.31 (s).

Example 40 and example 41:



[0352] Step 1: 29C (0.400 g, 2.06 mmol) and cesium carbonate (1.01 g, 3.09 mmol) were added to dry N,N-dimethylformamide (10 mL) in a 25 mL single-neck flask. The obtained mixture was reacted at 50°C for 30 min. A solution of 10E (0.748 g, 2.06 mmol) in N,N-dimethylformamide (2 mL) was added dropwise at 50°C. After the addition, the obtained mixture was reacted under stirring at 100°C overnight. After the reaction was completed, the reaction liquid was filtered. The filter cake was washed with N,N-dimethylformamide (4 mL). The filtrate was concentrated and then dissolved in water (15 mL) and ethyl acetate (10 mL). Liquid separation was performed. After the aqueous phase was extracted once with ethyl acetate (10 mL), the pH was adjusted to about 7 with saturated ammonium chloride solution. Then the aqueous phase was extracted with dichloromethane (20 mL × 3). The organic phase was dried over anhydrous sodium sulfate and then concentrated to obtain 40A crude product. The crude product was directly used in the next reaction.

[0353] LCMS m/z = 538.5 $[M+H]^+$;

reaction was completed, the reaction liquid was concentrated to obtain crude product 42B, which was directly used in the next reaction.

[0360] LCMS m/z = 257.1 $[M+H]^+$;

[0361] Step 2: The crude product 42B was dissolved in dichloromethane (10 mL) in a 25 mL single-neck flask. Trifluoroacetic acid (5 mL) was slowly added dropwise at 0-5°C. After the addition, the obtained mixture was reacted at room temperature overnight. After the reaction was completed, the reaction liquid was concentrated, and the organic phase was concentrated and then purified by column chromatography (petroleum ether/ethyl acetate = 2/1) to obtain 42C (0.250 g, yield 70%).

[0362] LCMS m/z = 213.2 $[M+H]^+$;

[0363] Step 3: 42C (0.250 g, 1.18 mmol) and cesium carbonate (0.577 g, 1.77 mmol) were added to dry N,N-dimethylformamide (5 mL) in a 25 mL single-neck flask. The obtained mixture was reacted at 50°C for 30 min. A solution of 10E (0.429 g, 1.18 mmol) in N,N-dimethylformamide (2 mL) was added dropwise at 50°C. After the addition, the obtained mixture was reacted under stirring at 80°C overnight. After the reaction was completed, the reaction liquid was filtered, and the filtrate was separated and purified by preparative liquid chromatography (instrument: waters 2767 preparative liquid chromatographic instrument; chromatographic column: SunFire@ Prep C18 (19 mm × 150 mm); composition of mobile phase: mobile phase A: acetonitrile; mobile phase B: water (containing 0.1% trifluoroacetic acid); gradient: gradient elution using 20%-70% acetonitrile; cycle time: 15 min) to obtain compound 42 (110 mg, yield 17%).

[0364] LCMS m/z = 556.0 $[M+H]^+$.

[0365] ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.57 (s, 1H), 8.34 (s, 1H), 7.92 – 7.87 (m, 1H), 7.83-7.80 (d, 1H), 7.73-7.70 (dd, 1H), 7.55-7.52 (dd, 1H), 7.44 (d, 1H), 6.51-6.22 (m, 1H), 4.52-4.43 (m , 2H), 4.08-4.06 (d, 2H), 3.91-3.88 (d, 2H), 2.47 – 2.42 (m, 2H), 2.04-2.00 (m , 2H).

[0366] ^{19}F NMR (376 MHz, DMSO-d_6) δ -98.98 (s), -120.45 (s), -126.75 (s).

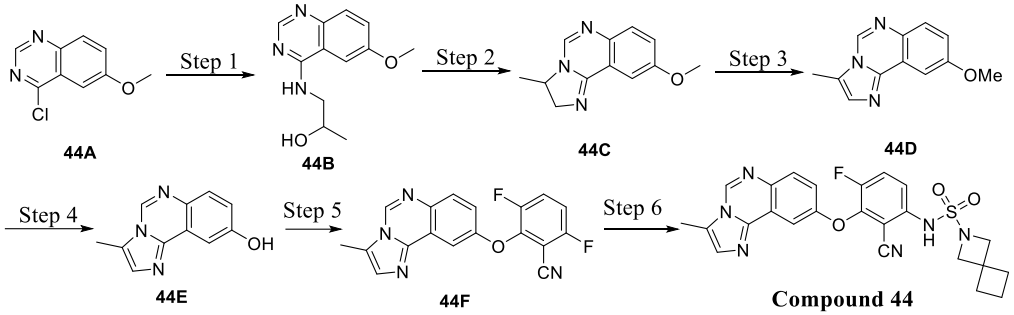
Example 43

acetonitrile; mobile phase B: water (containing 0.1% trifluoroacetic acid); gradient: gradient elution using 30%-70% acetonitrile; cycle time: 15 min) to obtain compound 43 (56 mg, yield: 6%).

