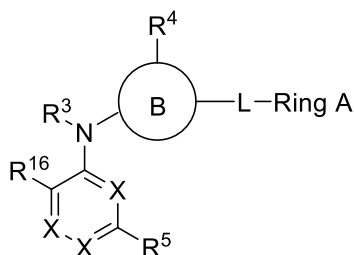


one or more of the conditions described herein without the side-effects associated with the inhibition of JAK2.

[0015] Accordingly there is a need to provide novel inhibitors having more effective or advantageous pharmaceutically relevant properties, like selectivity over other JAK kinases (especially JAK2).

SUMMARY

[0015a] In an aspect of the present disclosure, there is provided a compound of Formula (XII), or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof:



Formula (XII),

wherein:

Ring B is cycloalkyl, heterocycloalkyl, aryl, heteroaryl;

R^{16} is $-C(=O)NR^1R^2$, $-C(=N-CN)NR^1R^2$, $-P(=O)R^1R^2$, or $-C(=O)R^{11}$;

R^1 and R^2 are independently hydrogen, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_1 - C_6 deuteroalkyl,

C_1 - C_6 hydroxyalkyl, C_1 - C_6 aminoalkyl, C_2 - C_6 alkenyl, or C_2 - C_6 alkynyl;

R^3 is hydrogen, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, or C_1 - C_6 deuteroalkyl;

R^4 is hydrogen, deuterium, halogen, $-CN$, $-OR^b$, $-SR^b$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-NO_2$, $-NR^cR^d$, -

$NHS(=O)_2R^a$, $-S(=O)_2NR^cR^d$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)OR^b$, $-OC(=O)OR^b$, $-C(=O)NR^cR^d$, -

$OC(=O)NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, $-P(=O)R^bR^b$, C_1 - C_6 alkyl,

C_1 - C_6 haloalkyl, C_1 - C_6 deuteroalkyl, C_1 - C_6 hydroxyalkyl, C_1 - C_6 aminoalkyl, C_2 - C_6 alkenyl, or C_2 -

C_6 alkynyl;

or R^3 and R^4 are taken together to form an optionally substituted ring;

L is a bond or $-C(=O)-$;

Ring A is cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; each optionally substituted with one or more R^A ;

each R^A is independently deuterium, halogen, $-CN$, $-OR^b$, $-SR^b$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-NO_2$, $-NR^cR^d$, -

$NHS(=O)_2R^a$, $-S(=O)_2NR^cR^d$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)OR^b$, $-OC(=O)OR^b$, $-C(=O)NR^cR^d$, -

$OC(=O)NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl,

C_1 - C_6 deuteroalkyl, C_1 - C_6 hydroxyalkyl, C_1 - C_6 aminoalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, cycloalkyl,

heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl,

heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo,

deuterium, halogen, $-CN$, $-OR^b$, $-NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, $-C(=O)NR^cR^d$, C_1 - C_6 alkyl, or

C_1 - C_6 haloalkyl;

or two R^A on the same carbon are taken together to form an oxo;

or $-L$ -Ring A is absent;

each X is independently -CR^x- or -N-;

each R^x is independently hydrogen, deuterium, halogen, -CN, -OR^b, -SR^b, -S(=O)R^a, -S(=O)₂R^a, -NO₂, -NR^cR^d, -NHS(=O)₂R^a, -S(=O)₂NR^cR^d, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -C(=O)NR^cR^d, -OC(=O)NR^cR^d, -NR^bC(=O)NR^cR^d, -NR^bC(=O)R^a, -NR^bC(=O)OR^b, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, or C₂-C₆alkynyl;

R⁵ is halogen, -CN, -OR⁸, -SR⁸, -S(=O)R⁷, -S(=O)₂R⁷, -NO₂, -NR⁹R¹⁰, -NR⁸S(=O)R⁷, -NR⁸S(=O)₂R⁷, -S(=O)₂NR⁹R¹⁰, -C(=N-CN)R⁷, -C(=O)R⁷, -OC(=N-CN)R⁷, -OC(=O)R⁷, -C(=N-CN)OR⁸, -C(=O)OR⁸, -OC(=N-CN)OR⁸, -OC(=O)OR⁸, -C(=N-CN)NR⁹R¹⁰, -C(=O)NR⁹R¹⁰, -OC(=N-CN)NR⁹R¹⁰, -OC(=O)NR⁹R¹⁰, -NR⁸C(=N-CN)NR⁹R¹⁰, -NR⁸C(=O)NR⁹R¹⁰, -NR⁸C(=N-CN)R⁷, -NR⁸C(=N-OH)R⁷, -NR⁸C(=N-CN)OR⁸, -NR⁸C(=O)OR⁸, -NR⁸S(=O)(=NR⁸)R⁷, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₁-C₆heteroalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C₁-C₆alkyl(cycloalkyl), C₁-C₆alkyl(heterocycloalkyl), C₁-C₆alkyl(aryl), or C₁-C₆alkyl(heteroaryl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, C₁-C₆alkyl, or C₁-C₆haloalkyl;

R⁷ is C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

each R⁸ is independently hydrogen, CN, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

R⁹ and R¹⁰ are independently hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, C₁-C₆deuteroalkyl, C₁-C₆haloalkyl, C₁-C₆hydroxyalkyl, C₁-C₆hydroxydeuteroalkyl, cycloalkyl, or heterocycloalkyl;

or R⁹ and R¹⁰ are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

or R⁸ and R⁹ are taken together with the atoms to which they are attached to form a heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

R¹¹ is C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more R^{11a};

each R^{11a} is independently deuterium, halogen, -CN, -OR^b, -SR^b, -S(=O)R^a, -S(=O)₂R^a, -NO₂, -NR^cR^d, -NHS(=O)₂R^a, -S(=O)₂NR^cR^d, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -C(=O)NR^cR^d, -OC(=O)NR^cR^d, -NR^bC(=O)NR^cR^d, -NR^bC(=O)R^a, -NR^bC(=O)OR^b, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, or C₂-C₆alkynyl;

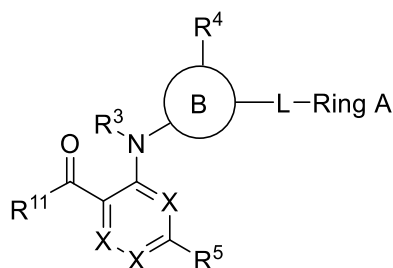
each R^a is independently C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

each R^b is independently hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

each R^c and R^d is independently hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

or R^c and R^d are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl.

[0015b] In another aspect of the present disclosure, there is also provided a compound of Formula (XIII), or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof:



Formula (XIII),

wherein:

Ring B is cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;

R³ is hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, or C₁-C₆deuteroalkyl;

R⁴ is hydrogen, deuterium, halogen, -CN, -OR^b, -SR^b, -S(=O)R^a, -S(=O)₂R^a, -NO₂, -NR^cR^d, -

NHS(=O)₂R^a, -S(=O)₂NR^cR^d, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -C(=O)NR^cR^d, -
OC(=O)NR^cR^d, -NR^bC(=O)NR^cR^d, -NR^bC(=O)R^a, -NR^bC(=O)OR^b, -P(=O)R^bR^b, C₁-C₆alkyl,
C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, or C₂-
C₆alkynyl;

or R³ and R⁴ are taken together to form an optionally substituted ring;

L is a bond or -C(=O)-;

Ring A is cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; each optionally substituted with one or more
R^A;

each R^A is independently deuterium, halogen, -CN, -OR^b, -SR^b, -S(=O)R^a, -S(=O)₂R^a, -NO₂, -NR^cR^d, -
NHS(=O)₂R^a, -S(=O)₂NR^cR^d, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -C(=O)NR^cR^d, -
OC(=O)NR^cR^d, -NR^bC(=O)NR^cR^d, -NR^bC(=O)R^a, -NR^bC(=O)OR^b, C₁-C₆alkyl, C₁-C₆haloalkyl,
C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl,
heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl,
heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo,
deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, C₁-C₆alkyl, or
C₁-C₆haloalkyl;

or two R^A on the same carbon are taken together to form an oxo;

or -L-Ring A is absent;

each X is independently -CR^x- or -N-;

each R^x is independently hydrogen, deuterium, halogen, -CN, -OR^b, -SR^b, -S(=O)R^a, -S(=O)₂R^a, -NO₂, -
NR^cR^d, -NHS(=O)₂R^a, -S(=O)₂NR^cR^d, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -
C(=O)NR^cR^d, -OC(=O)NR^cR^d, -NR^bC(=O)NR^cR^d, -NR^bC(=O)R^a, -NR^bC(=O)OR^b, C₁-C₆alkyl,
C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, or C₂-
C₆alkynyl;

R⁵ is halogen, -CN, -OR⁸, -SR⁸, -S(=O)R⁷, -S(=O)₂R⁷, -NO₂, -NR⁹R¹⁰, -NR⁸S(=O)R⁷, -NR⁸S(=O)₂R⁷, -
S(=O)₂NR⁹R¹⁰, -C(=N-CN)R⁷, -C(=O)R⁷, -OC(=N-CN)R⁷, -OC(=O)R⁷, -C(=N-CN)OR⁸, -C(=O)OR⁸,
-OC(=N-CN)OR⁸, -OC(=O)OR⁸, -C(=N-CN)NR⁹R¹⁰, -C(=O)NR⁹R¹⁰, -OC(=N-CN)NR⁹R¹⁰, -
OC(=O)NR⁹R¹⁰, -NR⁸C(=N-CN)NR⁹R¹⁰, -NR⁸C(=O)NR⁹R¹⁰, -NR⁸C(=N-CN)R⁷, -NR⁸C(=N-OH)R⁷,
-NR⁸C(=O)R⁷, -NR⁸C(=N-CN)OR⁸, -NR⁸C(=O)OR⁸, -NR⁸S(=O)(=NR⁸)R⁷, C₁-C₆alkyl,

C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₁-C₆heteroalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C₁-C₆alkyl(cycloalkyl), C₁-C₆alkyl(heterocycloalkyl), C₁-C₆alkyl(aryl), or C₁-C₆alkyl(heteroaryl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, C₁-C₆alkyl, or C₁-C₆haloalkyl;

R⁷ is C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

each R⁸ is independently hydrogen, CN, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

R⁹ and R¹⁰ are independently hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, C₁-C₆deuteroalkyl, C₁-C₆haloalkyl, C₁-C₆hydroxyalkyl, C₁-C₆hydroxydeuteroalkyl, cycloalkyl, or heterocycloalkyl;

or R⁹ and R¹⁰ are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

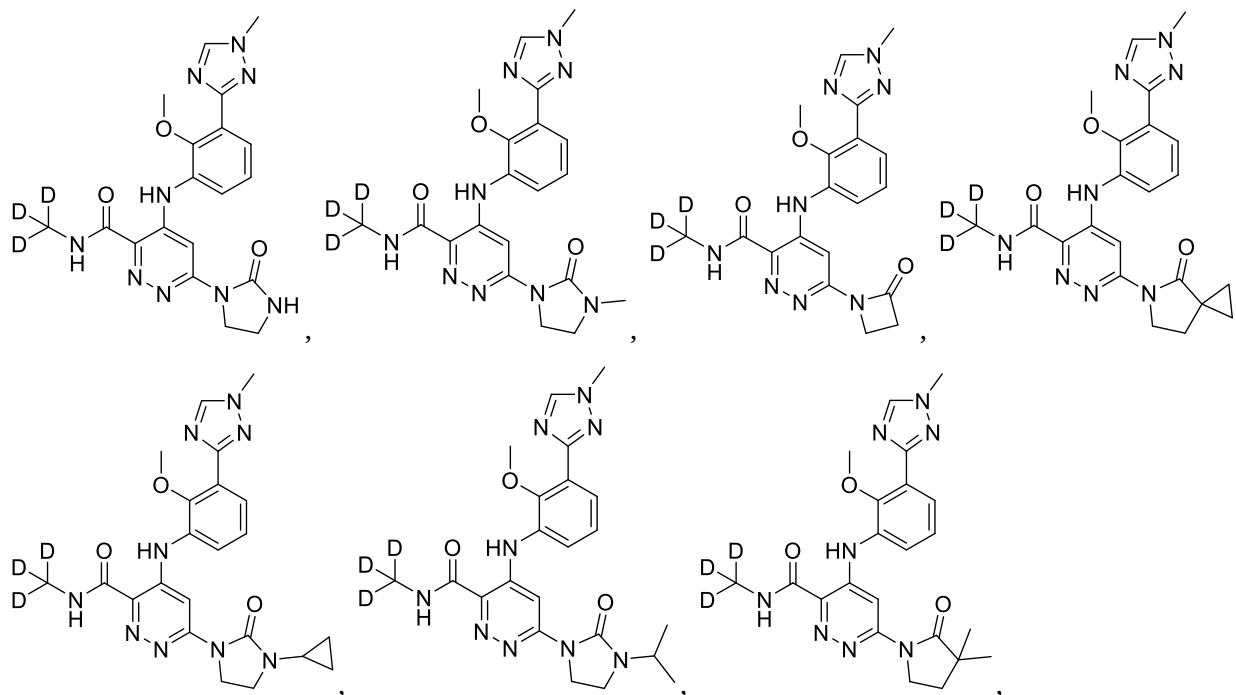
or R⁸ and R⁹ are taken together with the atoms to which they are attached to form a heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

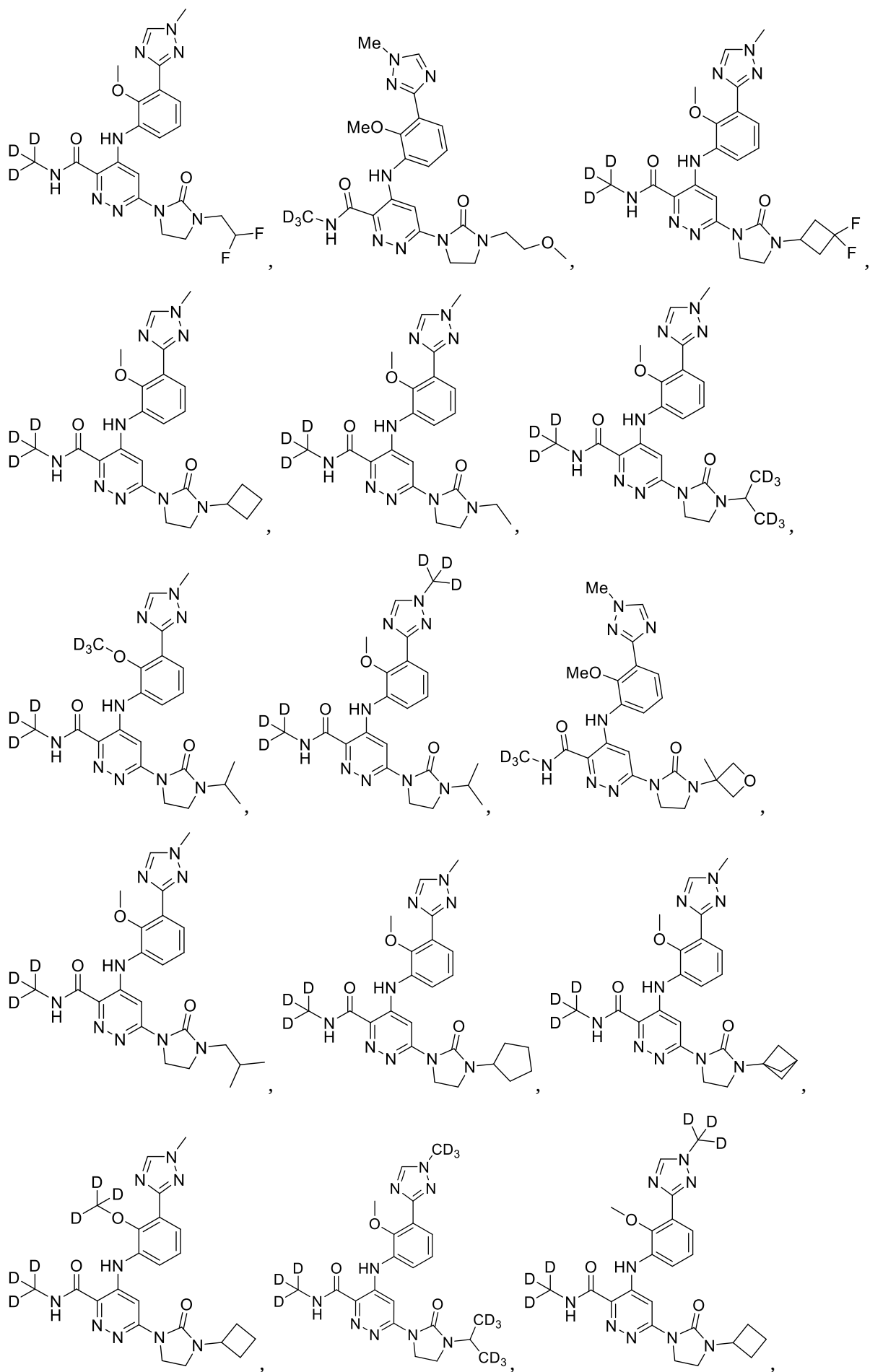
R¹¹ is C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more R^{11a};

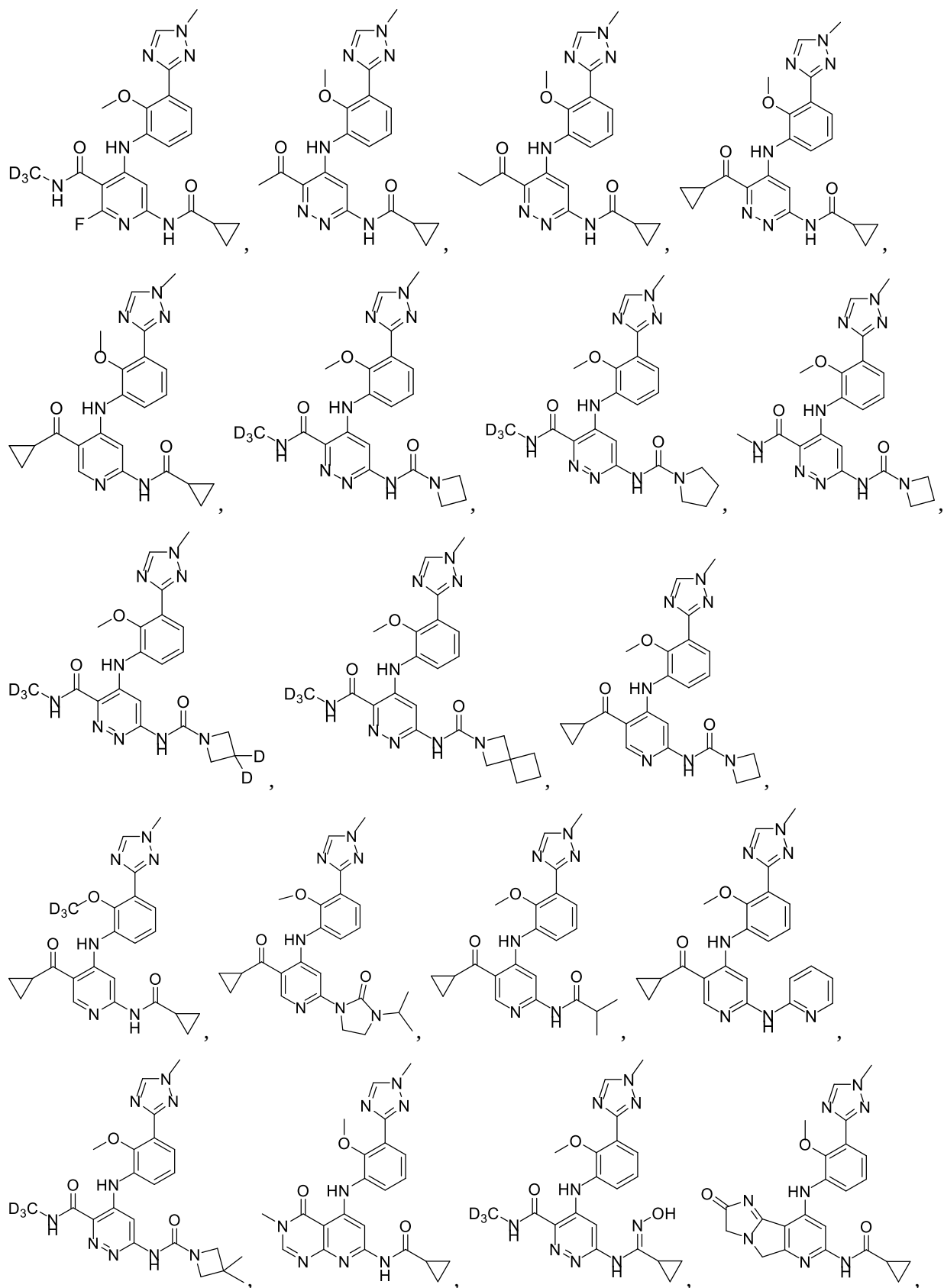
each R^{11a} is independently deuterium, halogen, -CN, -OR^b, -SR^b, -S(=O)R^a, -S(=O)₂R^a, -NO₂, -NR^cR^d, -NHS(=O)₂R^a, -S(=O)₂NR^cR^d, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -C(=O)NR^cR^d, -

