reduced pressure, then diluted by adding 1,2-dichloroethane (40 mL) and concentrated under reduced pressure again to give a crude product **2-2,** which was directly used in the next reaction.

[00168] Step 2: Synthesis of compound **2-3**

[00169] Compound **2-2** (1.35 g, 6.38 mmol) was dissolved in tetrahydrofuran (15 mL) at 20°C, and deuterated methylamine hydrochloride (225.19 mg, 3.19 mmol) and N,N-diisopropylethylamine (2.48 g, 19.15 mmol, 3.34 mL) were added. The mixture was stirred at 20 °C for 16 hours. The reaction solution was diluted with water (20 mL), and extracted with ethyl acetate (40 mL×3). The combined organic phase was washed with saturated brine (5 mL×2), dried over anhydrous sodium sulfate, and filtered. The filtrate was concentrated under reduced pressure, and then purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 10/1 ~ 5/1) to give a crude product. The crude product was separated by preparative HPLC (Waters Xbridge C18 150*50mm*10μm; mobile phase: [water (10mM ammonium bicarbonate)-acetonitrile]; acetonitrile%: 3%-33%, 11min) to give compound **2-3.**

[00170] MS *m/z*: 209[M+H]$^+$; ^{1}H NMR (400 MHz, DMSO-d$_6$) δ 8.90 (br s, 1H), 8.48 (s, 1H).

[00171] Step 3: Synthesis of compound **2-4**

[00172] Compound **2-3** (55.06 mg, 263.38 μmol) and compound **1-12** (70 mg, 239.43 μmol) were dissolved in tetrahydrofuran (3 mL) at 0°C under nitrogen, and lithium hexamethyldisilazide (1 M, 718.30 μL) was added dropwise. The mixture was stirred at 20 °C for 1 h. The reaction solution was quenched by adding aqueous ammonium chloride solution (10 mL) at 0 °C, diluted with water (10 mL), and extracted with ethyl acetate (20 mL×3). The combined organic phase was washed with saturated brine (5 mL×2), dried over anhydrous sodium sulfate, and filtered. The filtrate was concentrated under reduced pressure to give a crude product. The crude product was purified by thin layer chromatography (silica gel, petroleum ether/ethyl acetate = 1/5) to give compound **2-4.**

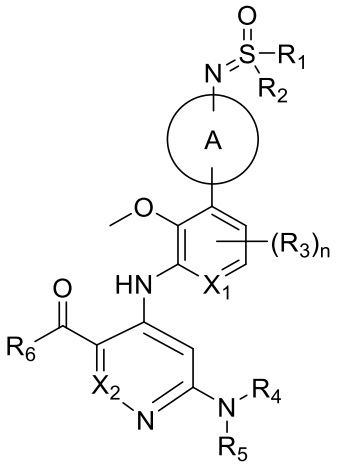
[00173] MS *m/z*: 465[M+H]$^+$

[00174] Step 4: Synthesis of compound **2**

[00175] Compound **2-4** (75 mg, 161.31 μmol) was dissolved in dioxane (2 mL). Cyclopropylformamide (41.18 mg, 483.93 μmol), cesium carbonate (157.67 mg, 483.93 μmol) and (2-dicyclohexylphosphino)-3,6-dimethoxy-2',4',6'-triisopropyl-1,1'-biphenyl)(2'-amino-1,1'-biphenyl-2-yl)palladium (II) mesylate (14.62 mg, 16.13 μmol) were added. The

CLAIMS

1. A compound of formula (II) or a pharmaceutically acceptable salt thereof,



(II) ,

wherein

ring A is 6-membered heteroaryl;

X_1 and X_2 are each independently selected from N and CH;

R_1 and R_2 are independently selected from C_{1-3} alkyl, wherein the C_{1-3} alkyl is optionally substituted with 1, 2, 3 or 4 R_a;

alternatively, R_1 and R_2 are taken together with the S atom to which they are attached to form 4- to 6-membered heterocycloalkyl, wherein the 4- to 6-membered heterocycloalkyl is optionally substituted with 1, 2, 3 or 4 R_a;

each R_3 is independently selected from hydrogen, deuterium, fluorine, chlorine, bromine, C_{1-3} alkyl and C_{1-3} alkoxy;