[0370] LCMS m/z = 538.1 $[M+H]^+$;

[0371] ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.35 (s, 1H), 7.81 (d, 1H), 7.77 (dd, 1H), 7.59 (d, 1H), 7.52 (dd, 1H), 6.52 - 6.23 (m, 1H), 4.49 (td, 2H), 3.83 (s, 4H), 2.08 - 2.11 (m, 4H), 1.77 - 1.70 (m, 2H).

Example 44



[0372] Step 1: 44A (4.5 g, 23.13 mmol) and isopropyl alcohol (50 mL) were added into a 250 mL single-neck flask. Then triethylamine (4.68 g, 46.26 mmol) and isopropanolamine (2.08 g, 27.76 mmol) were added. The obtained mixture was reacted at 80°C for 1 hr. After the reaction was completed, the reaction liquid was concentrated, slurried with ethyl acetate (50 mL), and filtered, and the filter cake was washed with petroleum ether (50 mL) to obtain 44B (5.30 g, yield 98%).

[0373] LCMS m/z = 234.3 $[M+H]^+$;

[0374] Step 2: Phosphorus oxychloride (60 mL) was added into a 250 mL single-neck flask. 44B (5.3 g, 22.72 mmol) was slowly added in portions at 0-5°C. After the addition, the obtained mixture was reacted at 110°C for 5 hrs. After the reaction was completed, the reaction liquid was concentrated, then water (100 mL) was slowly added to quench the reaction at 0-5°C, and extraction was performed with ethyl acetate (100 mL × 2). The organic phase was concentrated and then purified by column chromatography (petroleum ether/ethyl acetate = 1/1) to obtain 44C (3.6 g, yield 73%).

[0375] LCMS m/z = 216.2 $[M+H]^+$;

[0376] Step 3: 44C (2.80 g, 13.01 mmol) and acetonitrile (30 mL) were added into a 100 mL single-neck flask. Then alumina (2.65 g, 25.99 mmol) and potassium permanganate (3.08 g, 19.49 mmol) were added. After the addition, the obtained mixture was reacted under stirring at room temperature overnight. After the reaction was completed, the reaction liquid was filtered,

and the filtrate was concentrated and then purified by column chromatography (petroleum ether/ethyl acetate = 1/2) to obtain 44D (0.88 g, yield 31%).

[0377] LCMS m/z = 214.1 $[M+H]^+$;

[0378] ^{1}H NMR (400 MHz, DMSO-d6) δ 9.01 (s, 1H), 7.86-7.84 (d, 1H), 7.74-7.73 (d, 1H), 7.35 (s, 1H), 7.32-7.29 (dd, 1H), 3.94 (s, 3H), 2.58 (s, 3H).

[0379] Step 4: 44D (0.88 g, 4.13 mmol) and N,N-dimethylformamide (10 mL) were added into a 50 mL single-neck flask. Then sodium thioethylate (1.04 g, 12.35 mmol) was added. After the addition, nitrogen protection was performed. The obtained mixture was reacted under stirring at 130°C overnight. After the reaction was completed, the reaction liquid was concentrated. Dilute hydrochloric acid was added to adjust the pH to acidic. After concentration, a residue was obtained, The residue was purified by column chromatography (dichloromethane/methanol = 20/1) to obtain 44E (0.68 g, yield 82%).

[0380] LCMS m/z =200.1 $[M+H]^+$;

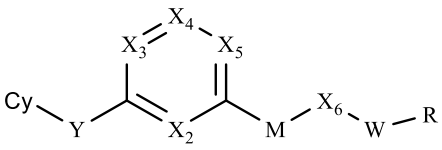
[0381] Step 5: 44E (0.30 g, 1.51 mmol) was dissolved in dry N,N-dimethylformamide (8 mL) in a 25 mL single-neck flask. Cesium carbonate (0.74 g, 2.26 mmol) was slowly added under an ice bath. After the addition, the obtained mixture was reacted under stirring at room temperature for 0.5 h. 2,3,6-trifluorobenzonitrile (0.28 g, 1.81 mmol) was slowly added dropwise under an ice bath. After the addition, the obtained mixture was reacted under stirring at room temperature overnight. After the reaction was completed, the reaction liquid was filtered, and the filtrate was concentrated and then purified by column chromatography (petroleum ether/ethyl acetate = 1/1) to obtain 44F (0.45 g, yield 88%).