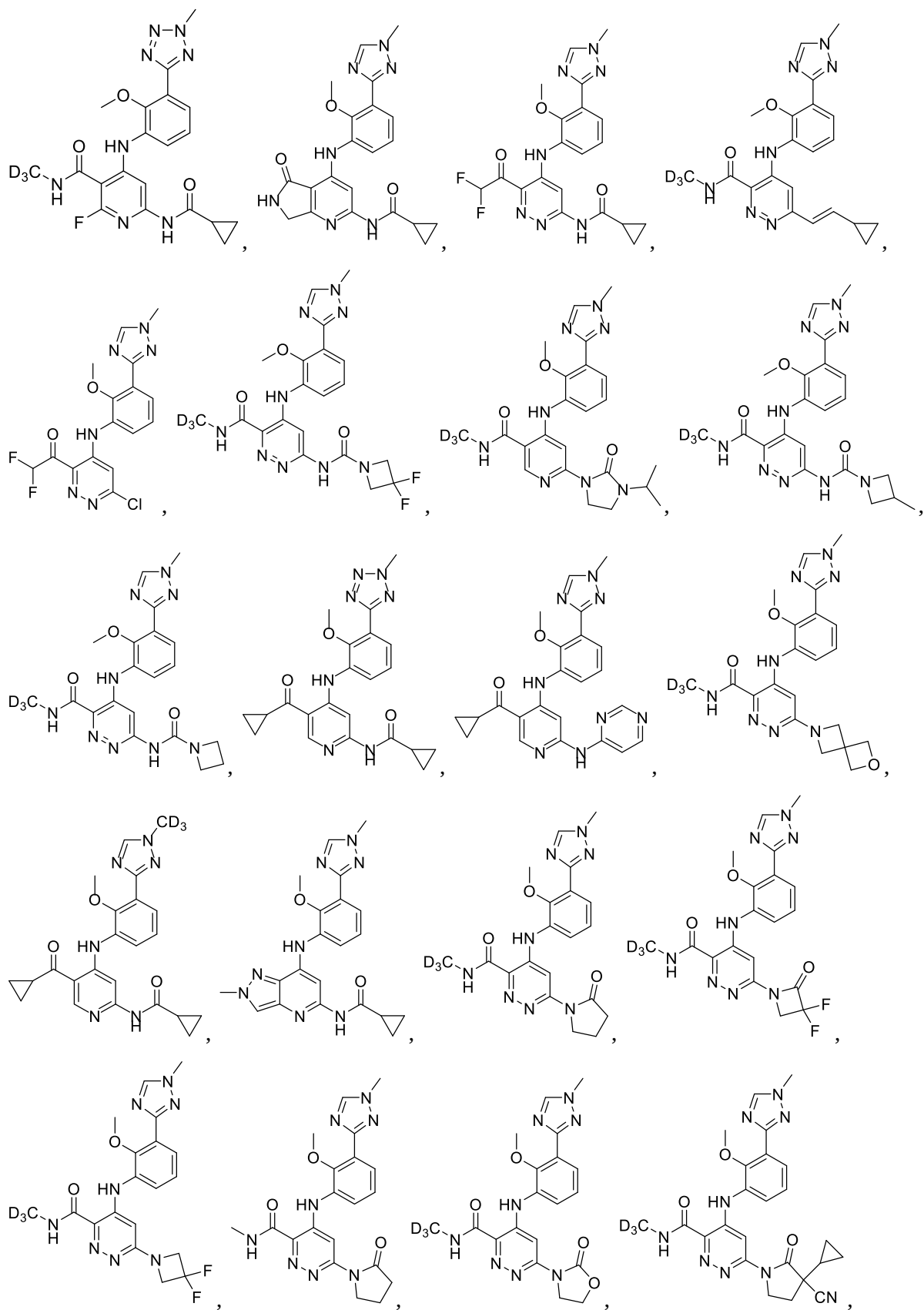
$\text{OC}(=\text{O})\text{NR}^{\text{c}}\text{R}^{\text{d}}$, $-\text{NR}^{\text{b}}\text{C}(=\text{O})\text{NR}^{\text{c}}\text{R}^{\text{d}}$, $-\text{NR}^{\text{b}}\text{C}(=\text{O})\text{R}^{\text{a}}$, $-\text{NR}^{\text{b}}\text{C}(=\text{O})\text{OR}^{\text{b}}$, $\text{C}_1\text{-C}_6\text{alkyl}$, $\text{C}_1\text{-C}_6\text{haloalkyl}$, $\text{C}_1\text{-C}_6\text{deuteroalkyl}$, $\text{C}_1\text{-C}_6\text{hydroxyalkyl}$, $\text{C}_1\text{-C}_6\text{aminoalkyl}$, $\text{C}_2\text{-C}_6\text{alkenyl}$, or $\text{C}_2\text{-C}_6\text{alkynyl}$;
 each R^{a} is independently $\text{C}_1\text{-C}_6\text{alkyl}$, $\text{C}_1\text{-C}_6\text{haloalkyl}$, $\text{C}_1\text{-C}_6\text{deuteroalkyl}$, $\text{C}_1\text{-C}_6\text{hydroxyalkyl}$, $\text{C}_1\text{-C}_6\text{aminoalkyl}$, $\text{C}_2\text{-C}_6\text{alkenyl}$, $\text{C}_2\text{-C}_6\text{alkynyl}$, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;
 wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, $-\text{CN}$, $-\text{OH}$, $-\text{OMe}$, $-\text{NH}_2$, $-\text{C}(=\text{O})\text{Me}$, $-\text{C}(=\text{O})\text{OH}$, $-\text{C}(=\text{O})\text{OMe}$, $\text{C}_1\text{-C}_6\text{alkyl}$, or $\text{C}_1\text{-C}_6\text{haloalkyl}$;
 each R^{b} is independently hydrogen, $\text{C}_1\text{-C}_6\text{alkyl}$, $\text{C}_1\text{-C}_6\text{haloalkyl}$, $\text{C}_1\text{-C}_6\text{deuteroalkyl}$, $\text{C}_1\text{-C}_6\text{hydroxyalkyl}$, $\text{C}_1\text{-C}_6\text{aminoalkyl}$, $\text{C}_2\text{-C}_6\text{alkenyl}$, $\text{C}_2\text{-C}_6\text{alkynyl}$, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;
 wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, $-\text{CN}$, $-\text{OH}$, $-\text{OMe}$, $-\text{NH}_2$, $-\text{C}(=\text{O})\text{Me}$, $-\text{C}(=\text{O})\text{OH}$, $-\text{C}(=\text{O})\text{OMe}$, $\text{C}_1\text{-C}_6\text{alkyl}$, or $\text{C}_1\text{-C}_6\text{haloalkyl}$;
 each R^{c} and R^{d} is independently hydrogen, $\text{C}_1\text{-C}_6\text{alkyl}$, $\text{C}_1\text{-C}_6\text{haloalkyl}$, $\text{C}_1\text{-C}_6\text{deuteroalkyl}$, $\text{C}_1\text{-C}_6\text{hydroxyalkyl}$, $\text{C}_1\text{-C}_6\text{aminoalkyl}$, $\text{C}_2\text{-C}_6\text{alkenyl}$, $\text{C}_2\text{-C}_6\text{alkynyl}$, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, $-\text{CN}$, $-\text{OH}$, $-\text{OMe}$, $-\text{NH}_2$, $-\text{C}(=\text{O})\text{Me}$, $-\text{C}(=\text{O})\text{OH}$, $-\text{C}(=\text{O})\text{OMe}$, $\text{C}_1\text{-C}_6\text{alkyl}$, or $\text{C}_1\text{-C}_6\text{haloalkyl}$;
 or R^{c} and R^{d} are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, $-\text{CN}$, $-\text{OH}$, $-\text{OMe}$, $-\text{NH}_2$, $-\text{C}(=\text{O})\text{Me}$, $-\text{C}(=\text{O})\text{OH}$, $-\text{C}(=\text{O})\text{OMe}$, $\text{C}_1\text{-C}_6\text{alkyl}$, or $\text{C}_1\text{-C}_6\text{haloalkyl}$.

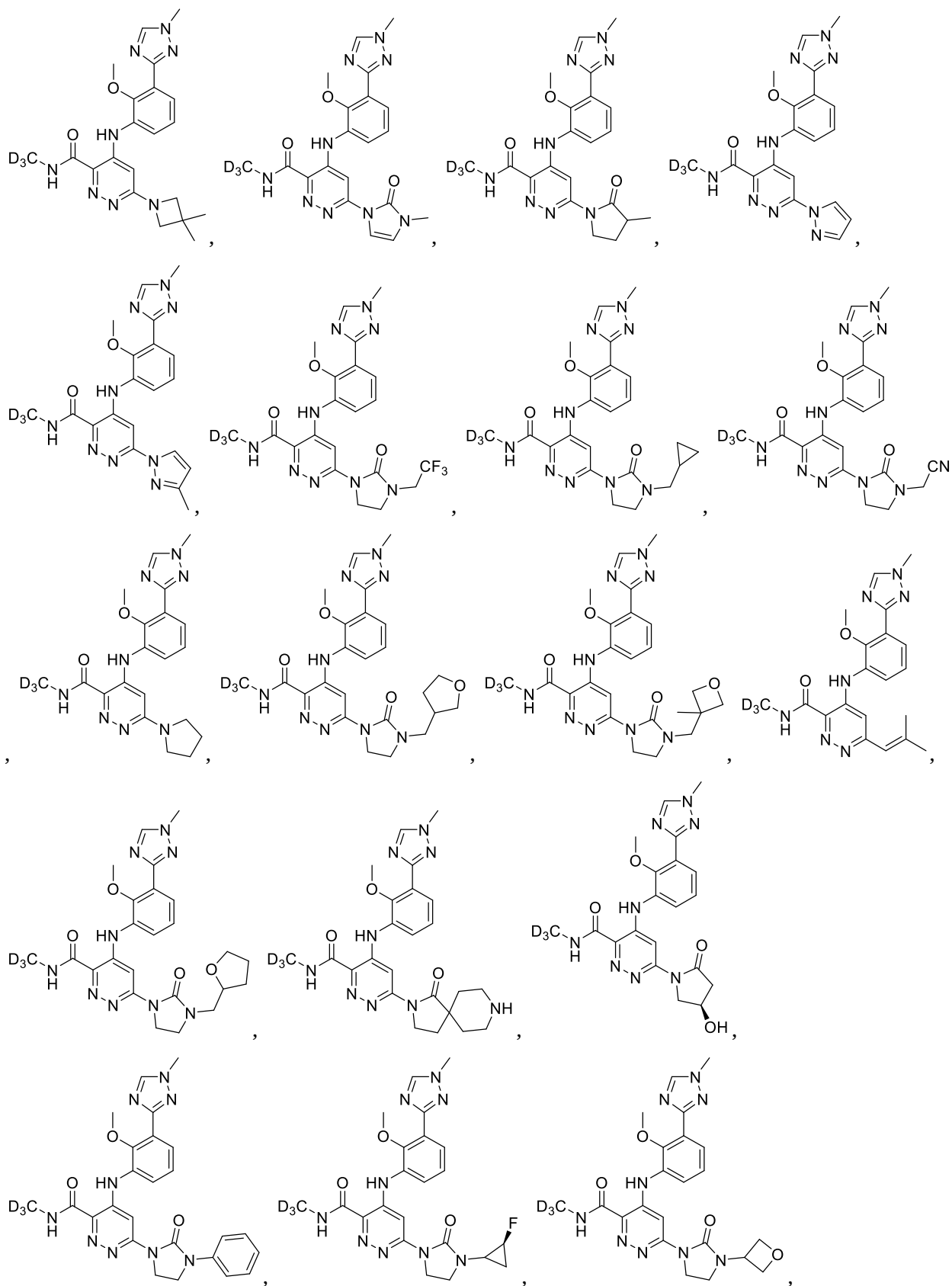
[0015c] In a further aspect of the present disclosure, there is provided a compound, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, selected from:

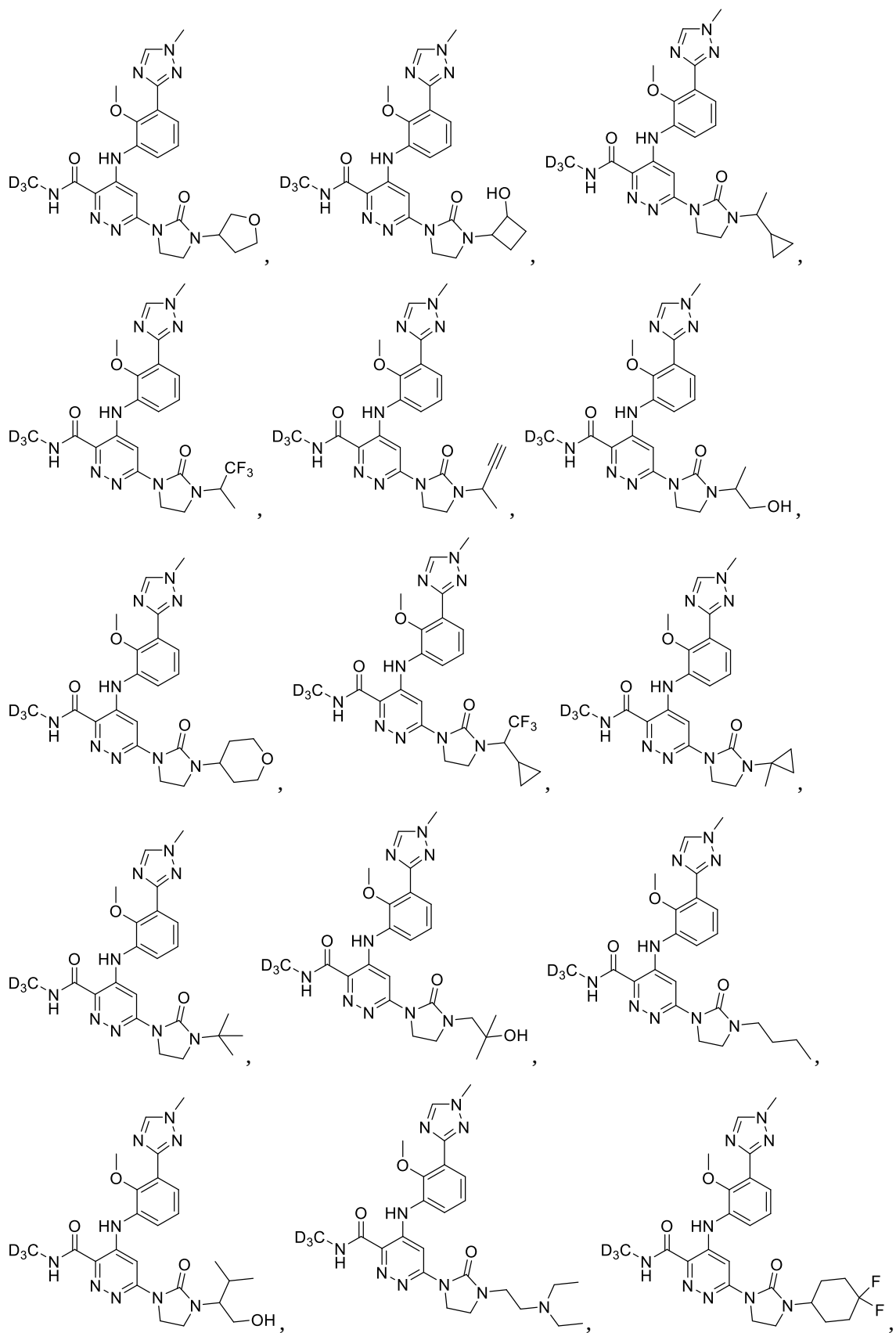


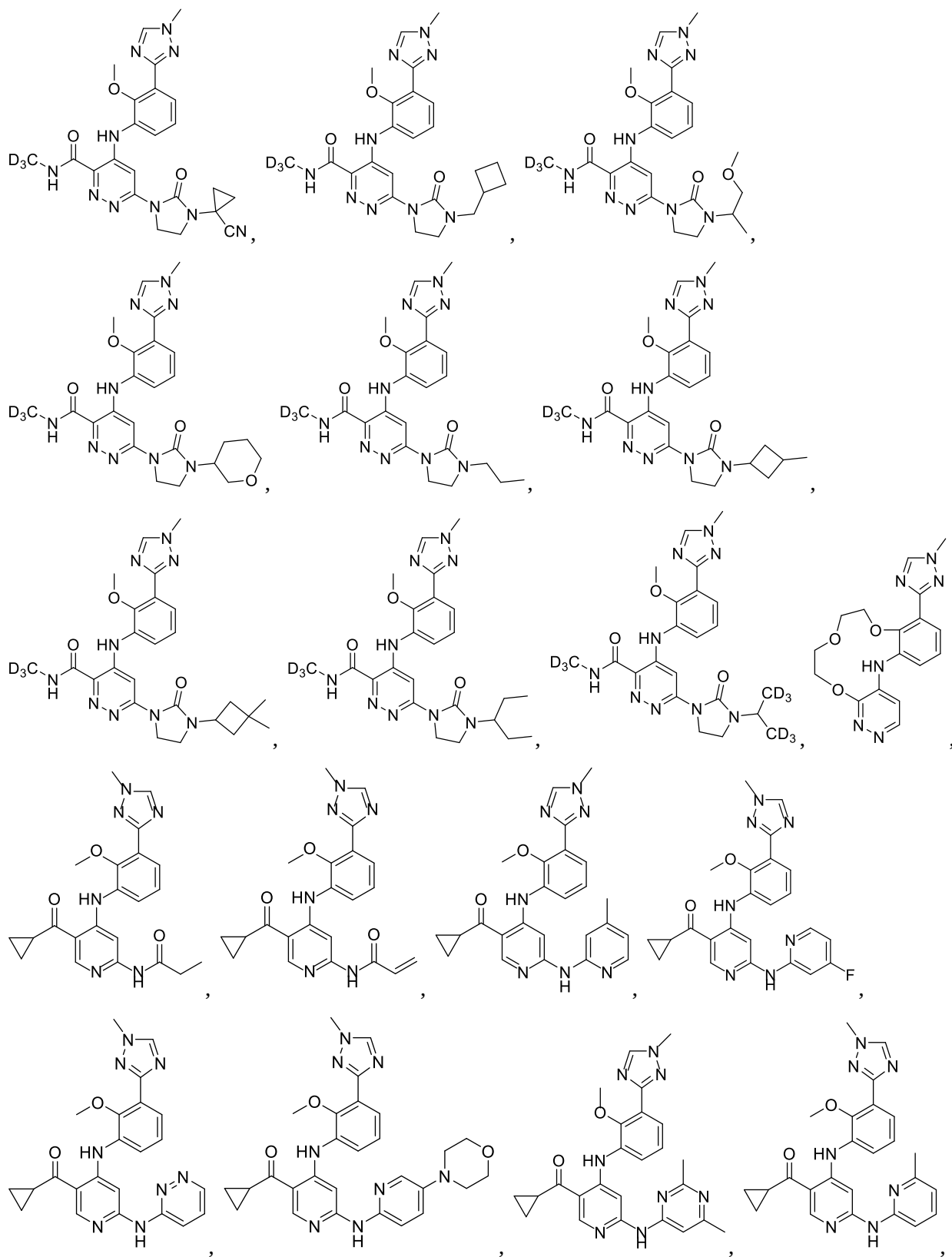


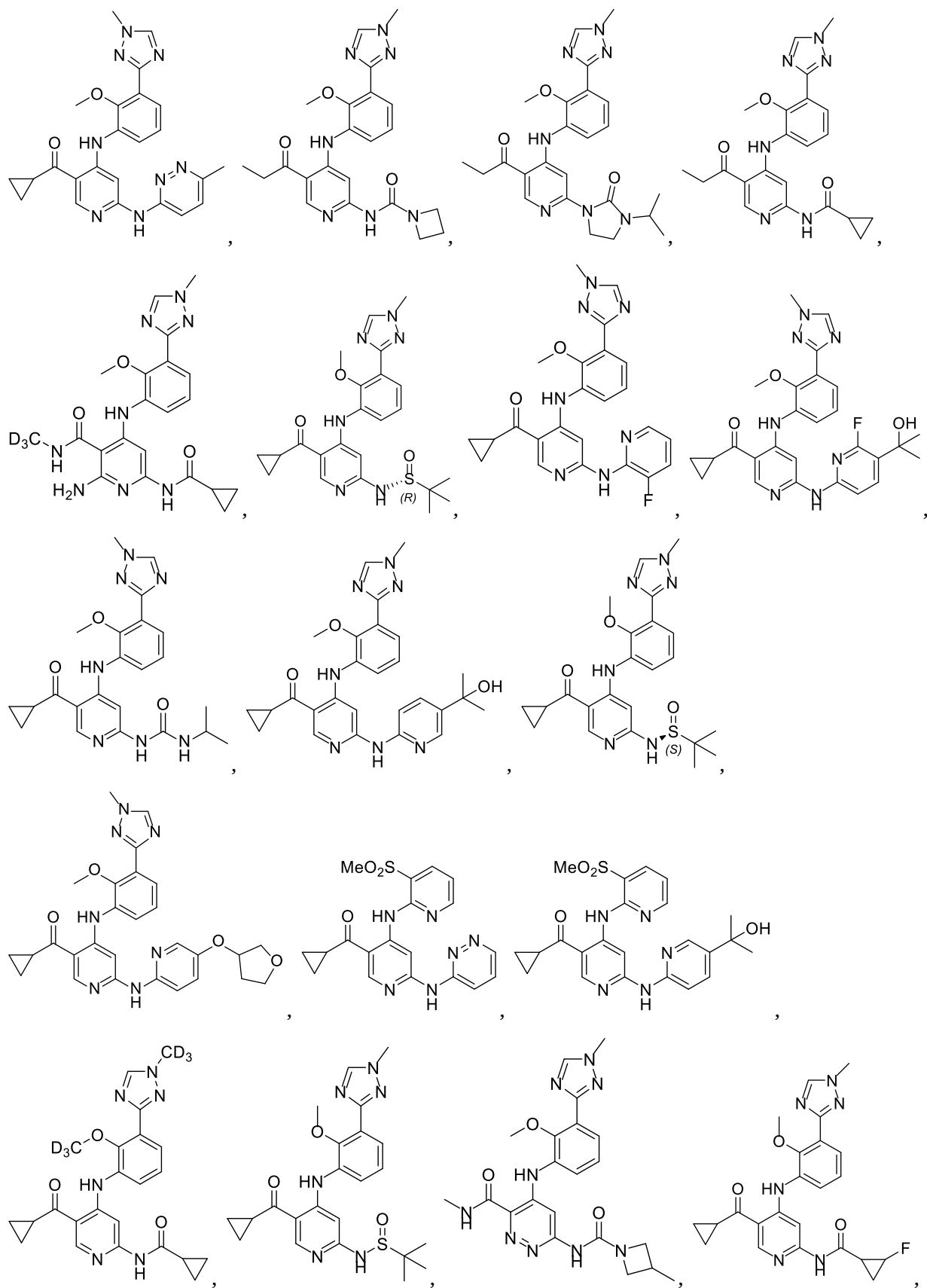


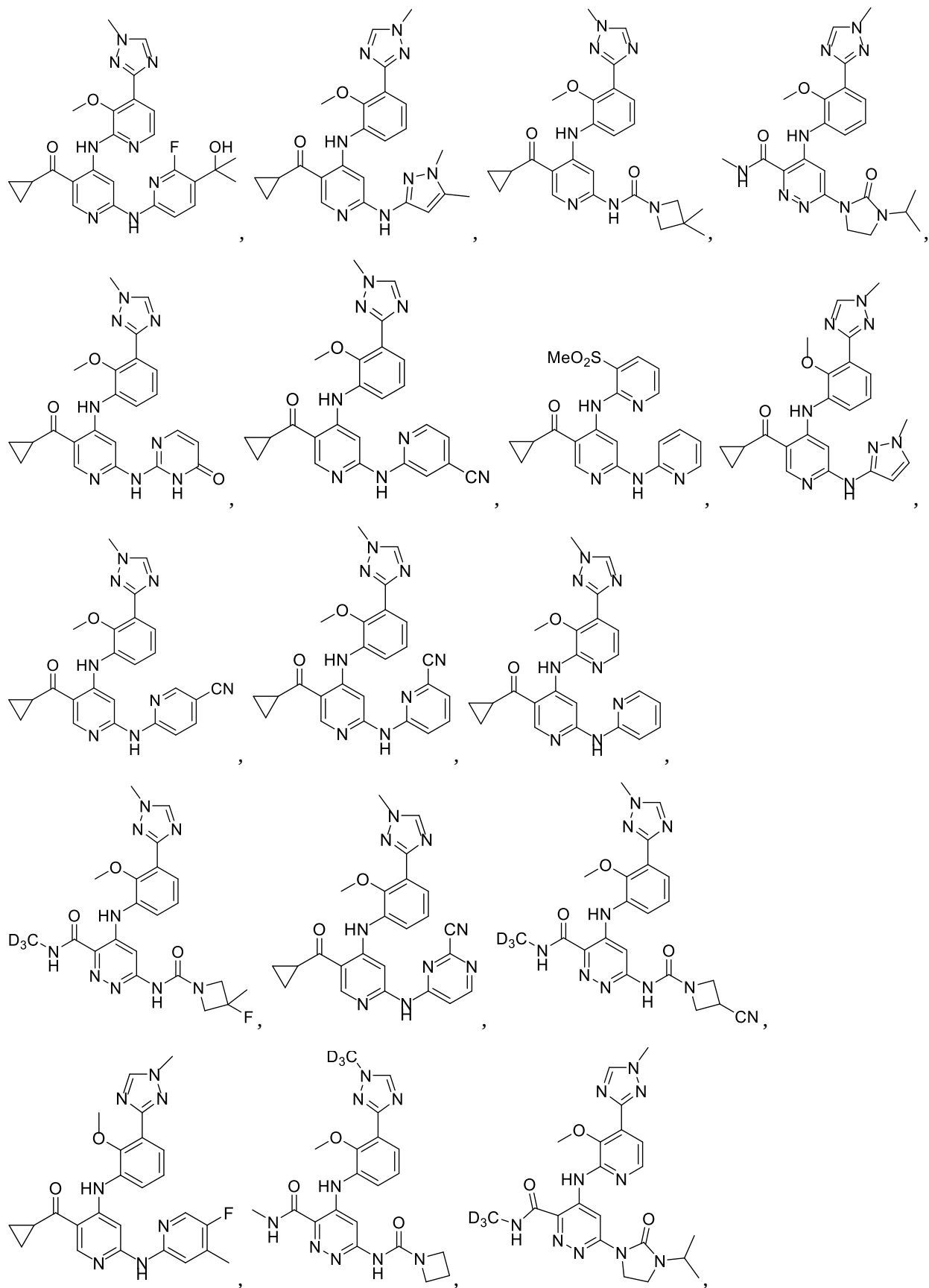


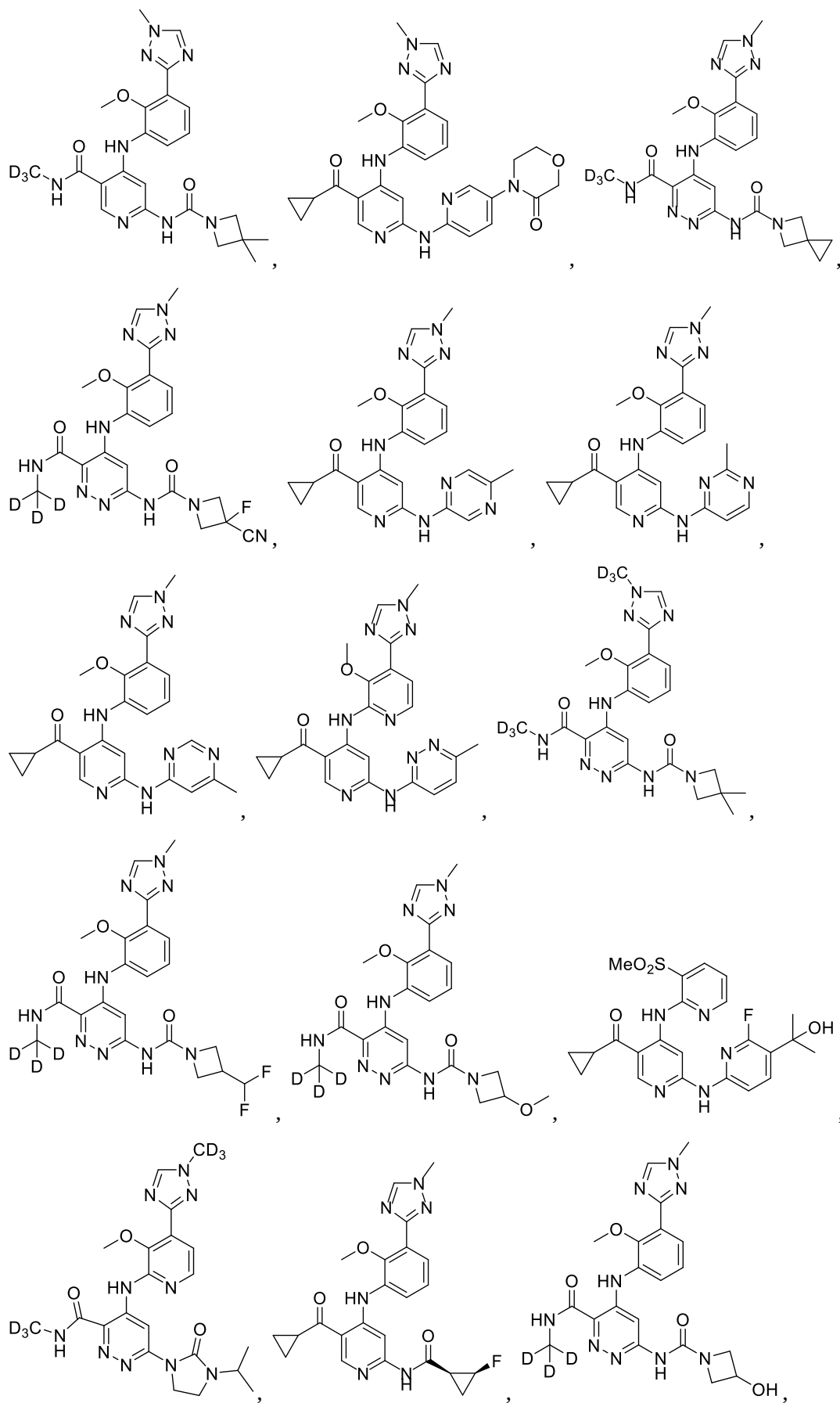


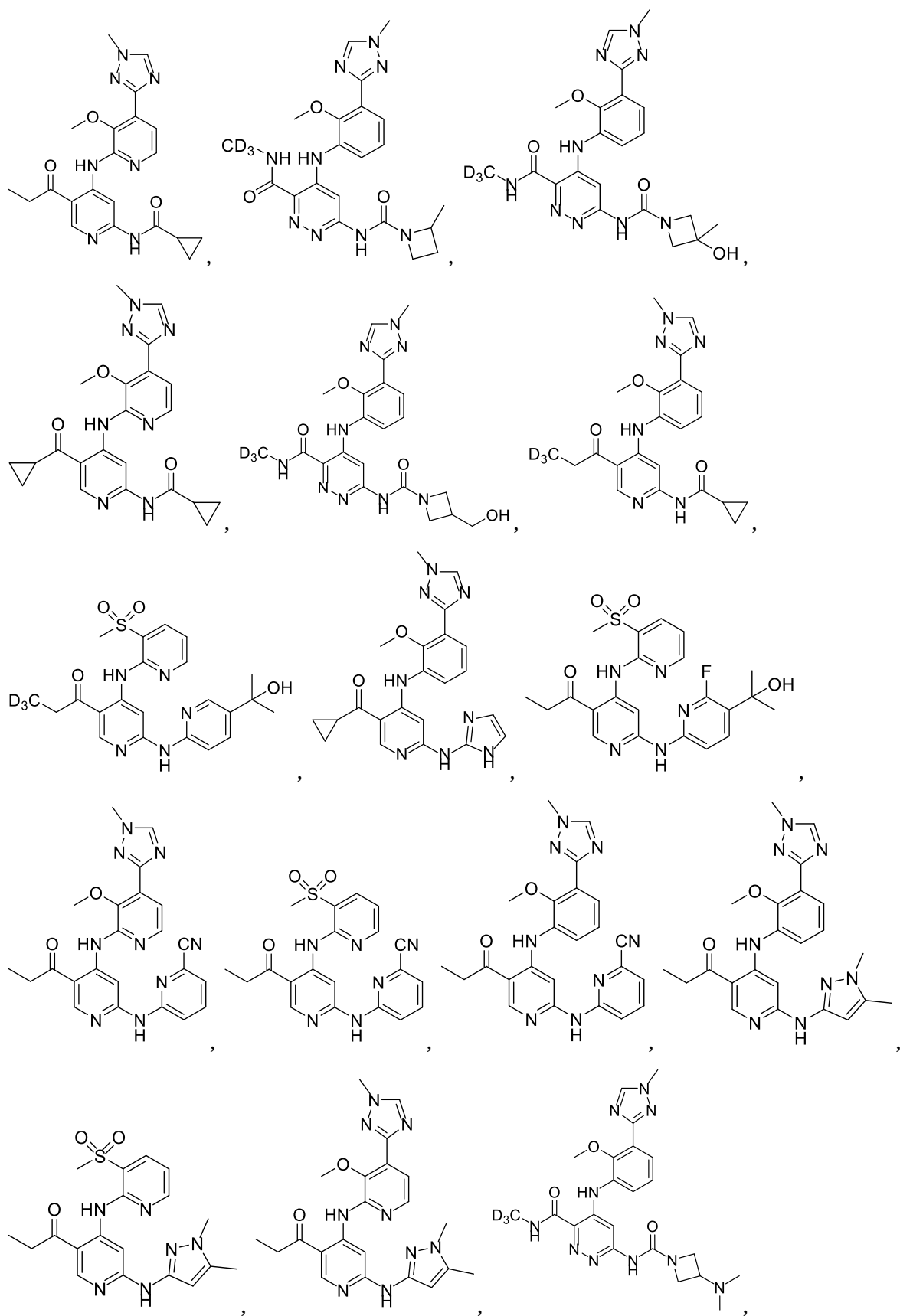


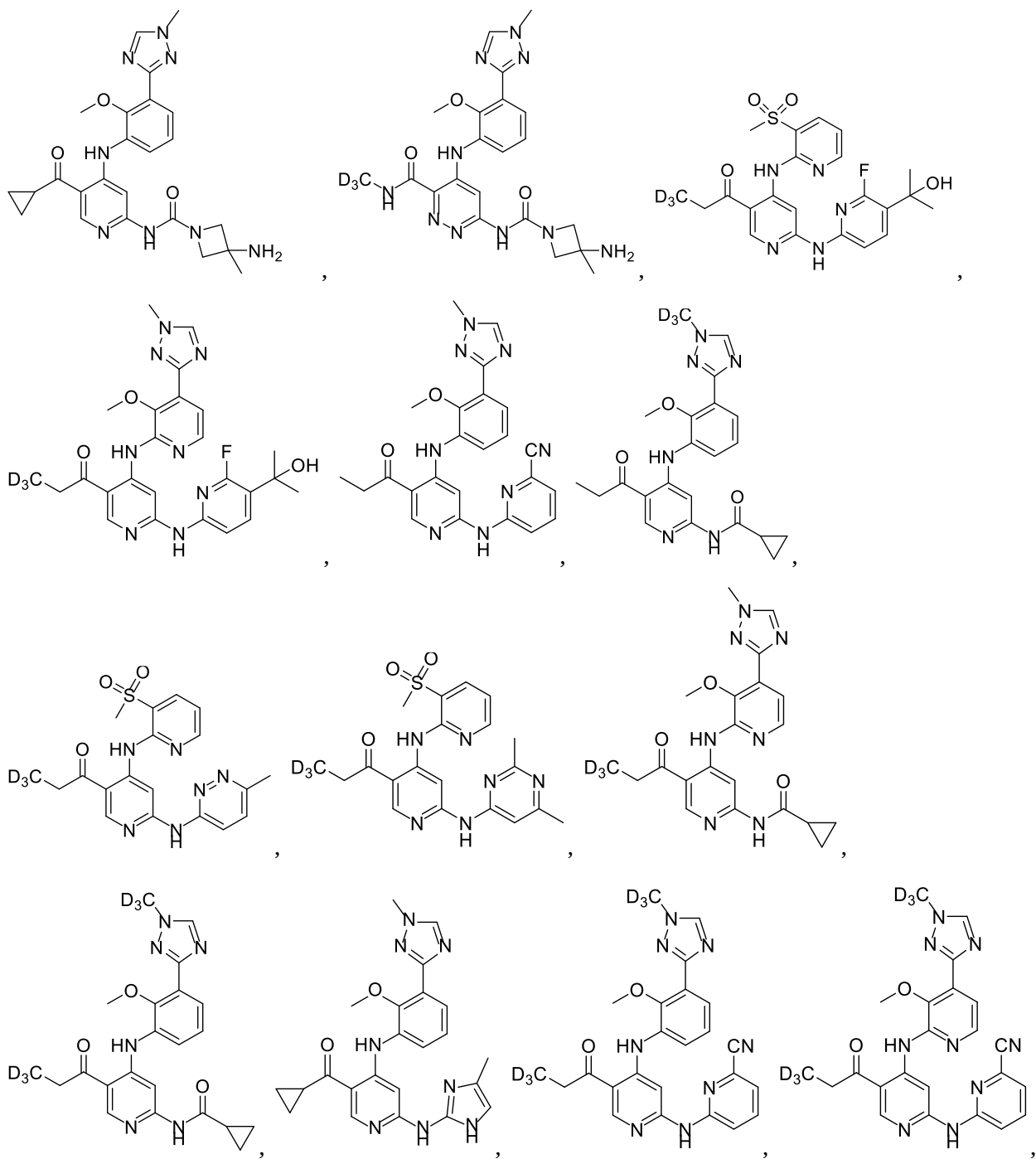


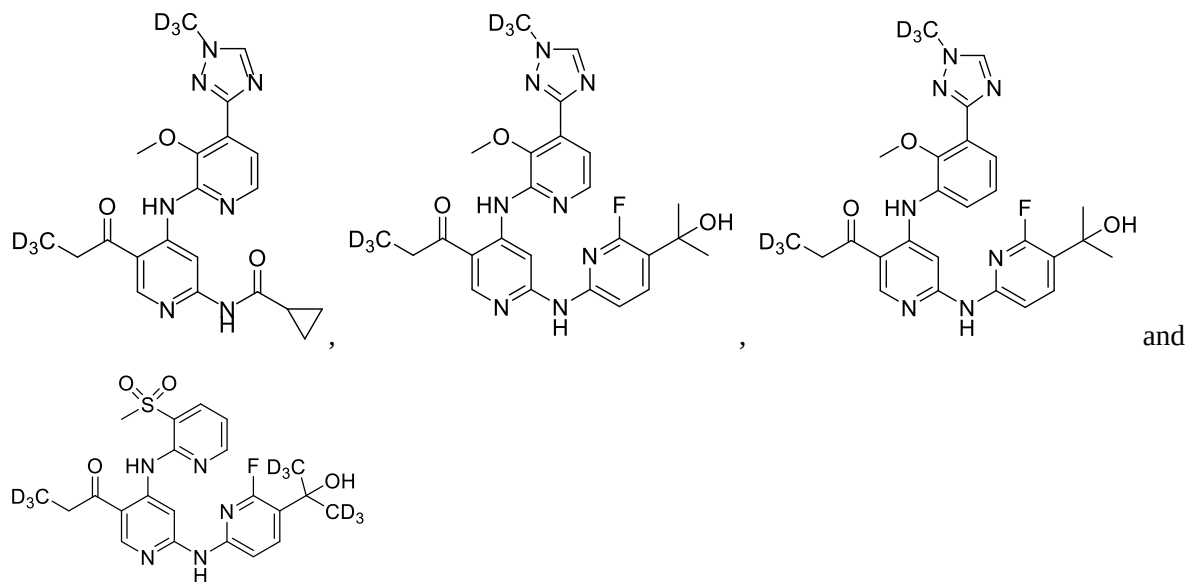