R_4 is selected from hydrogen, $-C(=O)R_{41}$, $-C(=O)NR_{42}R_{43}$, 5- to 10-membered heteroaryl and phenyl, wherein the 5- to 10-membered heteroaryl and phenyl are optionally substituted with 1, 2 or 3 R_b;

R_{41} is selected from C_{1-3} alkyl, C_{3-8} cycloalkyl, 5- to 6-membered heteroaryl, phenyl and 4- to 6-membered heterocycloalkyl, wherein the C_{1-3} alkyl, C_{3-8} cycloalkyl, 5- to 6-membered heteroaryl, phenyl and 4- to 6-membered heterocycloalkyl are optionally substituted with 1, 2, 3 or 4 R_c;

R_{42} is selected from hydrogen and C_{1-3} alkyl;

R_{43} is selected from C_{1-3} alkyl, C_{3-8} cycloalkyl, 5- to 6-membered heteroaryl and 4- to 6-membered heterocycloalkyl, wherein the C_{1-3} alkyl, C_{3-8} cycloalkyl, 5- to 6-membered heteroaryl and 4- to 6-membered heterocycloalkyl are optionally substituted with 1, 2, 3 or 4 R_c;

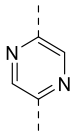
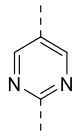
R_5 is selected from hydrogen and C_{1-3} alkyl;

R_6 is selected from C_{1-3} alkyl, C_{1-3} alkoxy, C_{3-6} cycloalkyl, -NH-C_{1-3} alkyl and -NH-C_{3-6} cycloalkyl, wherein the C_{1-3} alkyl, C_{1-3} alkoxy, C_{3-6} cycloalkyl, -NH-C_{1-3} alkyl and -NH-C_{3-6} cycloalkyl are optionally substituted with 1, 2, 3 or 4 R_d;

R_a, R_b, R_c and R_d are independently selected from H, deuterium, fluorine, chlorine, bromine, iodine, CN, NH_2, C_{1-3} alkyl and C_{1-3} alkoxy;

n is selected from 0, 1, 2 and 3.

2. The compound according to claim 1 or a pharmaceutically acceptable salt thereof, ring A is selected from  and ;

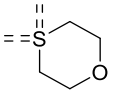
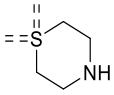
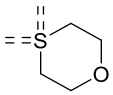
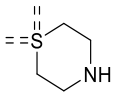
alternatively, ring A is selected from  and .

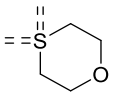
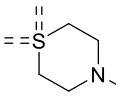
3. The compound according to claim 1 or a pharmaceutically acceptable salt thereof, R_1 and R_2 are independently selected from methyl, ethyl and propyl, wherein the methyl, ethyl and propyl are optionally substituted with 1, 2, 3 or 4 R_a;

alternatively, R_1 and R_2 are independently selected from methyl.

4. The compound according to claim 1 or a pharmaceutically acceptable salt thereof, R_1 and R_2 are taken together with the S atom to which they are attached to form 4- to 6-membered heterocycloalkyl, wherein the 4- to 6-membered heterocycloalkyl is optionally substituted with 1, 2, 3 or 4 R_a.

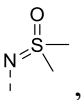
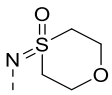
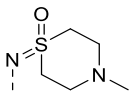
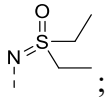
5. The compound according to claim 4 or a pharmaceutically acceptable salt thereof, the 4- to

6-membered heterocycloalkyl is selected from , , ,  and , wherein the , , ,  and  are optionally substituted with 1, 2, 3 or 4 R_a;

alternatively, the 4- to 6-membered heterocycloalkyl is selected from , , ,  and .