[0382] LCMS m/z =337.0 $[M+H]^+$;

[0383] Step 6: 1B (0.21 g, 1.16 mmol) and cesium carbonate (0.47 g, 1.46 mmol) were added to dry N,N-dimethylformamide (5 mL) in a 25 mL single-neck flask. The obtained mixture was reacted at 50°C for 30 min. A solution of 44F (0.36 g, 0.97 mmol) in N,N-dimethylformamide (1 mL) was added dropwise at 50°C. After the addition, the obtained mixture was reacted under stirring at 80°C for 4 hrs. After the reaction was completed, the reaction liquid was filtered. The filter cake was washed with N,N-dimethylformamide (2 mL). The filtrate was concentrated, and then ethyl acetate (15 mL) and water (15 mL) were added for dissolution. Liquid separation was performed, and the aqueous phase was adjusted to neutral pH with saturated ammonium chloride, and extracted with dichloromethane (20 mL × 3), The organic phases were combined,

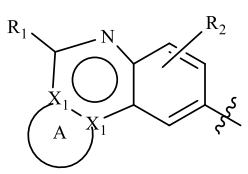
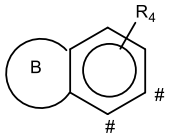
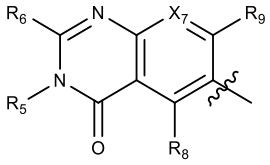
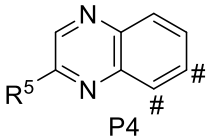
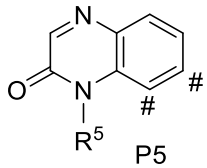
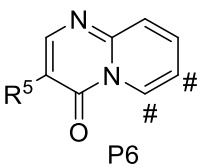
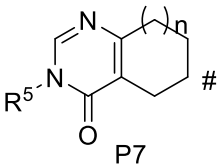
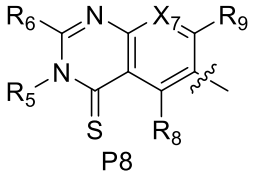
Claims

1. A compound represented by formula I, and a stereoisomer, deuterated product or pharmaceutically acceptable salt thereof,



I

wherein, Cy is selected from P1, P2, P3, P4, P5, P6, P7 or P8;


P1 ,

P2 ,

P3 ,

P4 ,

P5 ,

P6 ,

P7 ,

P8 ;

ring A is 5-membered or 6-membered heteroaryl containing 1 to 3 heteroatoms selected from N, S, and O, and the heteroaryl is optionally substituted with 1 or 2 groups selected from halogen, C_{1-4} alkoxy, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$, CN, C_{1-4} alkyl, haloC_{1-4} alkoxy and haloC_{1-4} alkyl;

ring B is 5-membered heterocyclic ring containing 1 to 3 heteroatoms selected from N, S, and O, and the heterocyclic ring is optionally substituted with 1 to 3 groups selected from =O, halogen, C_{1-4} alkyl, haloC_{1-4} alkyl, C_{1-4} alkoxy, OH and haloC_{1-4} alkoxy;

means that one point is selected to connect to Y;

n = 0 or 1;

each X_1 is independently N or C;

X_2 is N or CR_3;

X_3 is N or CR_{31};

X_4 is N or CR_{32};

X_5 is N or CR_{33};

X_6 is C(O), S(O) or S(O)$_2$;

X_7 is CR_7 or N;

R_1, R_2 and R_4 are independently H, halogen, OH, -NHC$_{1-4}$ alkyl, -N(C$_{1-4}$ alkyl)$_2$, CN, C$_{1-4}$ alkyl, C$_{1-4}$ alkoxy, haloC$_{1-4}$ alkoxy, haloC$_{1-4}$ alkyl, C$_{2-4}$ alkenyl or C$_{2-4}$ alkynyl;