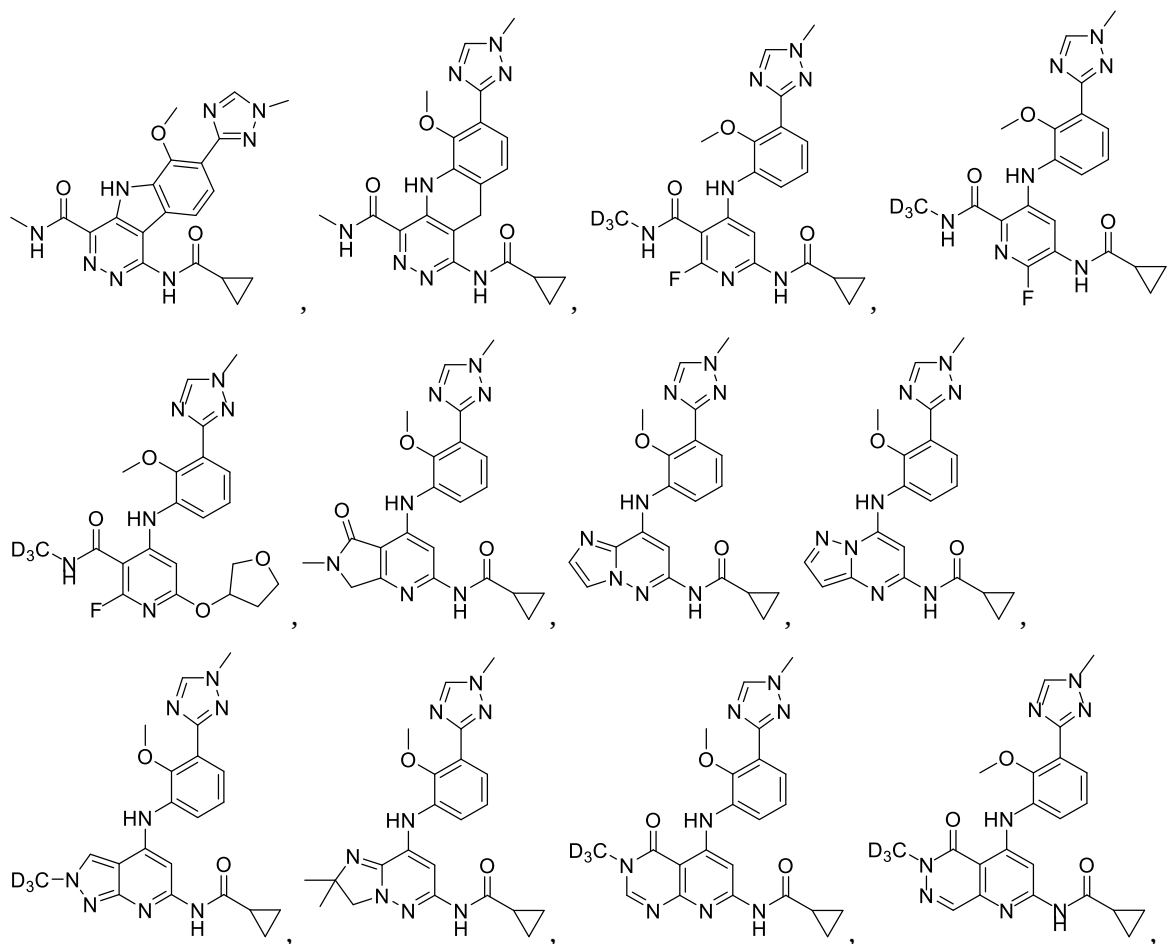




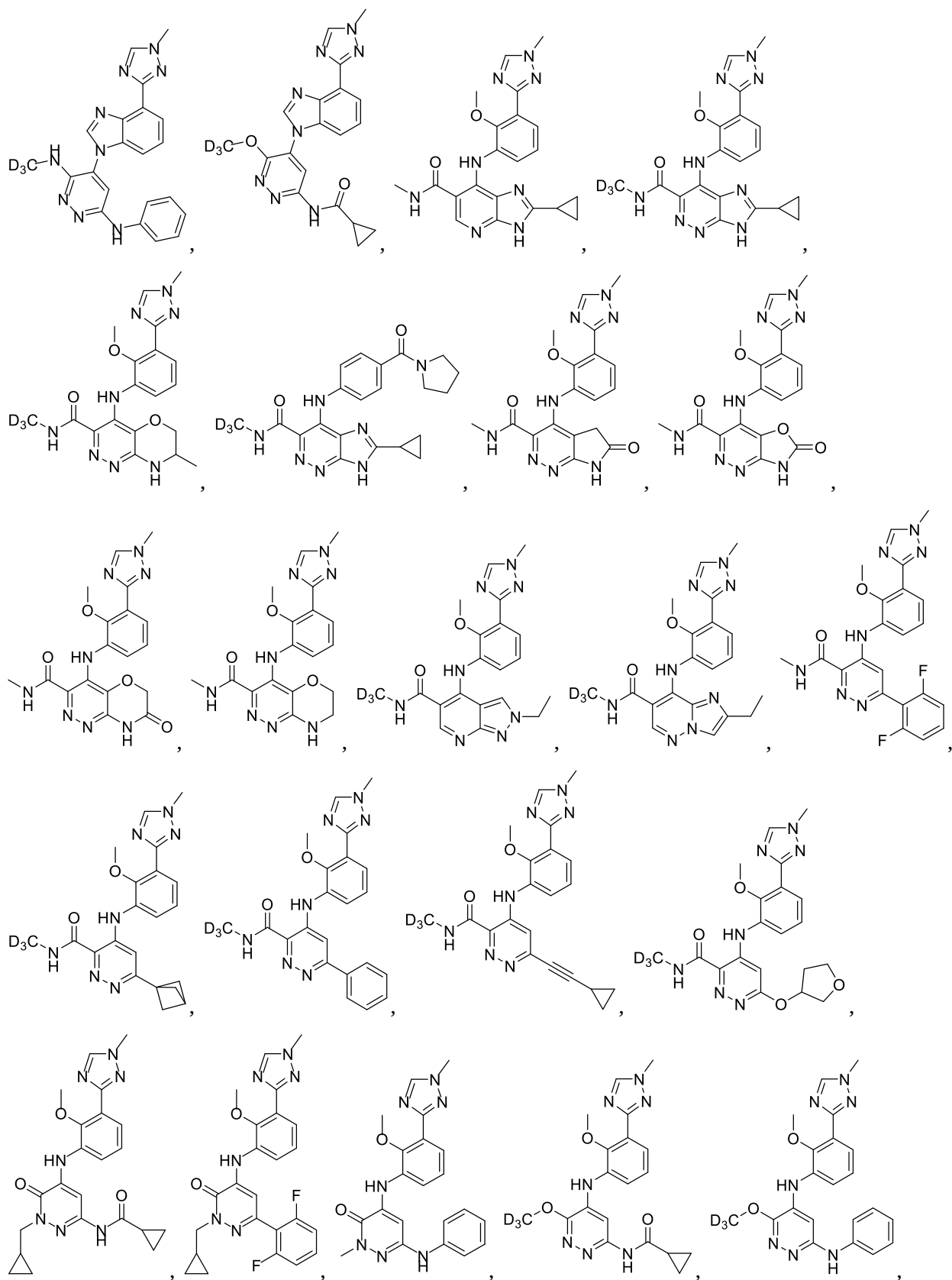


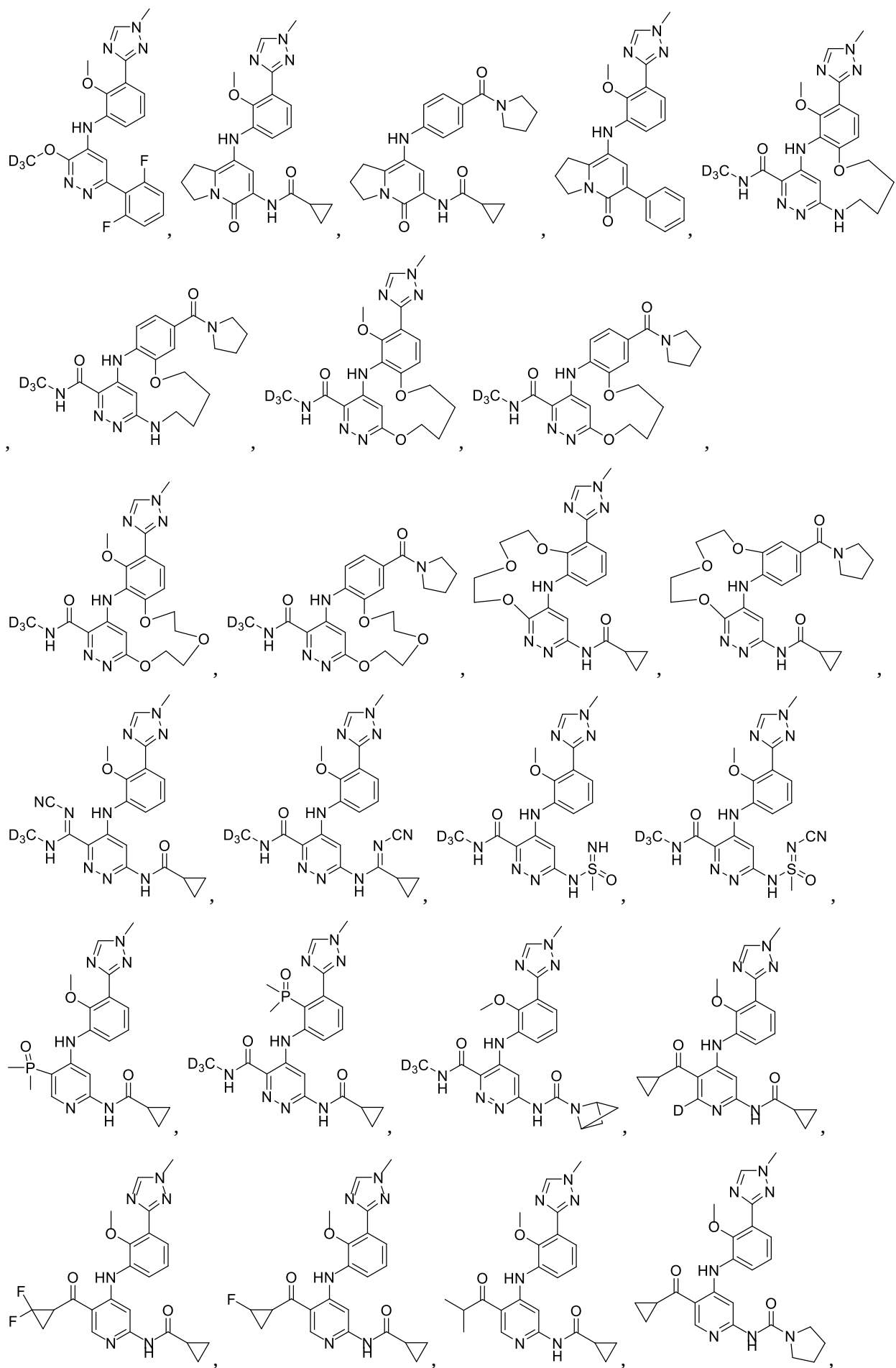


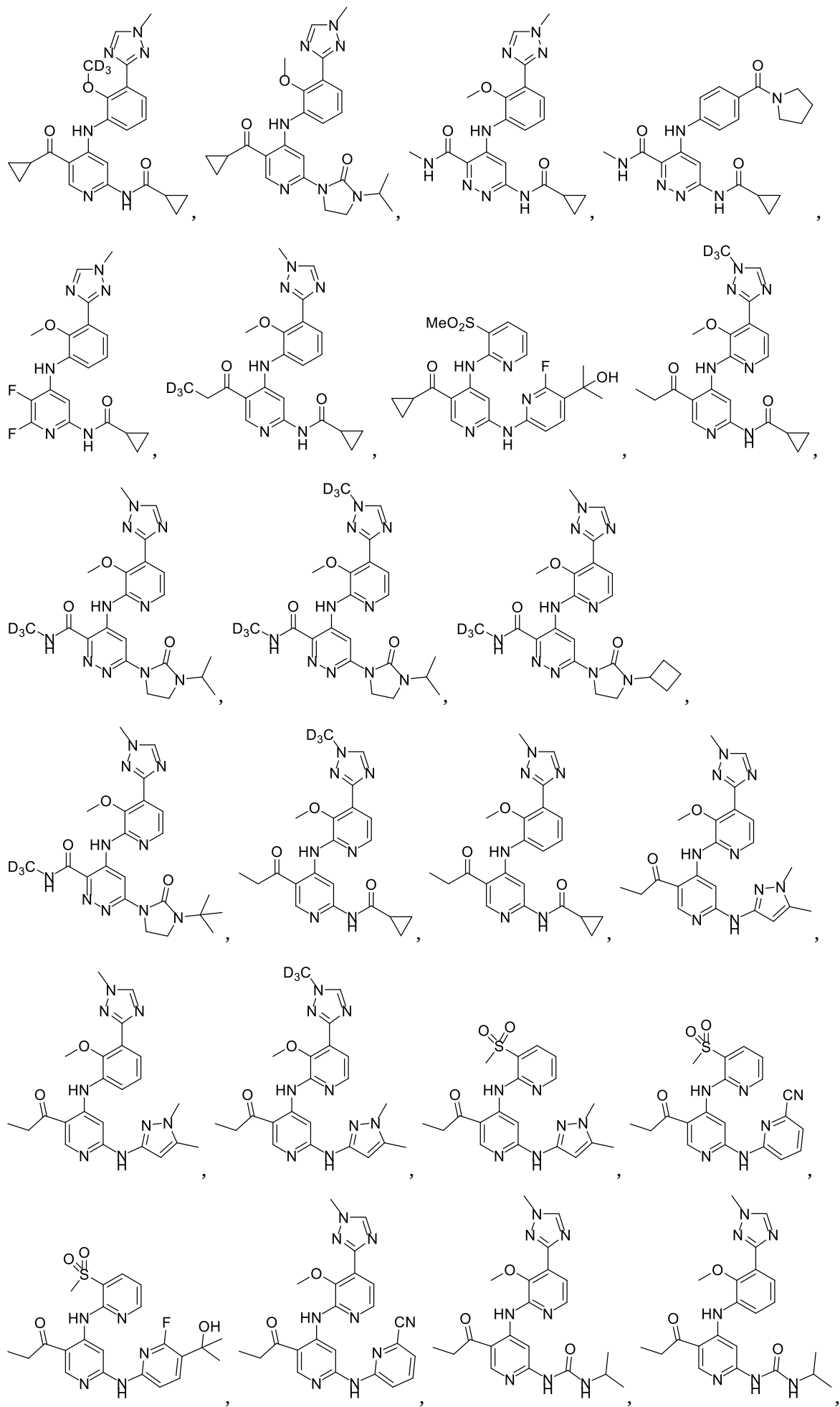
[0015d] In another aspect of the present disclosure, there is provided a compound, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, selected from:

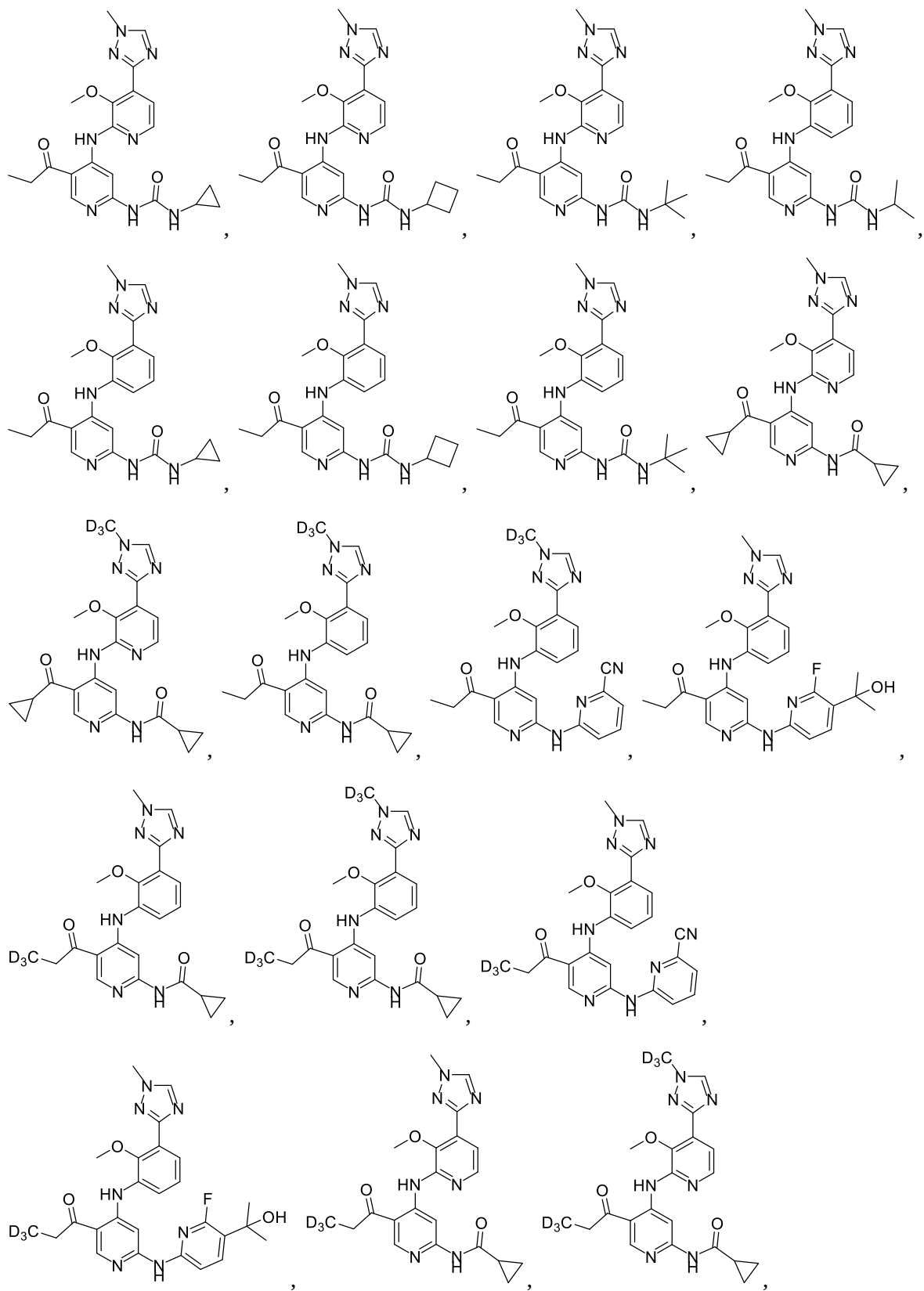


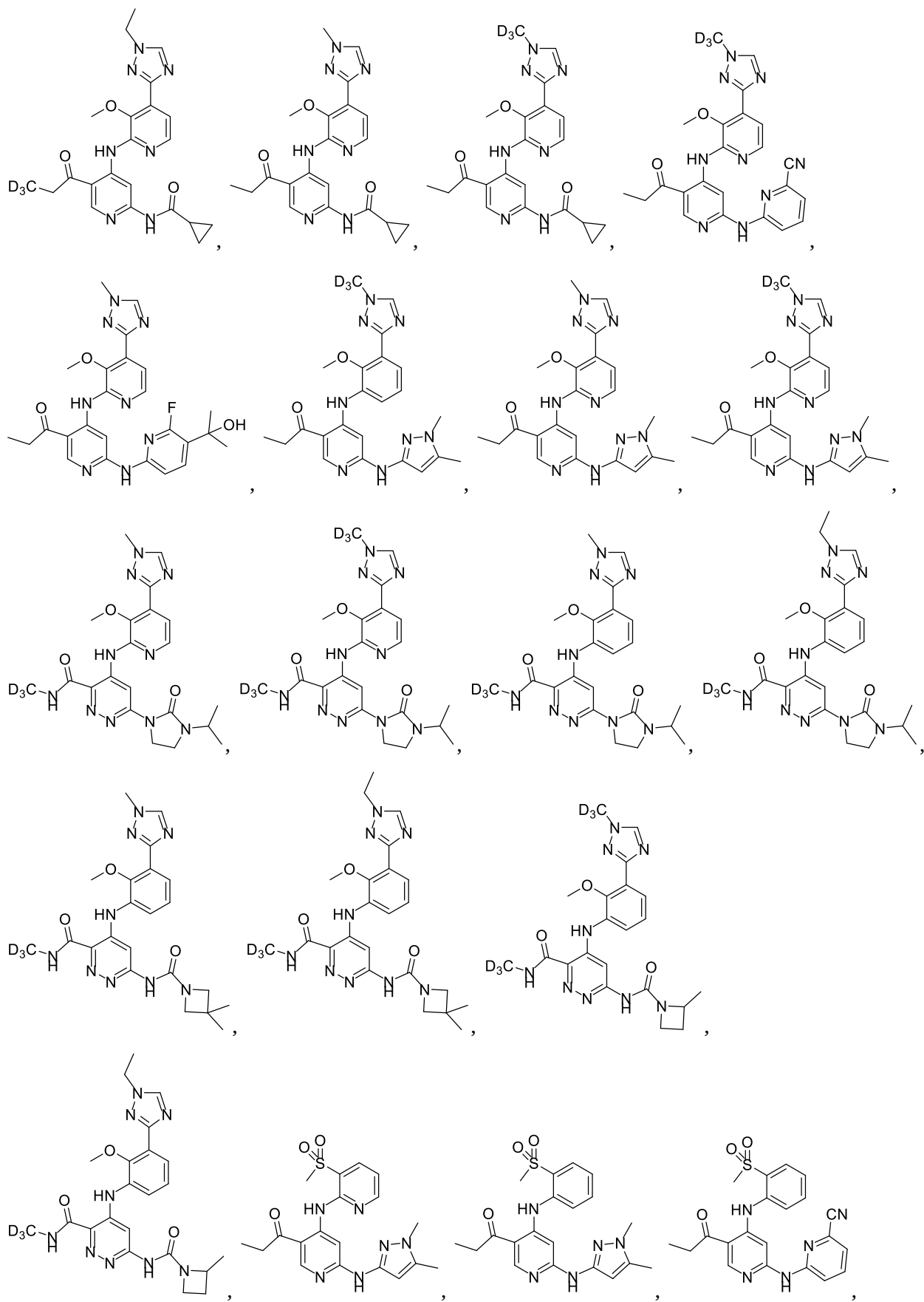


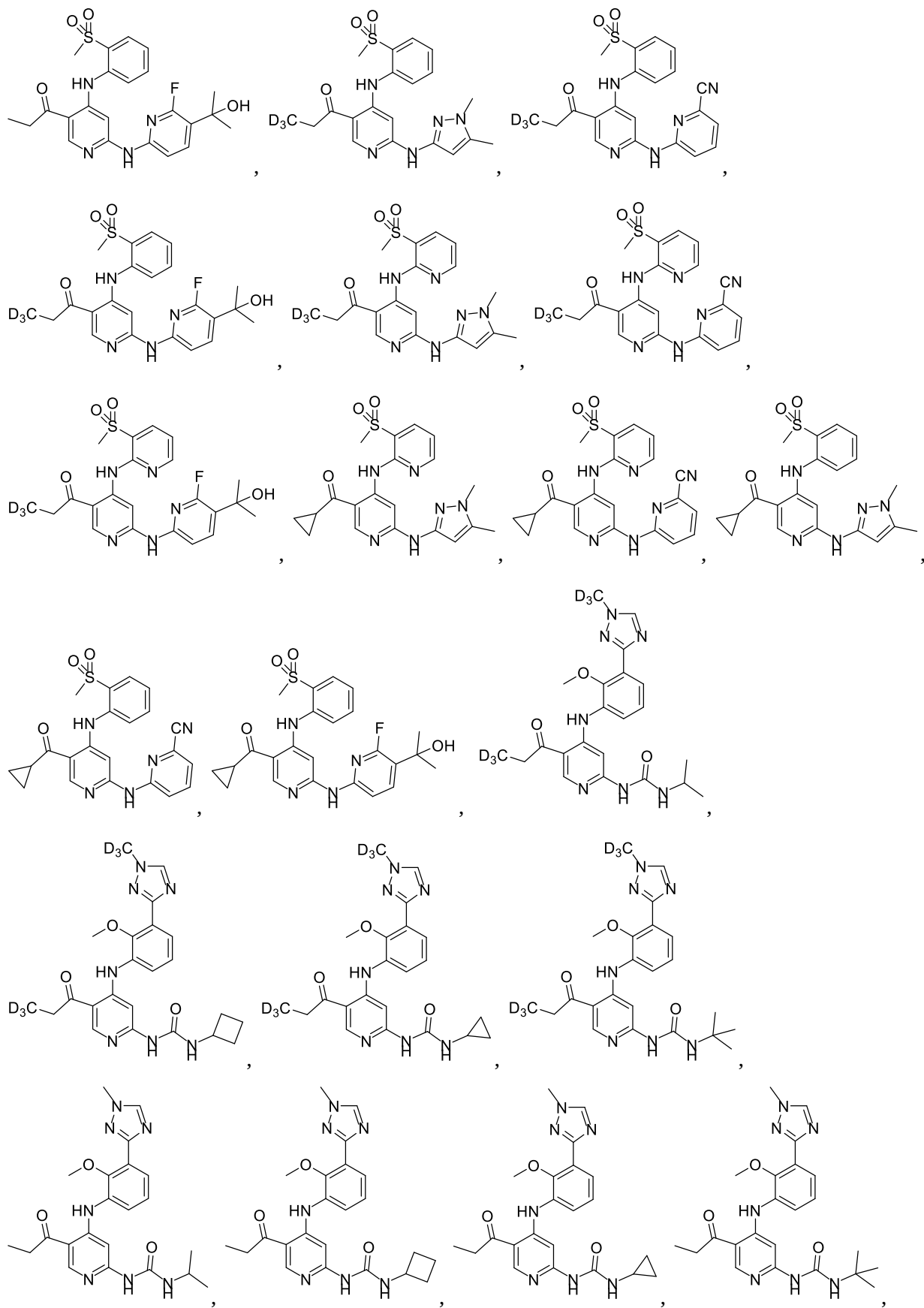


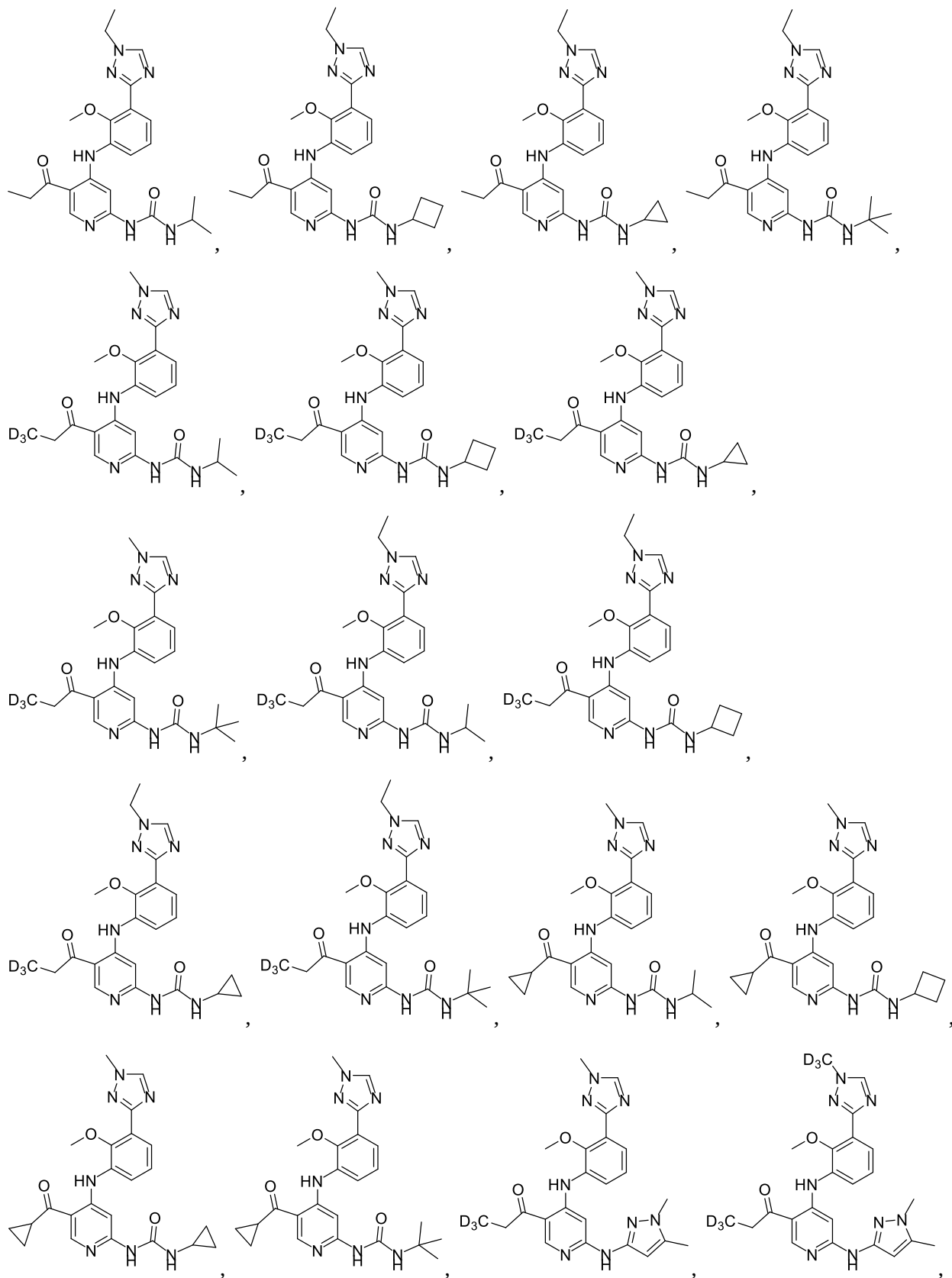


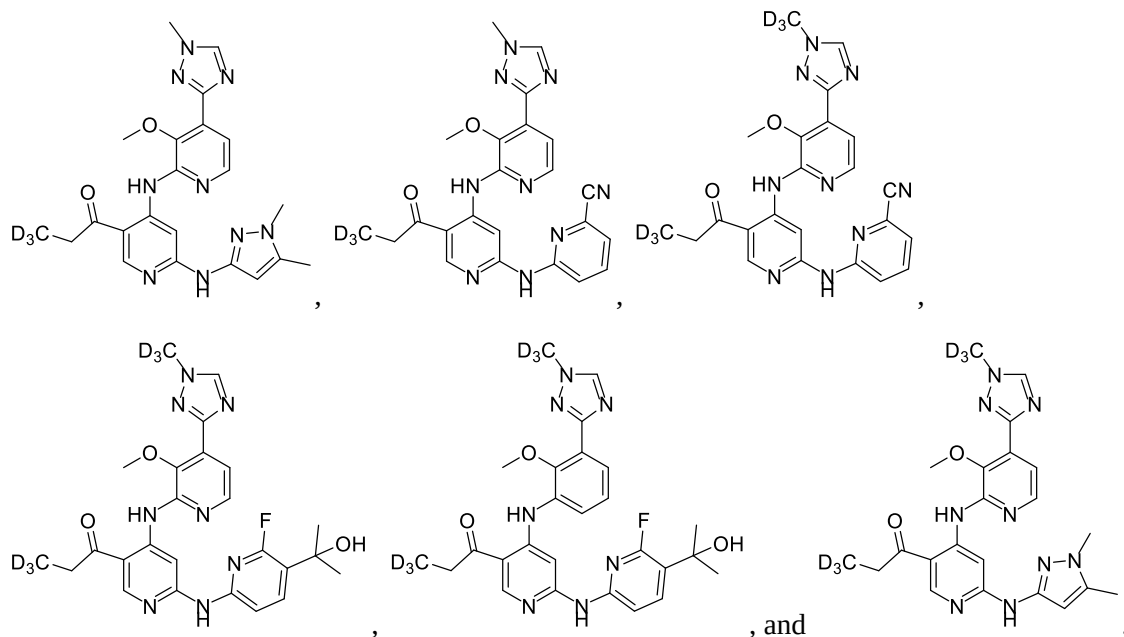












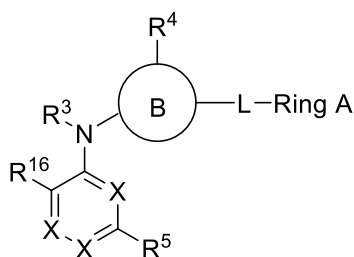
[0015e] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising a therapeutically effective amount of the compound, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof disclosed herein, and a pharmaceutically acceptable excipient.

[0015f] In another aspect of the present disclosure, there is provided a compound, or a pharmaceutically acceptable salt, stereoisomer or solvate thereof disclosed herein, for use in inhibiting a TYK2 enzyme in a patient or biological sample, or for use in treating a TYK2-mediated disorder.

[0015g] In a further aspect of the present disclosure, there is provided a use of a compound, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof disclosed herein, in the manufacture of a medicament for inhibiting a TYK2 enzyme in a patient or biological sample.

[0015h] In another aspect of the present disclosure, there is provided a use of a compound, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof disclosed herein, in the manufacture of a medicament for treating a TYK2-mediated disorder.

[0016] Disclosed herein is a compound of Formula (XII), or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof:



Formula (XII),

wherein:

Ring B is cycloalkyl, heterocycloalkyl, aryl, heteroaryl;

R^{16} is $-C(=O)NR^1R^2$, $-C(=N-CN)NR^1R^2$, $-P(=O)R^1R^2$, or $-C(=O)R^{11}$;

R^1 and R^2 are independently hydrogen, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_1 - C_6 deuteroalkyl,

C_1 - C_6 hydroxyalkyl, C_1 - C_6 aminoalkyl, C_2 - C_6 alkenyl, or C_2 - C_6 alkynyl;

R³ is hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, or C₁-C₆deuteroalkyl;

R⁴ is hydrogen, deuterium, halogen, -CN, -OR^b, -SR^b, -S(=O)R^a, -S(=O)₂R^a, -NO₂, -NR^cR^d, -NHS(=O)₂R^a, -S(=O)₂NR^cR^d, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -C(=O)NR^cR^d, -OC(=O)NR^cR^d, -NR^bC(=O)NR^cR^d, -NR^bC(=O)R^a, -NR^bC(=O)OR^b, -P(=O)R^bR^b, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, or C₂-C₆alkynyl;

or R³ and R⁴ are taken together to form an optionally substituted ring;

L is a bond or -C(=O)-;

Ring A is cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; each optionally substituted with one or more R^A;

each R^A is independently deuterium, halogen, -CN, -OR^b, -SR^b, -S(=O)R^a, -S(=O)₂R^a, -NO₂, -NR^cR^d, -NHS(=O)₂R^a, -S(=O)₂NR^cR^d, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -C(=O)NR^cR^d, -OC(=O)NR^cR^d, -NR^bC(=O)NR^cR^d, -NR^bC(=O)R^a, -NR^bC(=O)OR^b, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, C₁-C₆alkyl, or C₁-C₆haloalkyl;

or two R^A on the same carbon are taken together to form an oxo;

or -L-Ring A is absent;

each R^{11a} is independently deuterium, halogen, -CN, -OR^b, -SR^b, -S(=O)R^a, -S(=O)₂R^a, -NO₂, -NR^cR^d, -NHS(=O)₂R^a, -S(=O)₂NR^cR^d, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -C(=O)NR^cR^d, -OC(=O)NR^cR^d, -NR^bC(=O)NR^cR^d, -NR^bC(=O)R^a, -NR^bC(=O)OR^b, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, or C₂-C₆alkynyl;

each R^a is independently C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

each R^b is independently hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

each R^c and R^d is independently hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

or R^c and R^d are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl.