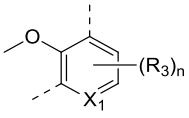
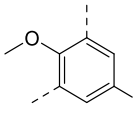
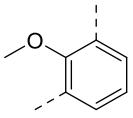
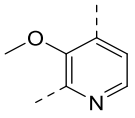
6. The compound according to any one of claims 1-5 or a pharmaceutically acceptable salt thereof, R_a is selected from hydrogen.

7. The compound according to claim 1 or a pharmaceutically acceptable salt thereof, wherein the compound has any one of the following definitions:

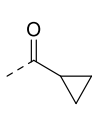
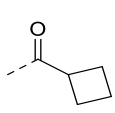
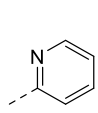
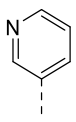
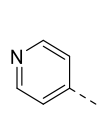
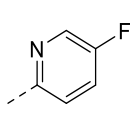
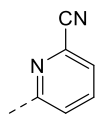
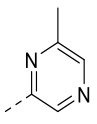
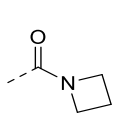
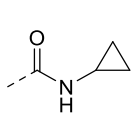
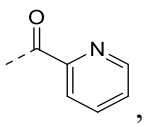
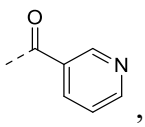
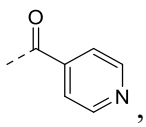
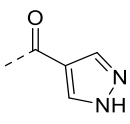
i) structural moiety  is selected from , , , ,  and ;

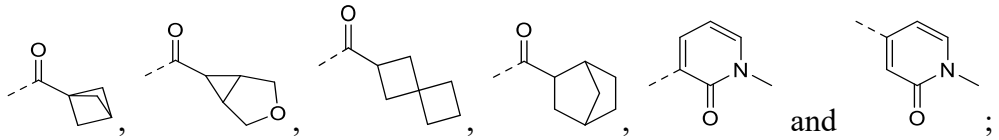
ii) X_1 is selected from N and CH;

iii) each R_3 is independently selected from hydrogen and fluorine;

iv) structural moiety  is selected from ,  and ;

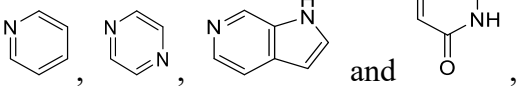
v) wherein R_b is selected from hydrogen, fluorine, CN and methyl;

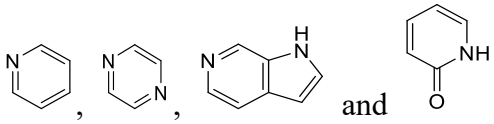
vi) R_4 is selected from , , , , , , , , , , , , , , ,



;

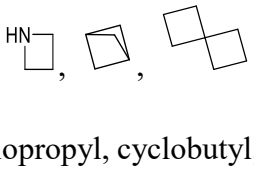
vii) R_5 is selected from hydrogen, methyl and ethyl.

8. The compound according to claim 1 or a pharmaceutically acceptable salt thereof, R_4 is selected from hydrogen, -C(O)R_{41}, -C(O)N$R_{42}R_{43}$, 

, wherein the 

are optionally substituted with 1, 2 or 3 R_b.

9. The compound according to claim 8 or a pharmaceutically acceptable salt thereof, wherein the compound has any one of the following definitions:

i) the R_{41} is selected from methyl, ethyl, propyl, cyclopropyl, cyclobutyl, 

, wherein the methyl, ethyl, propyl, cyclopropyl, cyclobutyl, are optionally substituted with 1, 2, 3 or 4 R_c;

ii) the R_{42} is selected from hydrogen;

iii) the R_{43} is selected from methyl, ethyl, propyl, cyclopropyl, and cyclobutyl, wherein the methyl, ethyl, propyl, cyclopropyl and cyclobutyl are optionally substituted with 1, 2, 3 or 4 R_c.

10. The compound according to any one of claims 8-9 or a pharmaceutically acceptable salt thereof, wherein R_c is selected from H.