R_3, R_{31}, R_{32}, and R_{33} are independently H, halogen, C$_{1-4}$ alkyl, haloC$_{1-4}$ alkyl, C$_{2-4}$ alkenyl, C$_{2-4}$ alkynyl, C$_{1-4}$ alkoxy, haloC$_{1-4}$ alkoxy, -NHC$_{1-4}$ alkyl, -N(C$_{1-4}$ alkyl)$_2$, CN or C$_{3-6}$ cycloalkyl, alternatively, R_{31} and R_{32}, or R_{32} and R_{33} together with the atoms to which they are attached form C$_{3-6}$ carbocyclic ring or 5-membered or 6-membered heterocyclic ring containing 1 to 3 heteroatoms selected from N, S, and O, and the carbocyclic ring or the heterocyclic ring is optionally substituted with 1 to 3 groups selected from halogen, C$_{1-4}$ alkyl, haloC$_{1-4}$ alkyl, C$_{1-4}$ alkoxy, OH, NH_2 and CN;

R_5 is C$_{1-4}$ alkyl, haloC$_{1-4}$ alkyl, C$_{3-6}$ cycloalkyl, 4-membered to 7-membered heterocycloalkyl containing 1-3 heteroatoms selected from N, S, and O, C$_{1-4}$ alkoxy, haloC$_{1-4}$ alkoxy or C$_{3-6}$ cycloalkyloxy, and is optionally substituted with 1 to 3 groups selected from halogen, -NHC$_{1-4}$ alkyl, -N(C$_{1-4}$ alkyl)$_2$, C$_{1-4}$ alkoxy, haloC$_{1-4}$ alkoxy, haloC$_{1-4}$ alkyl, CN, C$_{1-4}$ alkyl or =O;

R_6 is H, halogen, C$_{1-4}$ alkyl or haloC$_{1-4}$ alkyl;

alternatively, R_5 and R_6 together with the atoms to which they are attached form 5-membered or 6-membered heterocyclic ring containing 1 to 3 heteroatoms selected from N, S, and O, and the heterocyclic ring is optionally substituted with 1 to 3 groups selected from halogen, OH, NH_2, -NHC$_{1-4}$ alkyl, -N(C$_{1-4}$ alkyl)$_2$, CN and C$_{1-4}$ alkyl;

R_7, R_8, and R_9 are independently H, halogen, -NHC$_{1-4}$ alkyl, -N(C$_{1-4}$ alkyl)$_2$, CN, C$_{1-4}$ alkyl, C$_{2-4}$ alkenyl, C$_{2-4}$ alkynyl, haloC$_{1-4}$ alkyl, C$_{1-4}$ alkoxy or haloC$_{1-4}$ alkoxy;

Y is C$_{1-2}$ alkylene, O or NR_y;

R_y is H or C$_{1-4}$ alkyl;

M is C$_{1-2}$ alkylene, O or NR_m;

W is a bond, O or NR_w;

R_m and R_w are independently H or C$_{1-4}$ alkyl;

R is selected from C$_{1-4}$ alkyl, C$_{3-8}$ cycloalkyl, 4-membered to 10-membered heterocyclic ring containing 1 to 3 heteroatoms selected from N, S, and O, or -O-C$_{3-6}$ cycloalkyl, and the alkyl, cycloalkyl or heterocyclic ring is optionally substituted with 1 to 3 groups selected from halogen, C$_{1-4}$ alkyl, C$_{1-4}$ alkoxy, haloC$_{1-4}$ alkoxy, OH, NH_2, -NHC$_{1-4}$ alkyl, -N(C$_{1-4}$ alkyl)$_2$ and haloC$_{1-4}$ alkyl;

when Cy is P2, R is 4-membered to 10-membered saturated heterocycloalkyl containing 1 to 3 heteroatoms selected from N, S, and O, and is optionally substituted with 1 to 3 groups selected

from halogen, C_{1-4} alkyl, C_{1-4} alkoxy, haloC_{1-4} alkoxy, OH, NH_2, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$ and haloC_{1-4} alkyl.