[0018] Also disclosed herein is a pharmaceutical composition comprising a therapeutically effective amount of the compound disclosed herein, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, and a pharmaceutically acceptable excipient.

[0019] Also disclosed herein is a method of inhibiting a TYK2 enzyme in a patient or biological sample comprising contacting said patient or biological sample with a compound disclosed herein, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof.

[0020] Also disclosed herein is a method of treating a TYK2-mediated disorder comprising administering to a patient in need thereof a compound disclosed herein, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof. In some examples, the TYK2-mediated disorder is an autoimmune disorder, an inflammatory disorder, a proliferative disorder, an endocrine disorder, a neurological disorder, or a disorder associated with transplantation. In some examples, the disorder is associated with type I interferon, IL-10, IL-12, or IL-23 signaling.

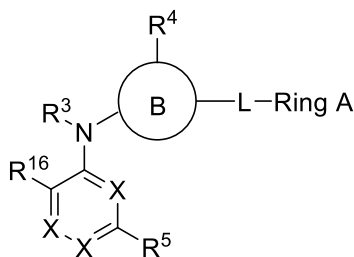
INCORPORATION BY REFERENCE

[0021] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference for the specific purposes identified herein.

CLAIMS

WHAT IS CLAIMED IS:

1. A compound of Formula (XII), or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof:



Formula (XII),

wherein:

Ring B is cycloalkyl, heterocycloalkyl, aryl, heteroaryl;

R¹⁶ is -C(=O)NR¹R², -C(=N-CN)NR¹R², -P(=O)R¹R², or -C(=O)R¹¹;

R¹ and R² are independently hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl,

C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, or C₂-C₆alkynyl;

R³ is hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, or C₁-C₆deuteroalkyl;

R⁴ is hydrogen, deuterium, halogen, -CN, -OR^b, -SR^b, -S(=O)R^a, -S(=O)₂R^a, -NO₂, -NR^cR^d, -

NHS(=O)₂R^a, -S(=O)₂NR^cR^d, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -C(=O)NR^cR^d, -

OC(=O)NR^cR^d, -NR^bC(=O)NR^cR^d, -NR^bC(=O)R^a, -NR^bC(=O)OR^b, -P(=O)R^bR^b, C₁-C₆alkyl,

C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, or C₂-

C₆alkynyl;

or R³ and R⁴ are taken together to form an optionally substituted ring;

L is a bond or -C(=O)-;

Ring A is cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; each optionally substituted with one or more R^A;

each R^A is independently deuterium, halogen, -CN, -OR^b, -SR^b, -S(=O)R^a, -S(=O)₂R^a, -NO₂, -NR^cR^d, -

NHS(=O)₂R^a, -S(=O)₂NR^cR^d, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -C(=O)NR^cR^d, -

OC(=O)NR^cR^d, -NR^bC(=O)NR^cR^d, -NR^bC(=O)R^a, -NR^bC(=O)OR^b, C₁-C₆alkyl, C₁-C₆haloalkyl,

C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl,

heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl,

heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo,

deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, C₁-C₆alkyl, or

C₁-C₆haloalkyl;

or two R^A on the same carbon are taken together to form an oxo;

or -L-Ring A is absent;

each X is independently -CR^x- or -N-;

each R^x is independently hydrogen, deuterium, halogen, -CN, -OR^b, -SR^b, -S(=O)R^a, -S(=O)₂R^a, -NO₂, -

NR^cR^d, -NHS(=O)₂R^a, -S(=O)₂NR^cR^d, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -

C(=O)NR^cR^d, -OC(=O)NR^cR^d, -NR^bC(=O)NR^cR^d, -NR^bC(=O)R^a, -NR^bC(=O)OR^b, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, or C₂-C₆alkynyl;

R⁵ is halogen, -CN, -OR⁸, -SR⁸, -S(=O)R⁷, -S(=O)₂R⁷, -NO₂, -NR⁹R¹⁰, -NR⁸S(=O)R⁷, -NR⁸S(=O)₂R⁷, -S(=O)₂NR⁹R¹⁰, -C(=N-CN)R⁷, -C(=O)R⁷, -OC(=N-CN)R⁷, -OC(=O)R⁷, -C(=N-CN)OR⁸, -C(=O)OR⁸, -OC(=N-CN)OR⁸, -OC(=O)OR⁸, -C(=N-CN)NR⁹R¹⁰, -C(=O)NR⁹R¹⁰, -OC(=N-CN)NR⁹R¹⁰, -OC(=O)NR⁹R¹⁰, -NR⁸C(=N-CN)NR⁹R¹⁰, -NR⁸C(=O)NR⁹R¹⁰, -NR⁸C(=N-CN)R⁷, -NR⁸C(=N-OH)R⁷, -NR⁸C(=N-CN)OR⁸, -NR⁸C(=O)OR⁸, -NR⁸S(=O)(=NR⁸)R⁷, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₁-C₆heteroalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C₁-C₆alkyl(cycloalkyl), C₁-C₆alkyl(heterocycloalkyl), C₁-C₆alkyl(aryl), or C₁-C₆alkyl(heteroaryl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, C₁-C₆alkyl, or C₁-C₆haloalkyl;

R⁷ is C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

each R⁸ is independently hydrogen, CN, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

R⁹ and R¹⁰ are independently hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, C₁-C₆deuteroalkyl, C₁-C₆haloalkyl, C₁-C₆hydroxyalkyl, C₁-C₆hydroxydeuteroalkyl, cycloalkyl, or heterocycloalkyl;

or R⁹ and R¹⁰ are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

or R⁸ and R⁹ are taken together with the atoms to which they are attached to form a heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

R¹¹ is C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more R^{11a};

each R^{11a} is independently deuterium, halogen, -CN, -OR^b, -SR^b, -S(=O)R^a, -S(=O)₂R^a, -NO₂, -NR^cR^d, -NHS(=O)₂R^a, -S(=O)₂NR^cR^d, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -C(=O)NR^cR^d, -OC(=O)NR^cR^d, -NR^bC(=O)NR^cR^d, -NR^bC(=O)R^a, -NR^bC(=O)OR^b, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, or C₂-C₆alkynyl;

each R^a is independently C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

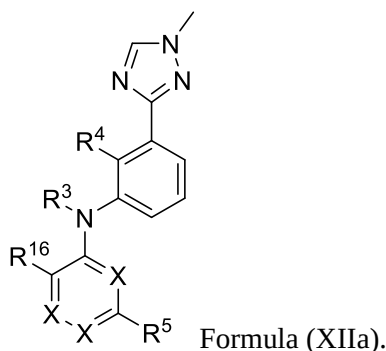
each R^b is independently hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

each R^c and R^d is independently hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

or R^c and R^d are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl.

2. The compound of claim 1, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
Ring B is aryl or heteroaryl.
3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
L is a bond.
4. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
Ring A is heterocycloalkyl or heteroaryl; each optionally substituted with one or more R^A.

5. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
Ring A is a 5-membered heterocycloalkyl or a 5-membered heteroaryl; each optionally substituted with one or more R^A.
6. The compound of any one of claims 1-5, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
each R^A is independently deuterium, halogen, C₁-C₆alkyl, C₁-C₆haloalkyl, or C₁-C₆deuteroalkyl.
7. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
R⁴ is hydrogen, deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, -OC(=O)NR^cR^d, C₁-C₆alkyl, C₁-C₆haloalkyl, or C₁-C₆deuteroalkyl.
8. The compound of any one of claims 1-7, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
R⁴ is hydrogen or -OR^b.
9. The compound of any one of claims 1-8, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein the compound is of formula (XIIa):



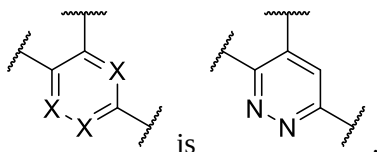
10. The compound of any one of claims 1-9, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
R³ is hydrogen.
11. The compound of any one of claims 1-10, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
R¹⁶ is -C(=O)NR¹R².
12. The compound of any one of claims 1-11, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
R¹ and R² are independently hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, or C₁-C₆deuteroalkyl.
13. The compound of any one of claims 1-12, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
R¹ is hydrogen.
14. The compound of any one of claims 1-13, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
R² is C₁-C₆alkyl or C₁-C₆deuteroalkyl.

15. The compound of any one of claims 1-14, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
 R^2 is C_1 - C_6 deuteroalkyl.

16. The compound of any one of claims 1-10, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
 R^{16} is $-C(=O)R^{11}$.

17. The compound of any one of claims 1-10 or 16, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
 R^{11} is C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, or cycloalkyl.

18. The compound of any one of claims 1-17, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:



19. The compound of any one of claims 1-18, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:

R^5 is $-NR^8C(=O)NR^9R^{10}$ or heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, $-CN$, $-OR^b$, $-NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, $-C(=O)NR^cR^d$, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_1 - C_6 deuteroalkyl, C_1 - C_6 hydroxyalkyl, C_1 - C_6 aminoalkyl, C_1 - C_6 heteroalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1 - C_6 alkyl(cycloalkyl), C_1 - C_6 alkyl(heterocycloalkyl), C_1 - C_6 alkyl(aryl), or C_1 - C_6 alkyl(heteroaryl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, $-CN$, $-OR^b$, $-NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, $-C(=O)NR^cR^d$, C_1 - C_6 alkyl, or C_1 - C_6 haloalkyl.

20. The compound of any one of claims 1-19, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:

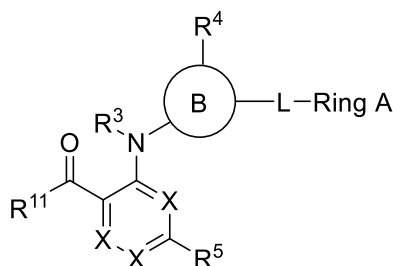
R^5 is heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, $-CN$, $-OR^b$, $-NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, $-C(=O)NR^cR^d$, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_1 - C_6 deuteroalkyl, C_1 - C_6 hydroxyalkyl, C_1 - C_6 aminoalkyl, C_1 - C_6 heteroalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1 - C_6 alkyl(cycloalkyl), C_1 - C_6 alkyl(heterocycloalkyl), C_1 - C_6 alkyl(aryl), C_1 - C_6 alkyl(heteroaryl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, $-CN$, $-OR^b$, $-NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, $-C(=O)NR^cR^d$, C_1 - C_6 alkyl, or C_1 - C_6 haloalkyl.

21. The compound of any one of claims 1-19, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
 R^5 is $-NR^8C(=O)NR^9R^{10}$.

22. The compound of any one of claims 1-21, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:

R^9 and R^{10} are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl.

23. A compound of Formula (XIII), or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof:



Formula (XIII),

wherein:

Ring B is cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;

R^3 is hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, or C₁-C₆deuteroalkyl;

R^4 is hydrogen, deuterium, halogen, -CN, -OR^b, -SR^b, -S(=O)R^a, -S(=O)₂R^a, -NO₂, -NR^cR^d, -NHS(=O)₂R^a, -S(=O)₂NR^cR^d, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -C(=O)NR^cR^d, -OC(=O)NR^cR^d, -NR^bC(=O)NR^cR^d, -NR^bC(=O)R^a, -NR^bC(=O)OR^b, -P(=O)R^bR^b, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, or C₂-C₆alkynyl;

or R^3 and R^4 are taken together to form an optionally substituted ring;

L is a bond or -C(=O)-;

Ring A is cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; each optionally substituted with one or more R^A;

each R^A is independently deuterium, halogen, -CN, -OR^b, -SR^b, -S(=O)R^a, -S(=O)₂R^a, -NO₂, -NR^cR^d, -NHS(=O)₂R^a, -S(=O)₂NR^cR^d, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -C(=O)NR^cR^d, -OC(=O)NR^cR^d, -NR^bC(=O)NR^cR^d, -NR^bC(=O)R^a, -NR^bC(=O)OR^b, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, C₁-C₆alkyl, or C₁-C₆haloalkyl;

or two R^A on the same carbon are taken together to form an oxo;

or -L-Ring A is absent;

each X is independently -CR^x- or -N-;

each R^x is independently hydrogen, deuterium, halogen, -CN, -OR^b, -SR^b, -S(=O)R^a, -S(=O)₂R^a, -NO₂, -NR^cR^d, -NHS(=O)₂R^a, -S(=O)₂NR^cR^d, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -

C(=O)NR^cR^d, -OC(=O)NR^cR^d, -NR^bC(=O)NR^cR^d, -NR^bC(=O)R^a, -NR^bC(=O)OR^b, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, or C₂-C₆alkynyl;

R⁵ is halogen, -CN, -OR⁸, -SR⁸, -S(=O)R⁷, -S(=O)₂R⁷, -NO₂, -NR⁹R¹⁰, -NR⁸S(=O)R⁷, -NR⁸S(=O)₂R⁷, -S(=O)₂NR⁹R¹⁰, -C(=N-CN)R⁷, -C(=O)R⁷, -OC(=N-CN)R⁷, -OC(=O)R⁷, -C(=N-CN)OR⁸, -C(=O)OR⁸, -OC(=N-CN)OR⁸, -OC(=O)OR⁸, -C(=N-CN)NR⁹R¹⁰, -C(=O)NR⁹R¹⁰, -OC(=N-CN)NR⁹R¹⁰, -OC(=O)NR⁹R¹⁰, -NR⁸C(=N-CN)NR⁹R¹⁰, -NR⁸C(=O)NR⁹R¹⁰, -NR⁸C(=N-CN)R⁷, -NR⁸C(=N-OH)R⁷, -NR⁸C(=O)R⁷, -NR⁸C(=N-CN)OR⁸, -NR⁸C(=O)OR⁸, -NR⁸S(=O)(=NR⁸)R⁷, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₁-C₆heteroalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C₁-C₆alkyl(cycloalkyl), C₁-C₆alkyl(heterocycloalkyl), C₁-C₆alkyl(aryl), or C₁-C₆alkyl(heteroaryl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, C₁-C₆alkyl, or C₁-C₆haloalkyl;

R⁷ is C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

each R⁸ is independently hydrogen, CN, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

R⁹ and R¹⁰ are independently hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, C₁-C₆deuteroalkyl, C₁-C₆haloalkyl, C₁-C₆hydroxyalkyl, C₁-C₆hydroxydeuteroalkyl, cycloalkyl, or heterocycloalkyl;

or R⁹ and R¹⁰ are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

or R⁸ and R⁹ are taken together with the atoms to which they are attached to form a heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

R¹¹ is C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more R^{11a};

each R^{11a} is independently deuterium, halogen, -CN, -OR^b, -SR^b, -S(=O)R^a, -S(=O)₂R^a, -NO₂, -NR^cR^d, -NHS(=O)₂R^a, -S(=O)₂NR^cR^d, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -C(=O)NR^cR^d, -OC(=O)NR^cR^d, -NR^bC(=O)NR^cR^d, -NR^bC(=O)R^a, -NR^bC(=O)OR^b, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, or C₂-C₆alkynyl;

each R^a is independently C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

each R^b is independently hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

each R^c and R^d is independently hydrogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl;

or R^c and R^d are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl.

24. The compound of claim 23, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:

Ring B is aryl or heteroaryl.

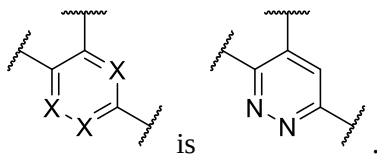
25. The compound of claim 23 or 24, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:

L is a bond.

26. The compound of any one of claims 23-25, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:

Ring A is a 5-membered heteroaryl optionally substituted with one or more R^A.

27. The compound of any one of claims 23-26, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
each R^A is independently deuterium, halogen, C₁-C₆alkyl, C₁-C₆haloalkyl, or C₁-C₆deuteroalkyl.
28. The compound of any one of claims 23-27, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
R⁴ is hydrogen, deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, -OC(=O)NR^cR^d, C₁-C₆alkyl, C₁-C₆haloalkyl, or C₁-C₆deuteroalkyl.
29. The compound of any one of claims 23-28, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
R⁴ is hydrogen or -OR^b.
30. The compound of any one of claims 23-29, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
R³ is hydrogen.
31. The compound of any one of claims 23-30, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
R¹¹ is C₁-C₆alkyl, C₁-C₆deuteroalkyl, C₁-C₆haloalkyl, or cycloalkyl.
32. The compound of any one of claims 23-31, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:



33. The compound of any one of claims 23-32, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
R⁵ is -NR⁸C(=O)R⁷, -NR⁸C(=O)NR⁹R¹⁰, or heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₁-C₆heteroalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C₁-C₆alkyl(cycloalkyl), C₁-C₆alkyl(heterocycloalkyl), C₁-C₆alkyl(aryl), or C₁-C₆alkyl(heteroaryl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, C₁-C₆alkyl, or C₁-C₆haloalkyl.
34. The compound of any one of claims 23-33, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:
R⁵ is heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆deuteroalkyl, C₁-C₆hydroxyalkyl, C₁-C₆aminoalkyl, C₁-C₆heteroalkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C₁-C₆alkyl(cycloalkyl),

C₁-C₆alkyl(heterocycloalkyl), C₁-C₆alkyl(aryl), C₁-C₆alkyl(heteroaryl),; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one or more oxo, deuterium, halogen, -CN, -OR^b, -NR^cR^d, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^cR^d, C₁-C₆alkyl, or C₁-C₆haloalkyl.

35. The compound of any one of claims 23-32, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:

R⁵ is -NR⁸C(=O)NR⁹R¹⁰.

36. The compound of any one of claims 23-35, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:

R⁹ and R¹⁰ are taken together with the nitrogen atom to which they are attached to form a

heterocycloalkyl optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl.