11. The compound according to claim 1 or a pharmaceutically acceptable salt thereof, R_6 is selected from methyl, ethyl, propyl, methoxy, ethoxy, cyclopropyl, cyclobutyl, -$NHCH_3$, -$NHCH_2CH_3$, -NH-cyclopropyl and -NH-cyclobutyl, wherein the methyl, ethyl, propyl, methoxy, ethoxy, cyclopropyl, cyclobutyl, -$NHCH_3$, -$NHCH_2CH_3$, -NH-cyclopropyl and -NH-

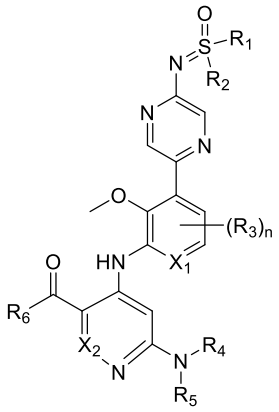
cyclobutyl are optionally substituted with 1, 2, 3 or 4 R_d;

alternatively, R_6 is selected from methyl, ethyl, -$NHCH_3$ and cyclopropyl, wherein the methyl, ethyl, -$NHCH_3$ and cyclopropyl are optionally substituted with 1, 2, 3 or 4 R_d;

alternatively, R_6 is selected from -CH_2CD_3, -CH_2CH_3, -$NHCD_3$, -CH_2OCH_3, -CH_3 and cyclopropyl.

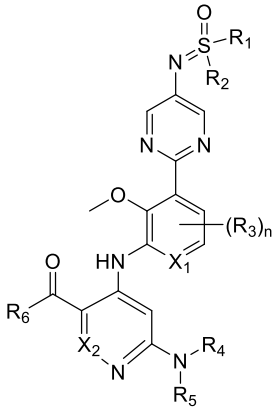
12. The compound according to claim 11 or a pharmaceutically acceptable salt thereof, R_d is selected from hydrogen, deuterium and methoxy.

13. The compound according to claim 1 or a pharmaceutically acceptable salt thereof, wherein the compound is represented by formula (II-1) or (II-2):



(II-1)

or

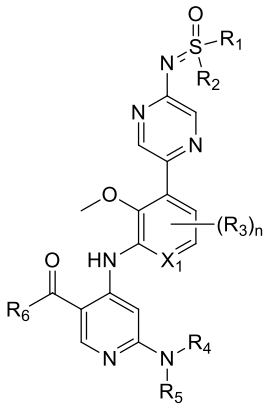


(II-2)

,

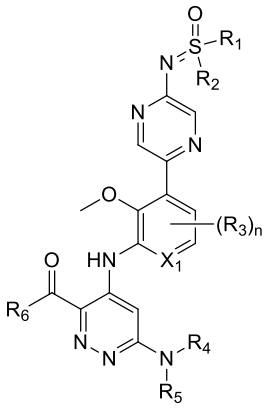
wherein R_1, R_2, R_3, R_4, R_5, R_6, X_1, X_2 and n are as defined in claim 1;

alternatively, the compound is represented by formula (II-1-1) or (II-1-2):



(II-1-1)

or

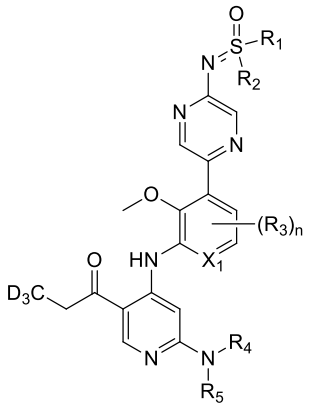


(II-1-2)

,

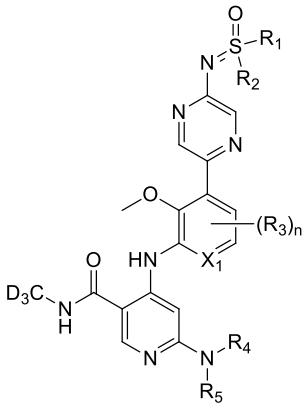
wherein R_1, R_2, R_3, R_4, R_5, R_6, X_1 and n are as defined in claim 12;

alternatively, the compound is represented by formula (II-1-1-1) or (II-1-1-2):