2. The compound, and the stereoisomer, the deuterated product, or the pharmaceutically acceptable salt thereof of claim 1,

wherein, ring A is 5-membered heteroaryl, and the heteroaryl is optionally substituted with 1 or 2 groups selected from halogen, C_{1-4} alkoxy, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$, CN, C_{1-4} alkyl, haloC_{1-4} alkoxy and haloC_{1-4} alkyl;

when Cy is P3, the compound meets at least one of the following conditions:

(1) R_5 is substituted or unsubstituted C_{3-6} cycloalkyl, substituted or unsubstituted 4-membered to 7-membered heterocycloalkyl containing 1-3 heteroatoms selected from N, S, and O, substituted or unsubstituted C_{3-6} cycloalkyloxy, substituted or unsubstituted C_{1-4} alkoxy or substituted or unsubstituted haloC_{1-4} alkoxy, R is C_{3-8} cycloalkyl, 4-membered to 10-membered heterocyclic ring containing 1 to 3 heteroatoms selected from N, S, and O, or -O-C_{3-6} cycloalkyl, and is optionally substituted with 1 to 3 groups selected from halogen, C_{1-4} alkyl, C_{1-4} alkoxy, haloC_{1-4} alkoxy, OH, NH_2, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$ and haloC_{1-4} alkyl;

(2) R_5 and R_6 together with the atoms to which they are attached form 5-membered or 6-membered heterocyclic ring containing 1 to 3 heteroatoms selected from N, S, and O, and the heterocyclic ring is optionally substituted with 1 to 3 groups selected from halogen, OH, NH_2, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$, CN and C_{1-4} alkyl;

(3) X_2 is N or CR_3, R_3 is C_{1-4} alkyl, haloC_{1-4} alkyl, C_{1-4} alkoxy, haloC_{1-4} alkoxy, C_{2-4} alkenyl, C_{2-4} alkynyl, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$ or CN, W is O;

(4) R_{31} and R_{32}, or R_{32} and R_{33} together with the atoms to which they are attached form C_{3-6} carbocyclic ring or 5-membered or 6-membered heterocyclic ring containing 1 to 3 heteroatoms selected from N, S, and O, and the carbocyclic ring or the heterocyclic ring is optionally substituted with 1 to 3 groups selected from halogen, C_{1-4} alkyl, haloC_{1-4} alkyl, C_{1-4} alkoxy, OH, NH_2 and CN;

(5) X_2 is N or CR_3, R_3 is C_{1-4} alkyl, haloC_{1-4} alkyl, C_{1-4} alkoxy, haloC_{1-4} alkoxy, C_{2-4} alkenyl, C_{2-4} alkynyl, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$ or CN, W is NR_w, R is C_{3-8} cycloalkyl or 4-membered to 10-membered heterocyclic ring containing 1 to 3 heteroatoms selected from N, S, and O, and is optionally substituted with 1 to 3 groups selected from halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, OH, NH_2, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$ and haloC_{1-4} alkyl;

(6) X_2 is N or CR_3, X_6 is SO or SO_2, W is a bond, R_3 is C_{1-4} alkyl, haloC_{1-4} alkyl, C_{1-4} alkoxy, haloC_{1-4} alkoxy, C_{2-4} alkenyl, C_{2-4} alkynyl, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$ or CN, R is C_{3-4} cycloalkyl or 4-membered monocyclic heterocycloalkyl containing 1 to 3 heteroatoms selected from N, S, and O, 6-membered to 8-membered monocyclic heterocycloalkyl, 5-membered or 6-membered monocyclic heteroaryl, 5-membered to 10-membered fused heterocycloalkyl, 5-membered to 10-membered bridged heterocycloalkyl or 6-membered to 10-membered spirocyclic heterocycloalkyl, and is optionally substituted with 1 to 3 groups selected from halogen, C_{1-4} alkyl, C_{1-4} alkoxy, OH, NH_2, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$ and haloC_{1-4} alkyl;

(7) X_6 is CO, X_2 is N or CR_3, W is a bond, R_3 is C_{1-4} alkyl, haloC_{1-4} alkyl, C_{1-4} alkoxy, haloC_{1-4} alkoxy, C_{2-4} alkenyl, C_{2-4} alkynyl, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$ or CN;

(8) at least one of X_2, X_3, X_4, and X_5 is N, when X_2 is CR_3, R_3 is H, C_{1-4} alkyl, haloC_{1-4} alkyl, C_{1-4} alkoxy, haloC_{1-4} alkoxy, C_{2-4} alkenyl, C_{2-4} alkynyl, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$ or CN;

(9) X_2 is N or CR_3, R_3 is H, C_{1-4} alkyl, haloC_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} alkoxy, haloC_{1-4} alkoxy, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$ or CN, R_8 is halogen, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$, CN, C_{1-4} alkoxy or haloC_{1-4} alkoxy.