(II-1-1-1)

or

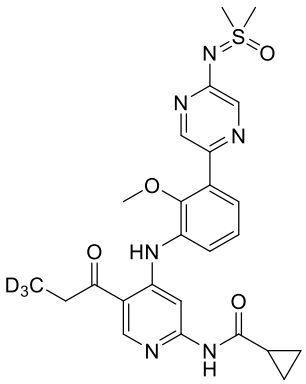


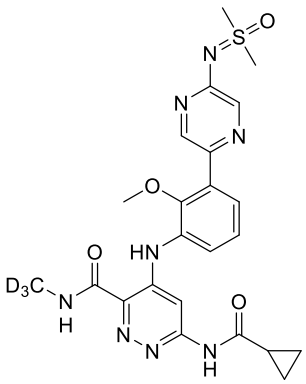
(II-1-1-2)

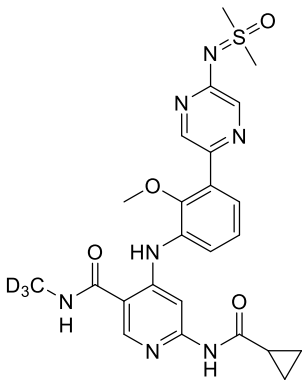
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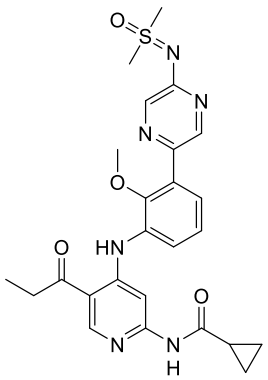
wherein R_1, R_2, R_3, R_4, R_5, X_1 and n are as defined in claim 1.

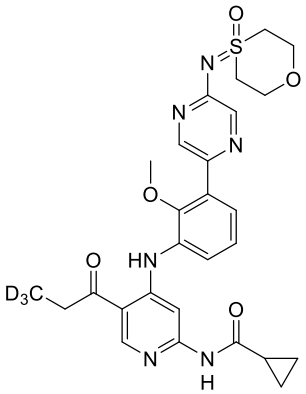
14. A compound, which is one of the following compounds, or a pharmaceutically acceptable salt thereof,