3. The compound, and the stereoisomer, the deuterated product, or the pharmaceutically acceptable salt thereof of claim 2,

wherein, R_3, R_{31}, R_{32}, and R_{33} are independently H, halogen, C_{1-4} alkyl, haloC_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} alkoxy, haloC_{1-4} alkoxy, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$, CN or C_{3-6} cycloalkyl, alternatively, R_{31} and R_{32}, or R_{32} and R_{33} together with the atoms to which they are attached form C_{3-6} cycloalkyl or 5-membered or 6-membered heterocycloalkyl containing 1 to 3 heteroatoms selected from N, S, and O, and the cycloalkyl or the heterocycloalkyl is optionally substituted with 1 to 3 groups selected from halogen, C_{1-4} alkyl, haloC_{1-4} alkyl, C_{1-4} alkoxy, OH, NH_2 and CN;

R_5 is C_{1-4} alkyl, haloC_{1-4} alkyl, C_{3-6} cycloalkyl, 4-membered to 7-membered heterocycloalkyl containing 1-3 heteroatoms selected from N, S, and O, C_{1-4} alkoxy, haloC_{1-4} alkoxy or C_{3-6} cycloalkyloxy, and is optionally substituted with 1 to 3 groups selected from halogen, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$, C_{1-4} alkoxy, haloC_{1-4} alkoxy, haloC_{1-4} alkyl, CN, C_{1-4} alkyl and =O;

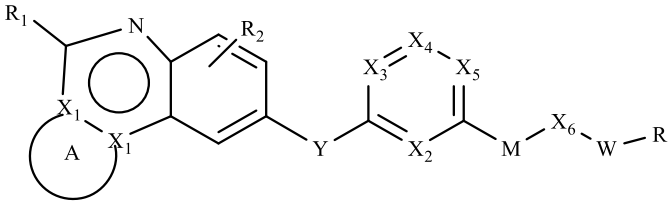
R_6 is H, halogen, C_{1-4} alkyl or haloC_{1-4} alkyl;

alternatively, R_5 and R_6 together with the atoms to which they are attached form 5-membered or 6-membered heterocycloalkyl containing 1 to 3 heteroatoms selected from N, S, and O, and

the heterocycloalkyl is optionally substituted with 1 to 3 groups selected from halogen, OH, NH_2, $-NHC_{1-4}$ alkyl, $-N(C_{1-4}$ alkyl$)_2$, CN and C_{1-4} alkyl;

R is selected from C_{1-4} alkyl, C_{3-8} cycloalkyl, 4-membered to 10-membered heterocycloalkyl containing 1 to 3 heteroatoms selected from N, S, and O, or $-O-C_{3-6}$ cycloalkyl, and the alkyl, the cycloalkyl or the heterocycloalkyl is optionally substituted with 1 to 3 groups selected from halogen, C_{1-4} alkyl, C_{1-4} alkoxy, haloC_{1-4} alkoxy, OH, NH_2, $-NHC_{1-4}$ alkyl, $-N(C_{1-4}$ alkyl$)_2$ and haloC_{1-4} alkyl.

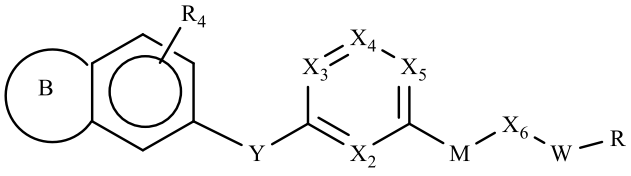
4. The compound, and the stereoisomer, the deuterated product, or the pharmaceutically acceptable salt thereof of claim 3, the compound having the structure as shown in formula I-1,



I-1

wherein, R is selected from C_{1-4} alkyl, C_{3-8} cycloalkyl or 4-membered to 7-membered monocyclic heterocycloalkyl containing 1 to 3 heteroatoms selected from N, S, and O, 5-membered to 10-membered fused heterocycloalkyl, 5-membered to 10-membered bridged heterocycloalkyl or 6-membered to 10-membered spirocyclic heterocycloalkyl, and is optionally substituted with 1 to 3 groups selected from halogen, C_{1-4} alkyl, C_{1-4} alkoxy, haloC_{1-4} alkoxy, OH, NH_2, $-NHC_{1-4}$ alkyl, $-N(C_{1-4}$ alkyl$)_2$ and haloC_{1-4} alkyl.