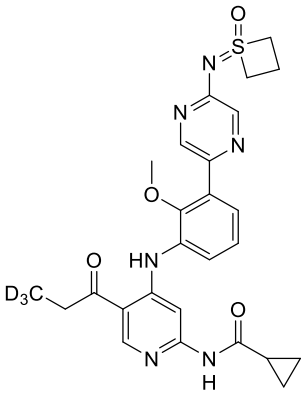


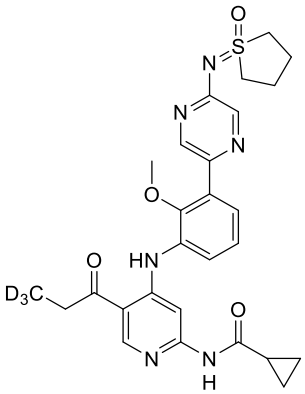


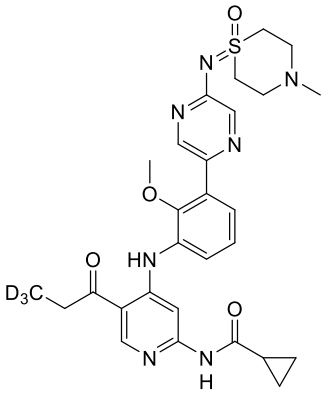


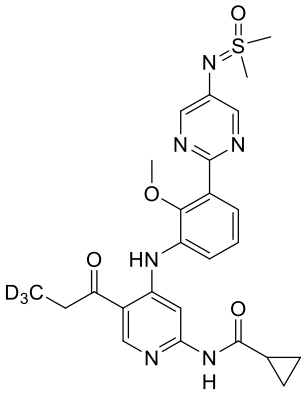


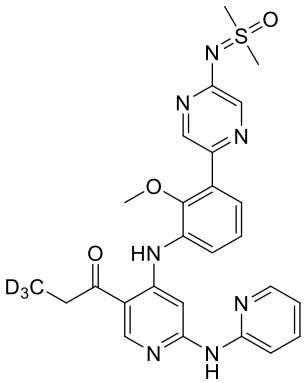


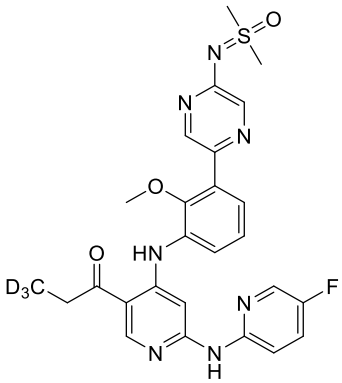


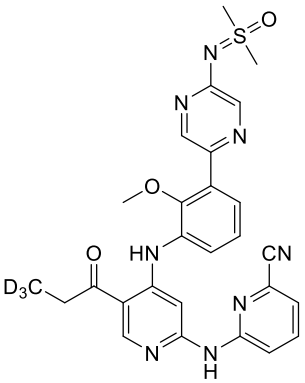


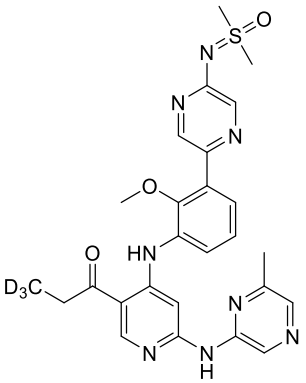


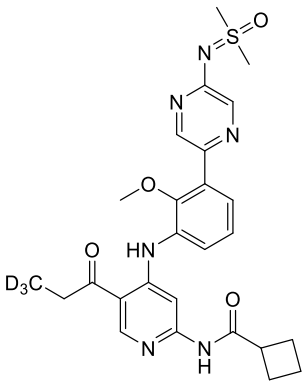


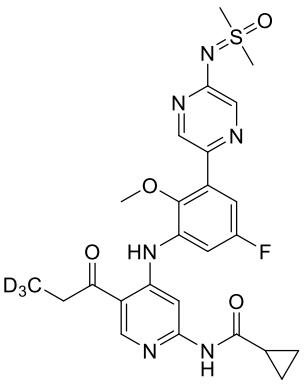


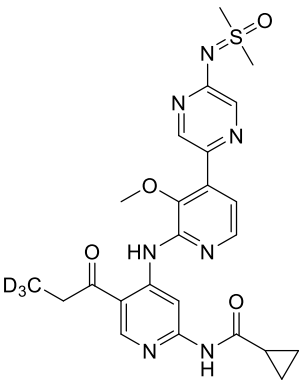


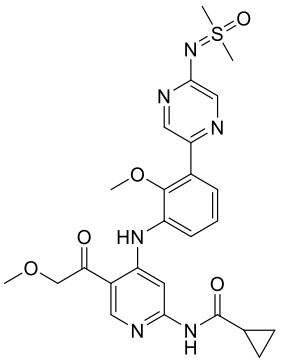


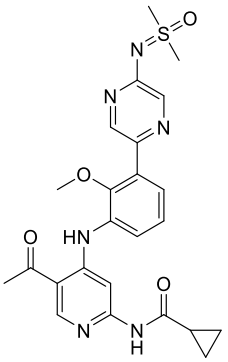


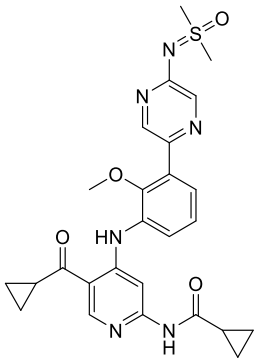


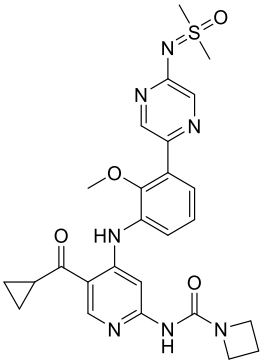


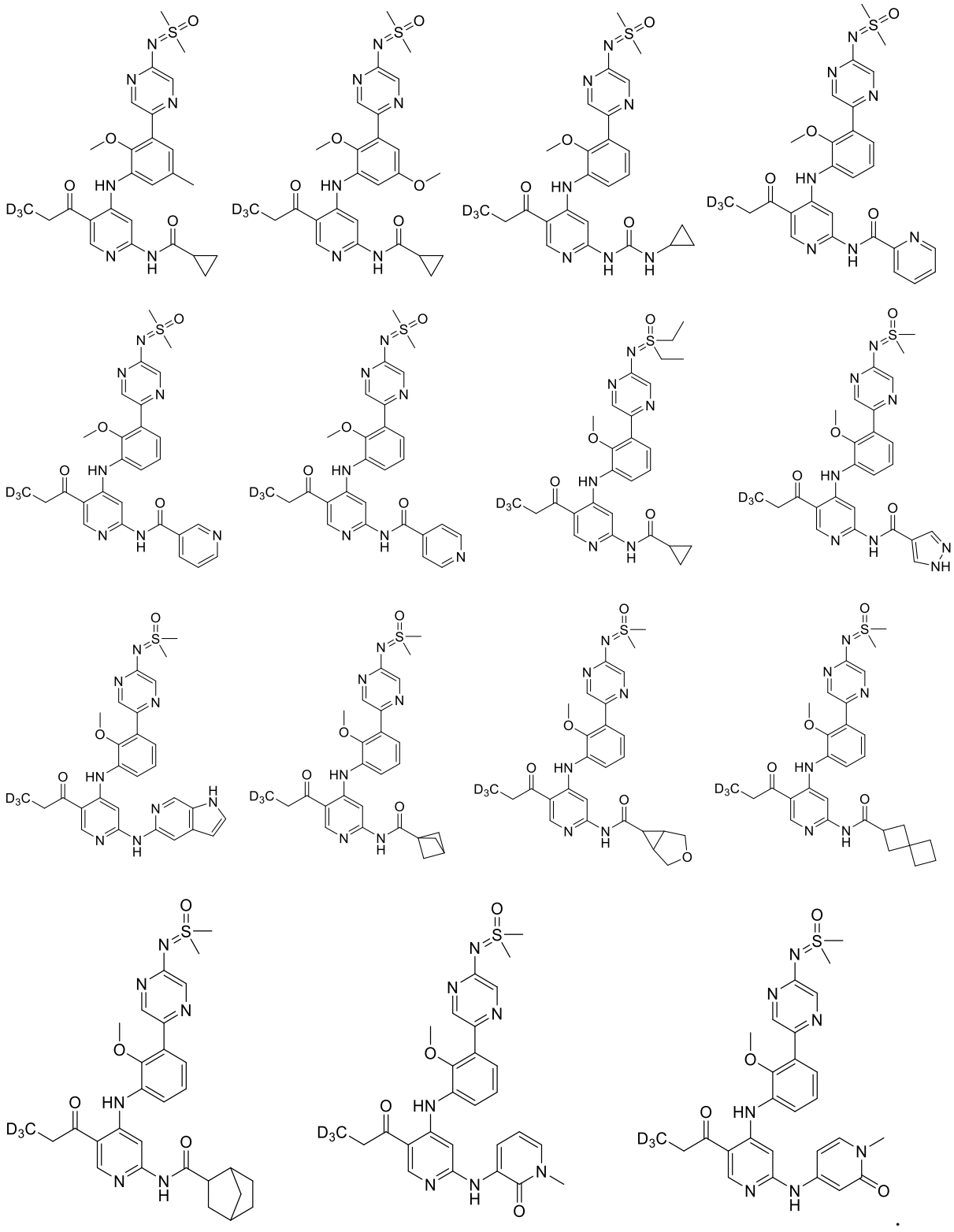












15. A compound according to any one of claims 1-14, or a pharmaceutically acceptable salt thereof, for use in the treatment of a disease related to Tyk2 JH2.