5. The compound, and the stereoisomer, the deuterated product, or the pharmaceutically acceptable salt thereof of claim 3, the compound having the structure as shown in formula I-2,



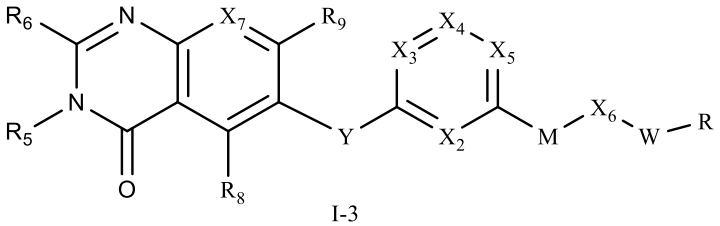
I-2

wherein, ring B is 5-membered heteroaryl or 5-membered heterocycloalkyl containing 1 to 3 heteroatoms selected from N, S, and O, and is optionally substituted with 1 to 3 groups selected from =O, halogen, C_{1-4} alkyl, haloC_{1-4} alkyl, C_{1-4} alkoxy, OH and haloC_{1-4} alkoxy;

R is saturated 4-membered to 7-membered monocyclic heterocycloalkyl containing 1 to 3 heteroatoms selected from N, S, and O, saturated 5-membered to 10-membered fused

heterocycloalkyl, saturated 5-membered to 10-membered bridged heterocycloalkyl or saturated 6-membered to 10-membered spirocyclic heterocycloalkyl, and is optionally substituted with 1 to 3 groups selected from halogen, C_{1-4} alkyl, C_{1-4} alkoxy, haloC_{1-4} alkoxy, OH, NH_2, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$ and haloC_{1-4} alkyl.

6. The compound, and the stereoisomer, the deuterated product, or the pharmaceutically acceptable salt thereof of claim 3, wherein the compound has the structure as shown in formula I-3,



I-3

.

7. The compound, and the stereoisomer, the deuterated product, or the pharmaceutically acceptable salt thereof of claim 6, wherein

R_6 and R_9 are H; Y is O; M is NH;

X_2 is N or CR_3, X_6 is SO or SO_2, and W is a bond;

R_3 is C_{1-4} alkyl, haloC_{1-4} alkyl, C_{1-4} alkoxy, haloC_{1-4} alkoxy, C_{2-4} alkenyl, C_{2-4} alkynyl, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$ or CN; R is 4-membered monocyclic heterocycloalkyl containing 1 to 3 heteroatoms selected from N, S, and O, 6-membered to 8-membered monocyclic heterocycloalkyl, 5-membered or 6-membered monocyclic heteroaryl, 5-membered to 10-membered fused heterocycloalkyl, 5-membered to 10-membered bridged heterocycloalkyl, 6-membered to 10-membered spirocyclic heterocycloalkyl or -O-C_{3-6} cycloalkyl, and the 4-membered monocyclic heterocycloalkyl is substituted with 1 to 3 groups selected from halogen, C_{1-4} alkyl, C_{1-4} alkoxy, OH, NH_2, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$ and haloC_{1-4} alkyl, the 6-membered to 8-membered monocyclic heterocycloalkyl, the 5-membered or 6-membered monocyclic heteroaryl, the 5-membered to 10-membered fused heterocycloalkyl, the 5-membered to 10-membered bridged heterocycloalkyl or the 6-membered to 10-membered spirocyclic heterocycloalkyl is optionally substituted with 1 to 3 groups selected from halogen, C_{1-4} alkyl, C_{1-4} alkoxy, OH, NH_2, -NHC_{1-4} alkyl, -N(C_{1-4} alkyl)$_2$ and haloC_{1-4} alkyl.

8. The compound, and the stereoisomer, the deuterated product, or the pharmaceutically acceptable salt thereof of claim 7, wherein

X_2 is CR_3; X_3 is CR_{31}; X_4 is CR_{32}; X_5 is CH; X_6 is SO_2; X_7 is CH;

R_3 is C_{1-2} alkyl, haloC_{1-2} alkyl, C_{1-2} alkoxy, haloC_{1-2} alkoxy, C_{2-4} alkenyl, C_{2-4} alkynyl, -NHC_{1-2} alkyl, -N(C_{1-2} alkyl)$_2$ or CN;

each of R_{31} and R_{32} is independently H, F, Cl, C_{1-2} alkyl, haloC_{1-2} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-2} alkoxy, haloC_{1-2} alkoxy, -NHC_{1-2} alkyl, -N(C_{1-2} alkyl)$_2$, CN or C_{3-6} cycloalkyl;

R_5 is C_{1-2} alkyl, CN or =O substituted C_{1-2} alkyl, haloC_{1-2} alkyl, C_{3-4} cycloalkyl, 4-membered to 7-membered heterocycloalkyl containing 1-3 heteroatoms selected from N, S, and O, C_{1-2} alkoxy, haloC_{1-2} alkoxy or C_{3-4} cycloalkyloxy;

R_8 is selected from H, F, Cl, CN, C_{1-2} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, haloC_{1-2} alkyl, C_{1-2} alkoxy or haloC_{1-2} alkoxy;

R is 4-membered or 5-membered monocyclic heterocycloalkyl containing 1 to 3 heteroatoms selected from N, S, and O, 6-membered to 8-membered monocyclic heterocycloalkyl, 5-membered or 6-membered monocyclic heteroaryl, 5-membered to 10-membered fused heterocycloalkyl, 5-membered to 10-membered bridged heterocycloalkyl, 6-membered to 10-membered spirocyclic heterocycloalkyl or -O-C_{3-6} cycloalkyl, and the 4-membered monocyclic heterocycloalkyl is substituted with 1 to 3 groups selected from F, Cl, C_{1-2} alkyl, C_{1-2} alkoxy, OH, NH_2, -NHC_{1-2} alkyl, -N(C_{1-2} alkyl)$_2$ and haloC_{1-2} alkyl, the 6-membered to 8-membered monocyclic heterocycloalkyl, the 5-membered or 6-membered monocyclic heteroaryl, the 5-membered to 10-membered fused heterocycloalkyl, the 5-membered to 10-membered bridged heterocycloalkyl, the 6-membered to 10-membered spirocyclic heterocycloalkyl or the C_{3-6} cycloalkyl is optionally substituted with 1 to 3 groups selected from F, Cl, C_{1-2} alkyl, C_{1-2} alkoxy, OH, NH_2, -NHC_{1-2} alkyl, -N(C_{1-2} alkyl)$_2$ and haloC_{1-2} alkyl.

9. The compound, and the stereoisomer, the deuterated product, or the pharmaceutically acceptable salt thereof of claim 8, wherein,

R_3 is CN;

each of R_{31} and R_{32} is independently H, F, Cl or C_{3-6} cycloalkyl;

R_5 is selected from C_{1-2} alkyl, haloC_{1-2} alkyl, C_{1-2} alkoxy, or CN or =O substituted C_{1-2} alkyl;

R_8 is H;

R is 6-membered to 10-membered spirocyclic heterocycloalkyl containing 1 to 3 heteroatoms selected from N, S, and O, 4-membered or 5-membered monocyclic heterocycloalkyl containing 1 to 3 heteroatoms selected from N, S, and O, or -O-C_{3-6} cycloalkyl, and the 6-membered to 10-membered spirocyclic heterocycloalkyl, the 4-membered or 5-membered monocyclic

heterocycloalkyl or the C_{3-6} cycloalkyl is optionally substituted with 1 to 3 groups selected from F, Cl, C_{1-2} alkyl or C_{1-2} alkoxy.

10. The compound, and the stereoisomer, the deuterated product, or the pharmaceutically acceptable salt thereof of claim 1, wherein the compound is selected from one of the structures in Table 1 or Table 2.
11. A pharmaceutical composition or pharmaceutical preparation, comprising the compound, and the stereoisomer, the deuterated product or the pharmaceutically acceptable salt thereof of any one of claims 1 to 10, and a pharmaceutically acceptable carrier and/or excipient.
12. The pharmaceutical composition or pharmaceutical preparation of claim 11, wherein the pharmaceutical composition or pharmaceutical preparation comprises 1 mg-1500 mg of the compound, and the stereoisomer, the deuterated product or the pharmaceutically acceptable salt thereof of any one of claims 1 to 10, and the pharmaceutically acceptable carrier and/or excipient.
13. Use of the compound, and the stereoisomer, the deuterated product or the pharmaceutically acceptable salt thereof of any one of claims 1 to 10 in the preparation of a drug for the treatment/prevention of a BRAF-mediated disease; the disease is preferably a tumor, more preferably a brain tumor; amount of the compound, or the stereoisomer, the deuterated product or the pharmaceutically acceptable salt thereof is preferably 1 mg-1500 mg.