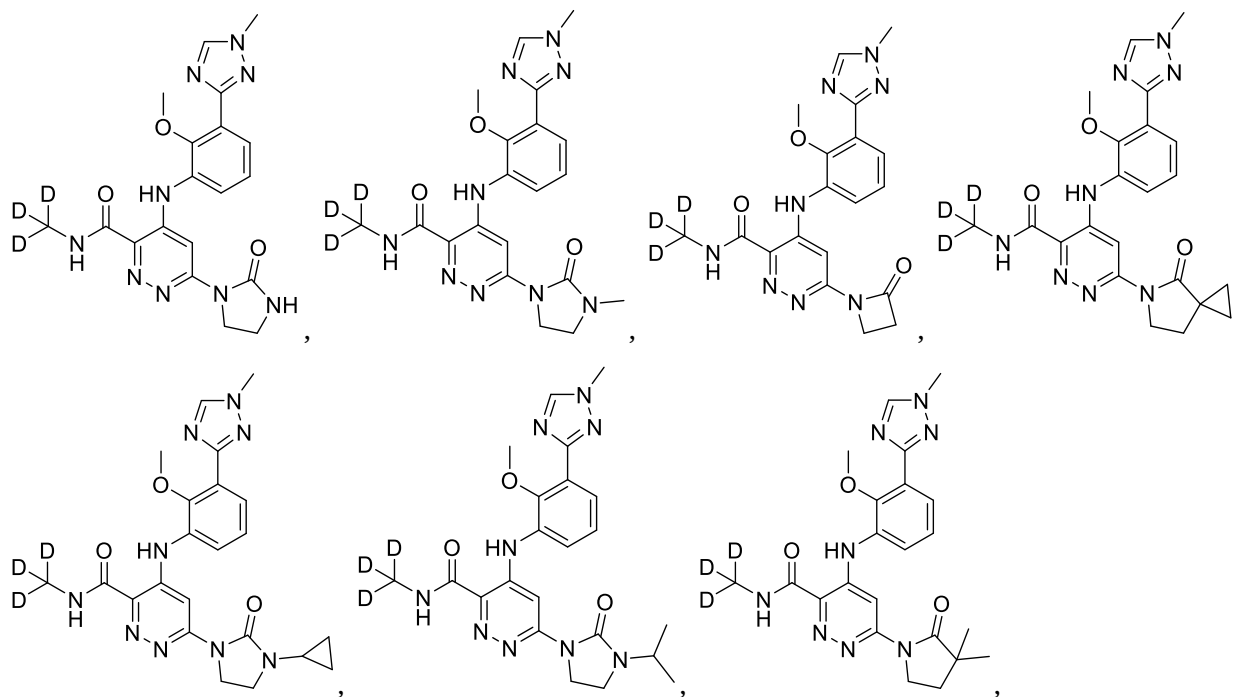
37. The compound of any one of claims 23-32, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:

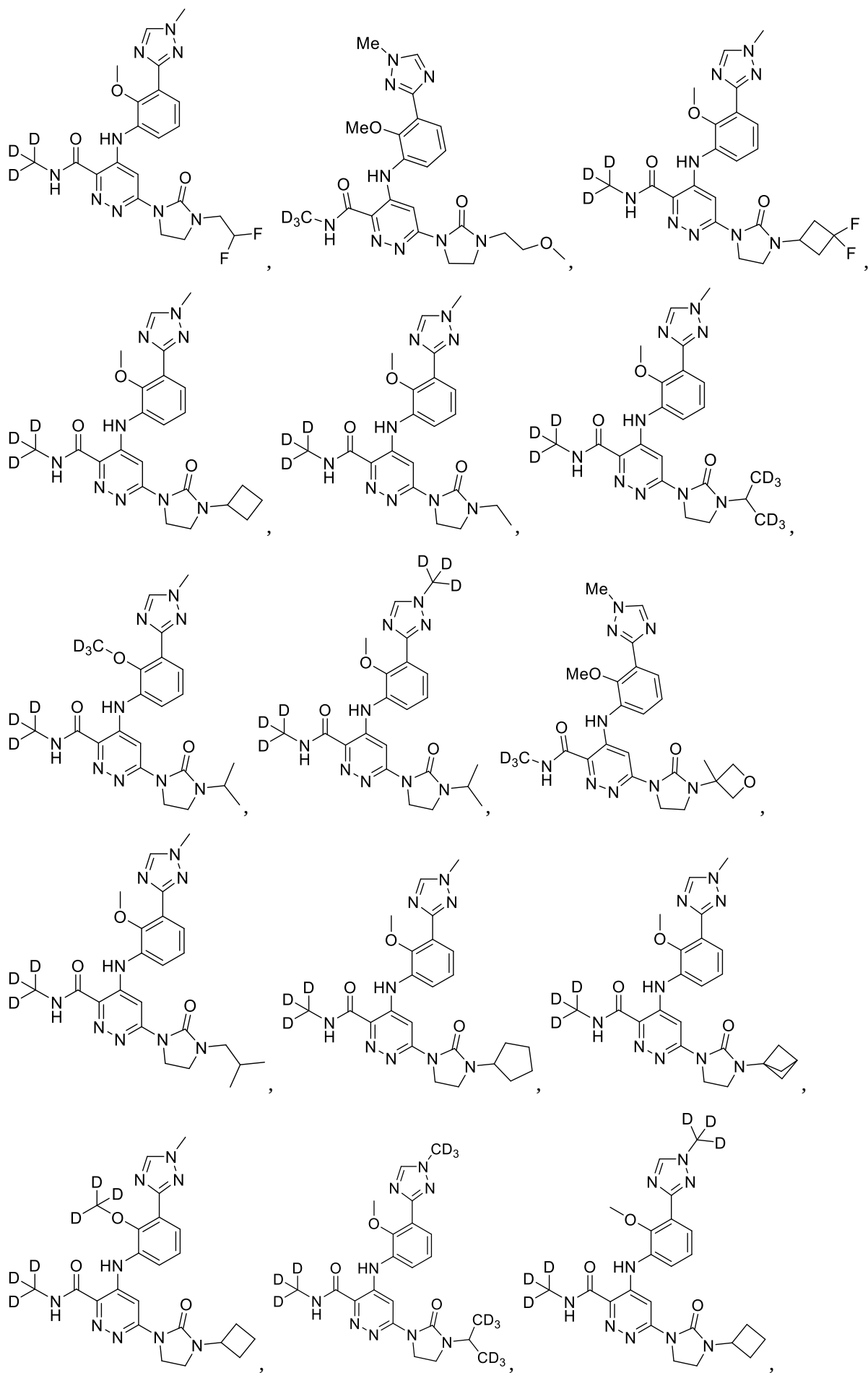
R⁵ is -NR⁸C(=O)R⁷.

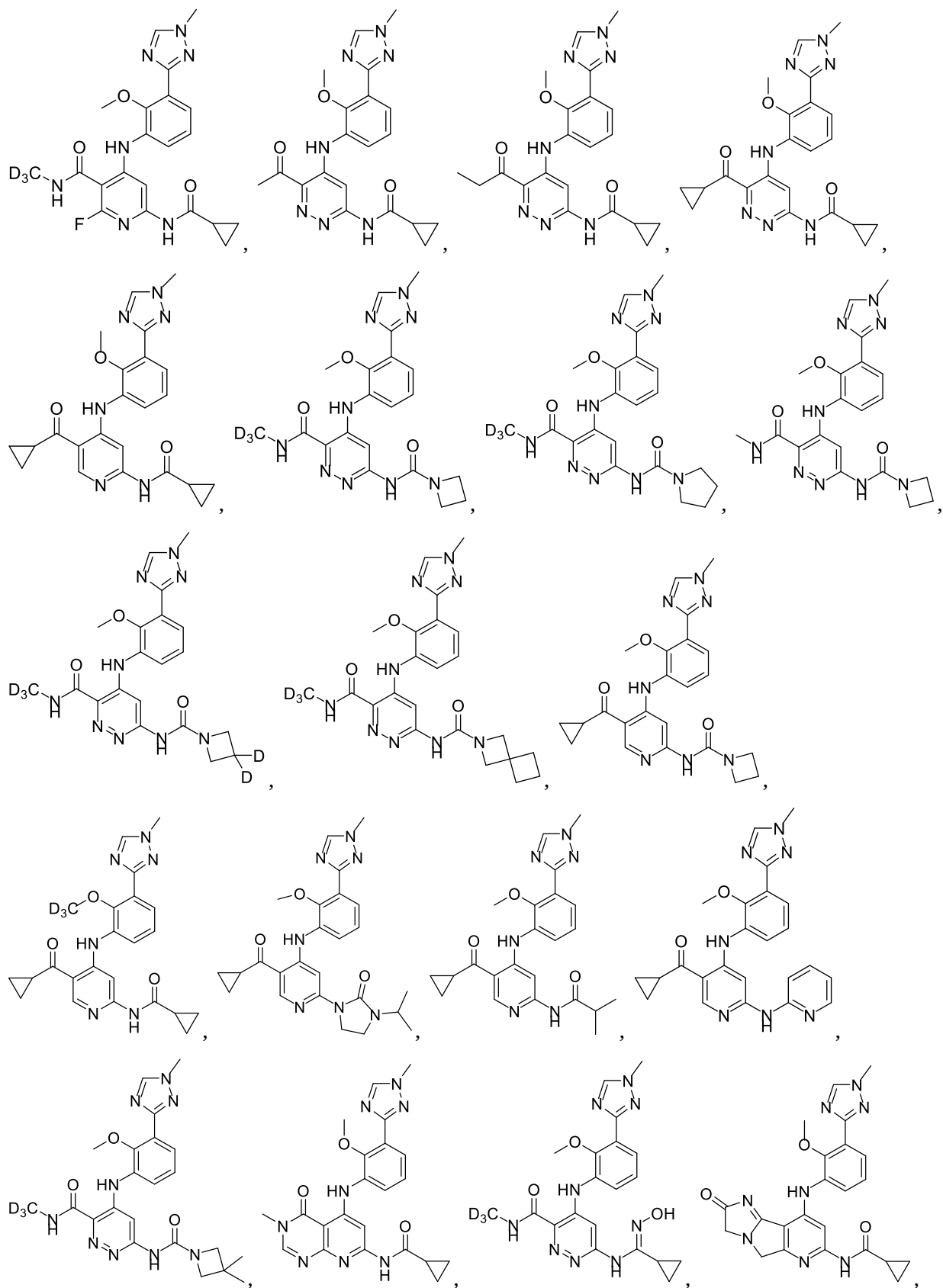
38. The compound of any one of claims 23-32 or 37, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, wherein:

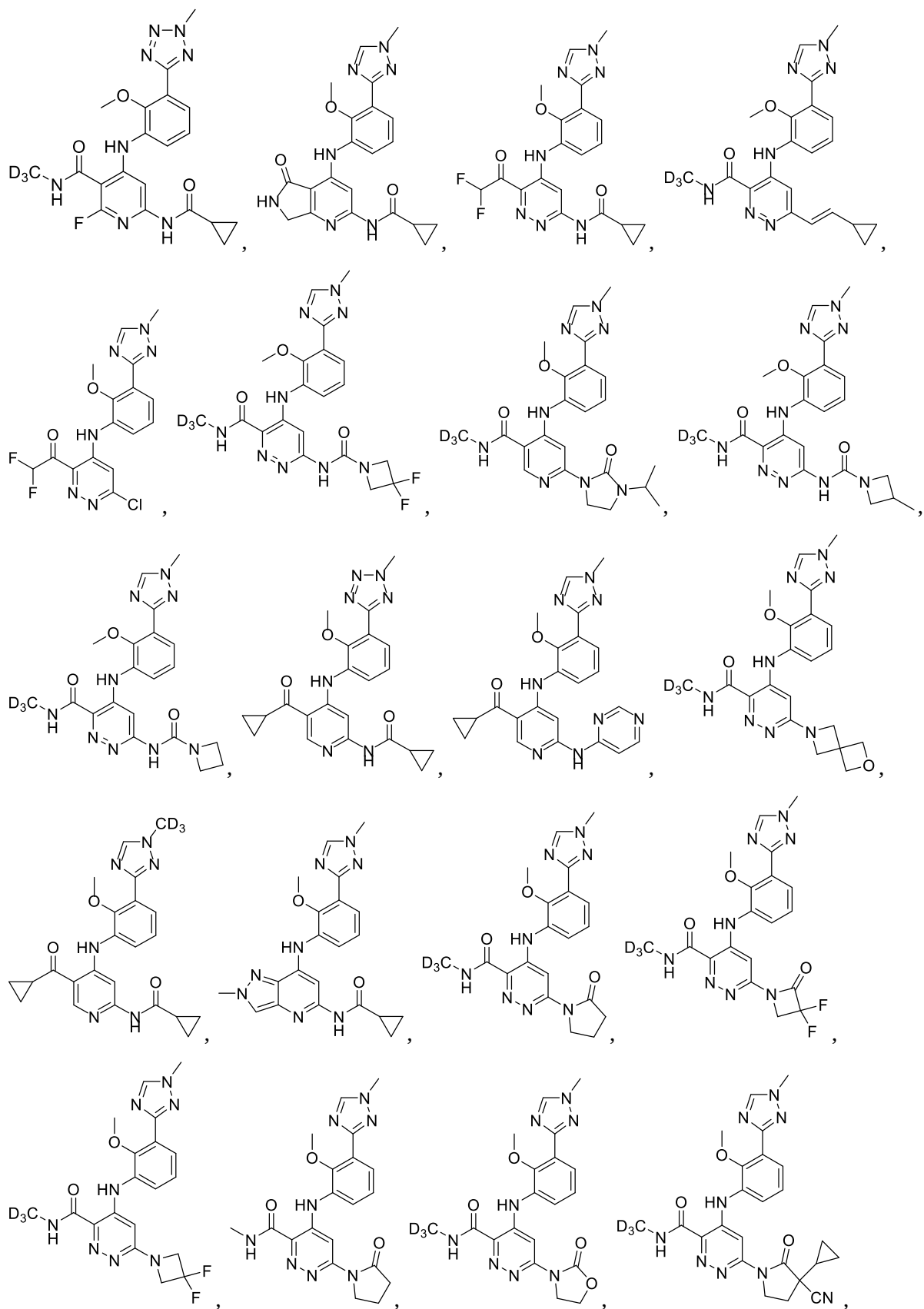
R⁷ is cycloalkyl optionally substituted with one or more oxo, deuterium, halogen, -CN, -OH, -OMe, -NH₂, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C₁-C₆alkyl, or C₁-C₆haloalkyl.

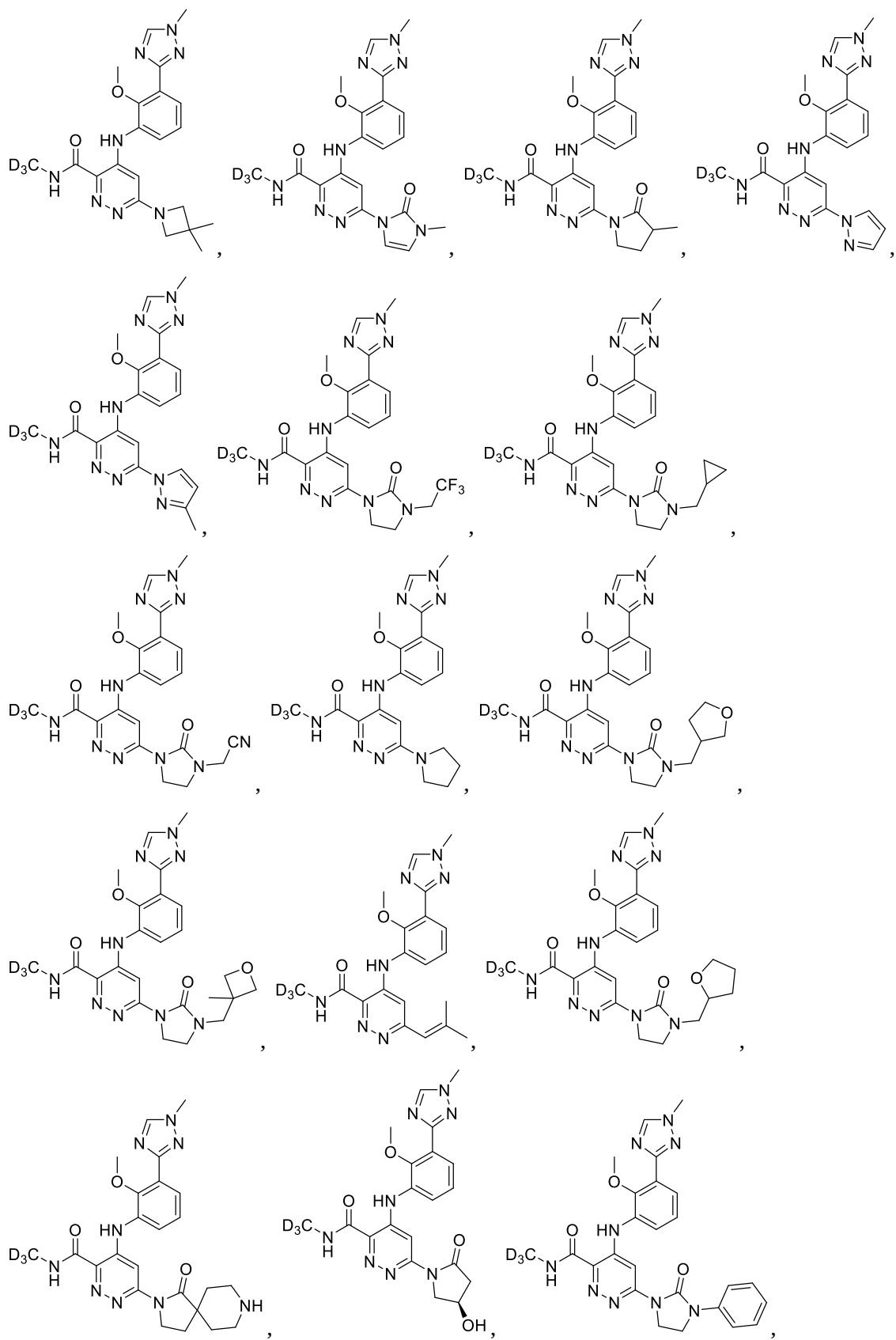
39. A compound, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, selected from:

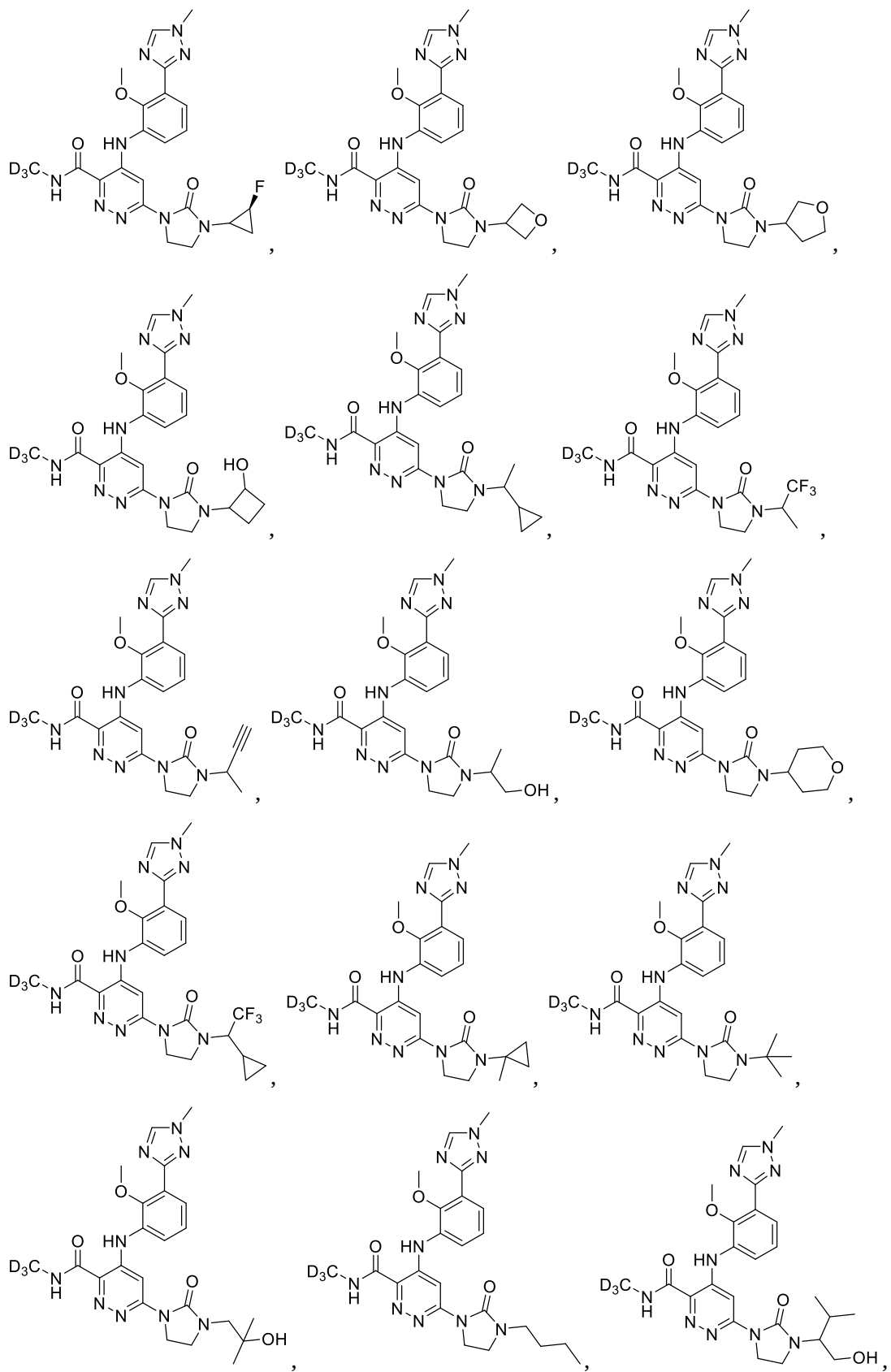


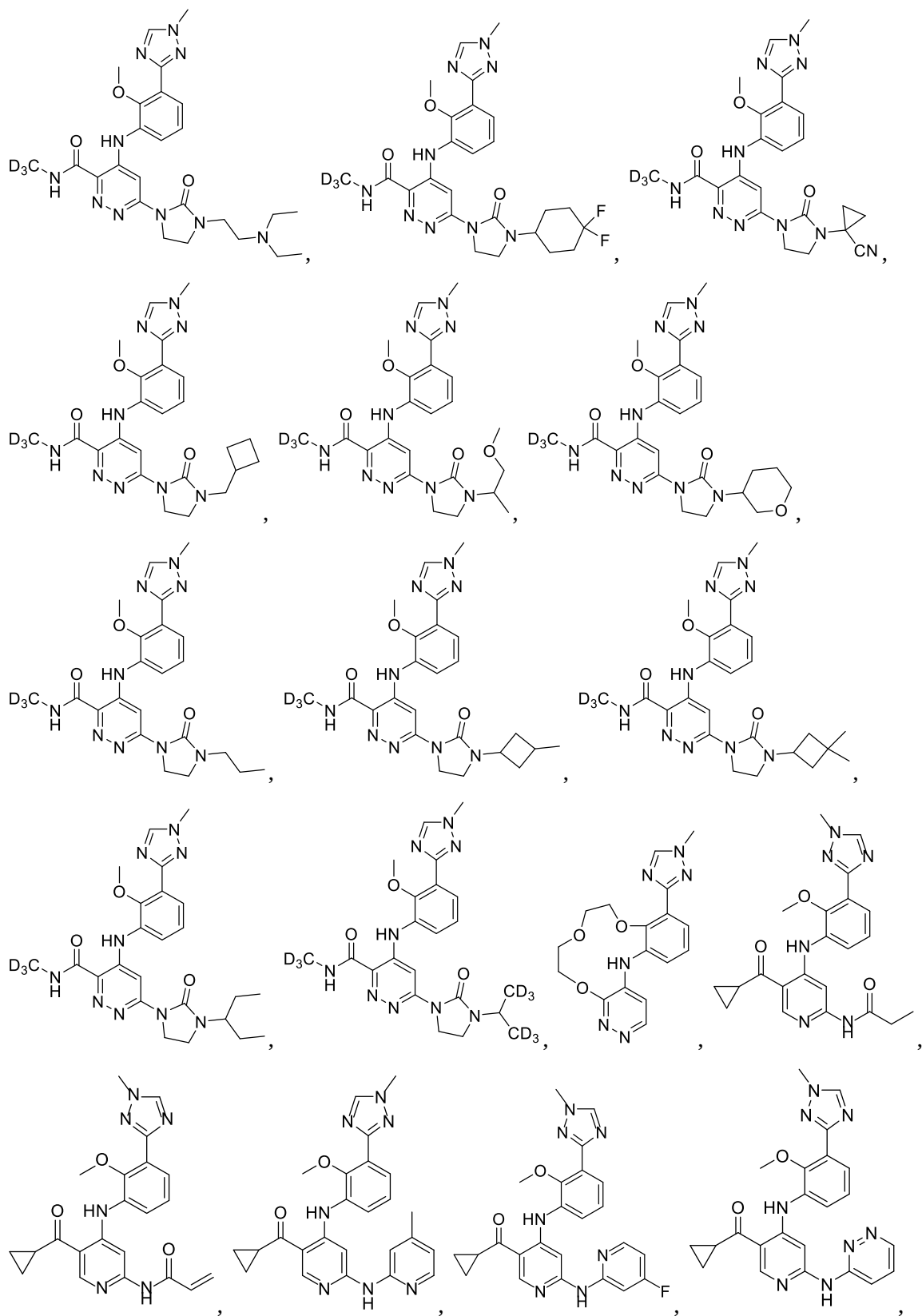


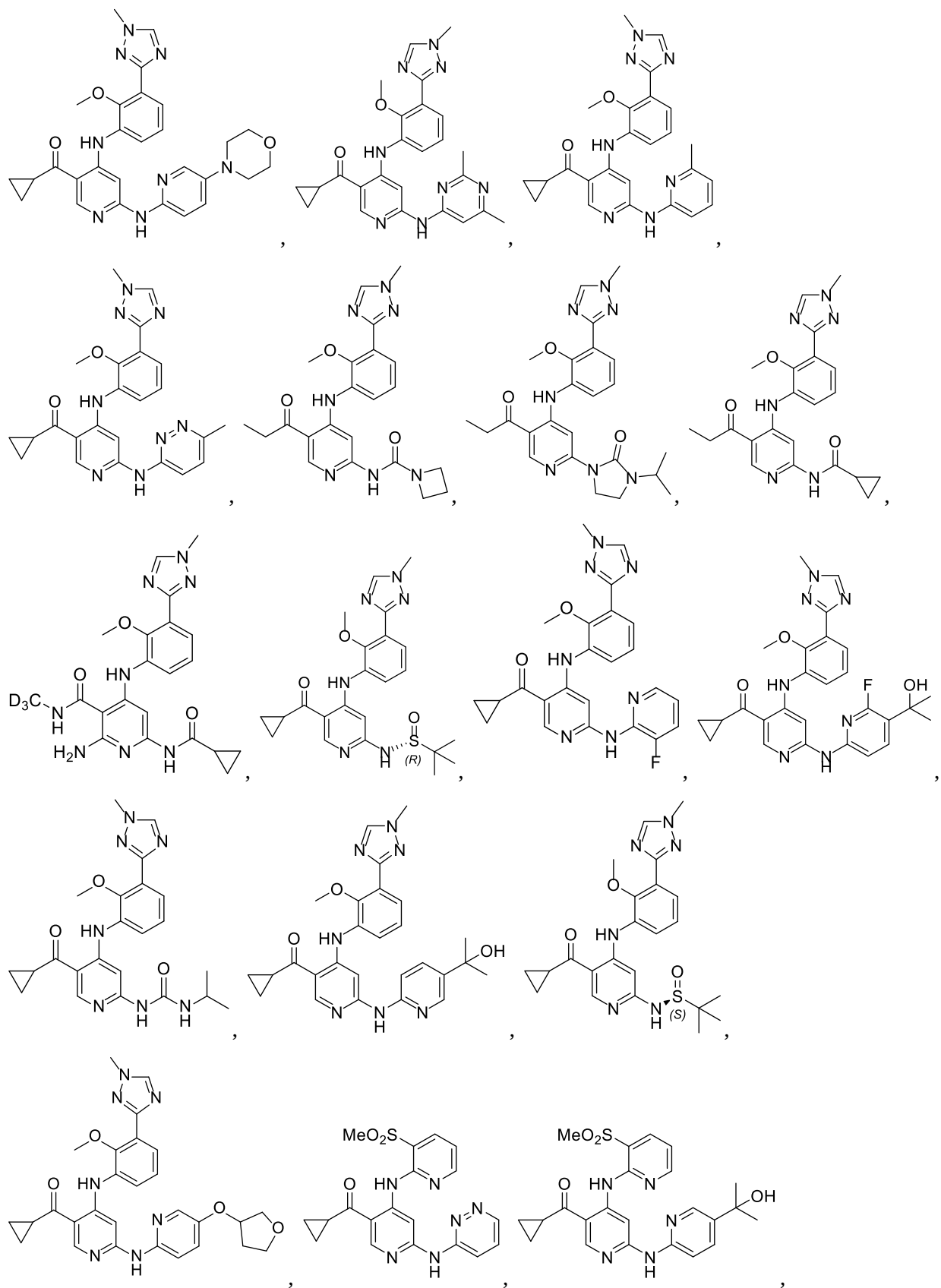


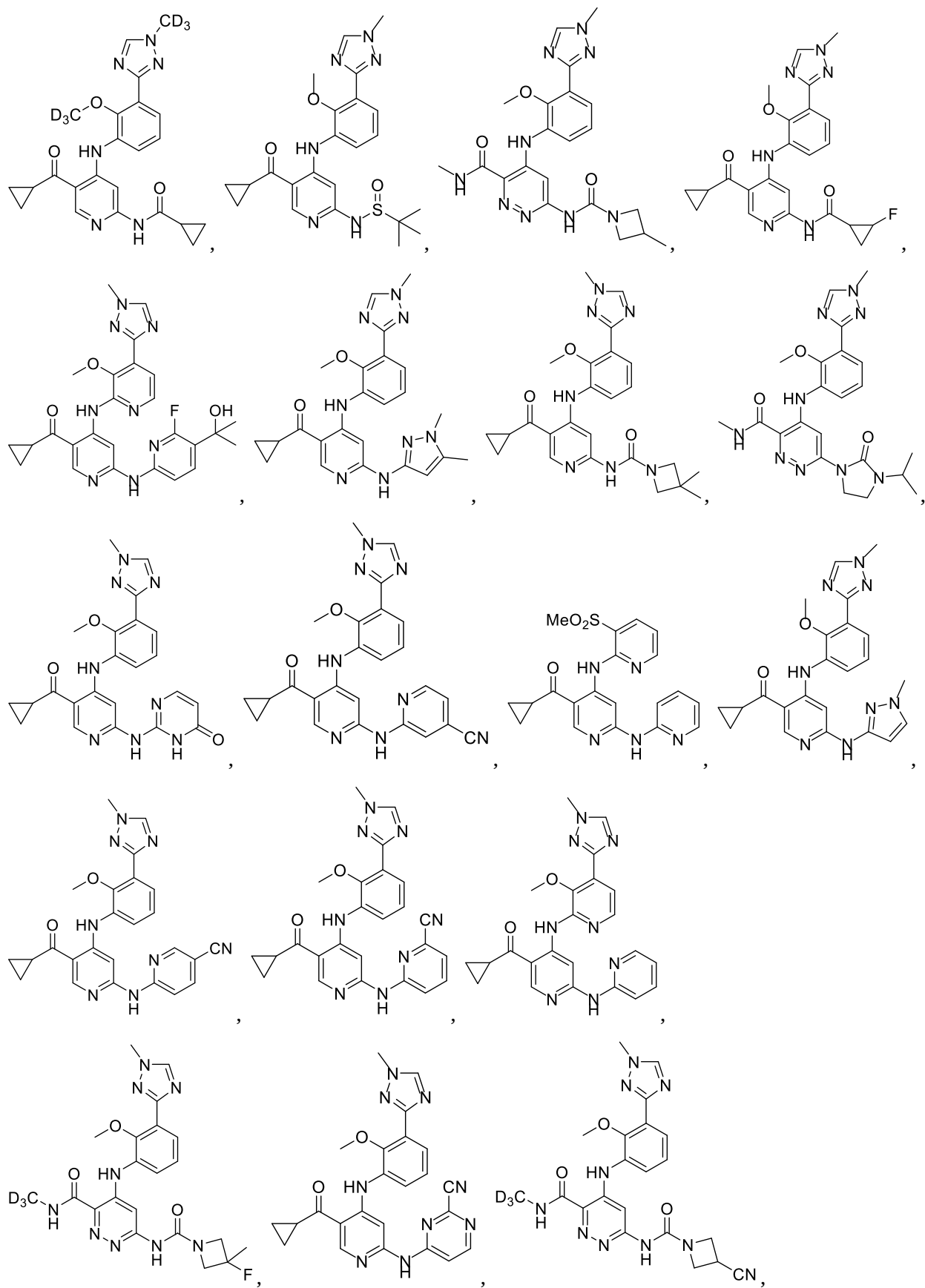


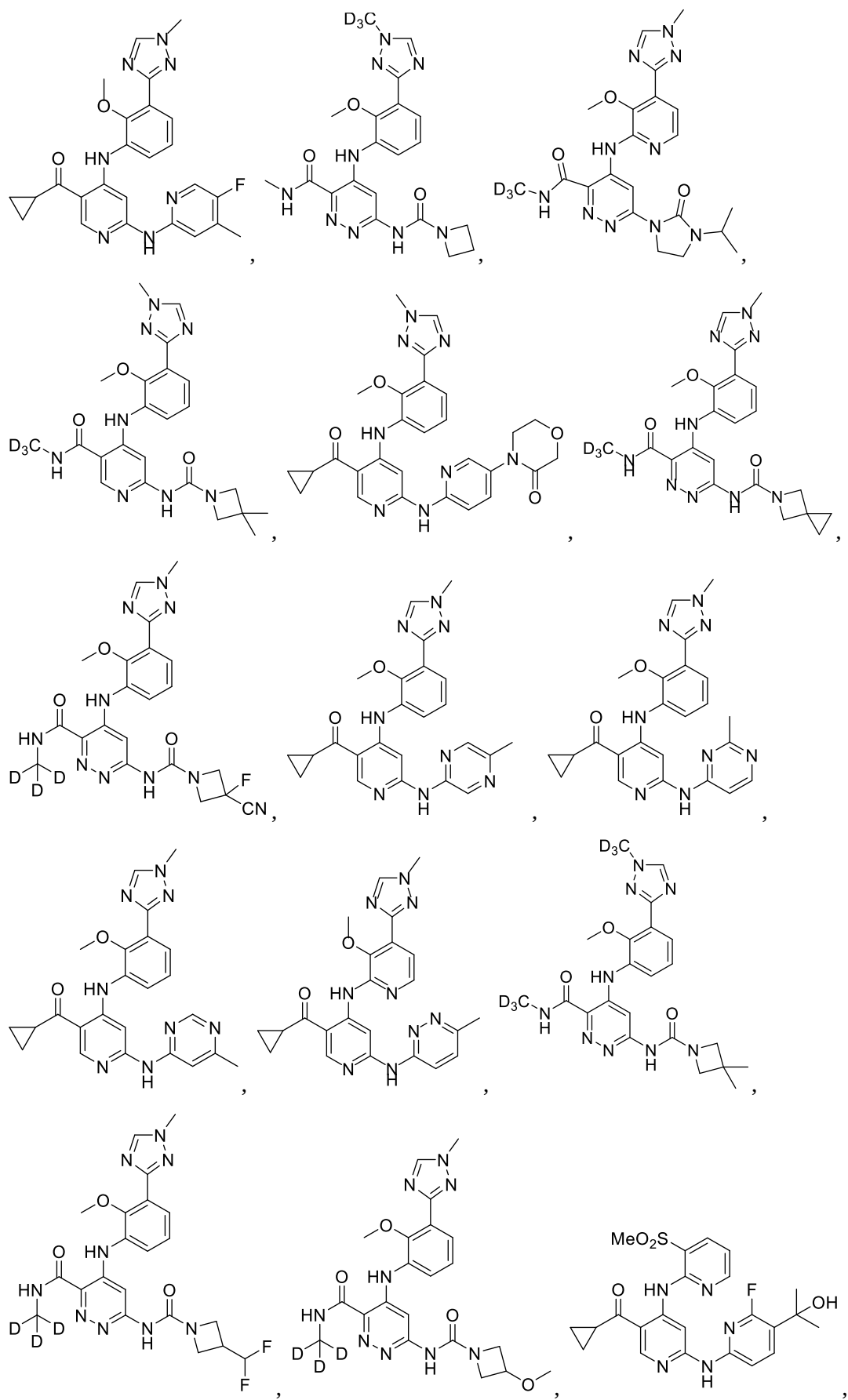


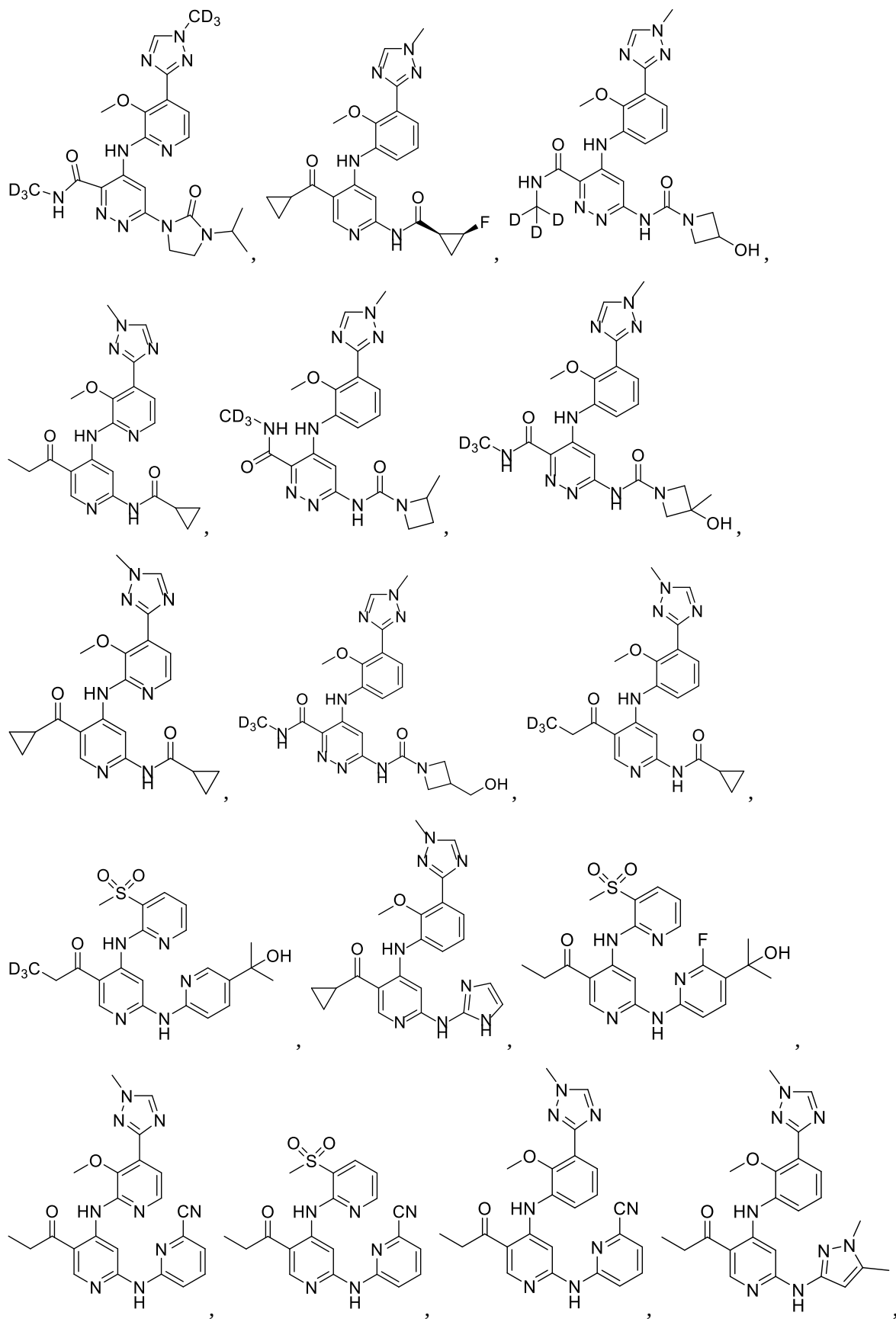


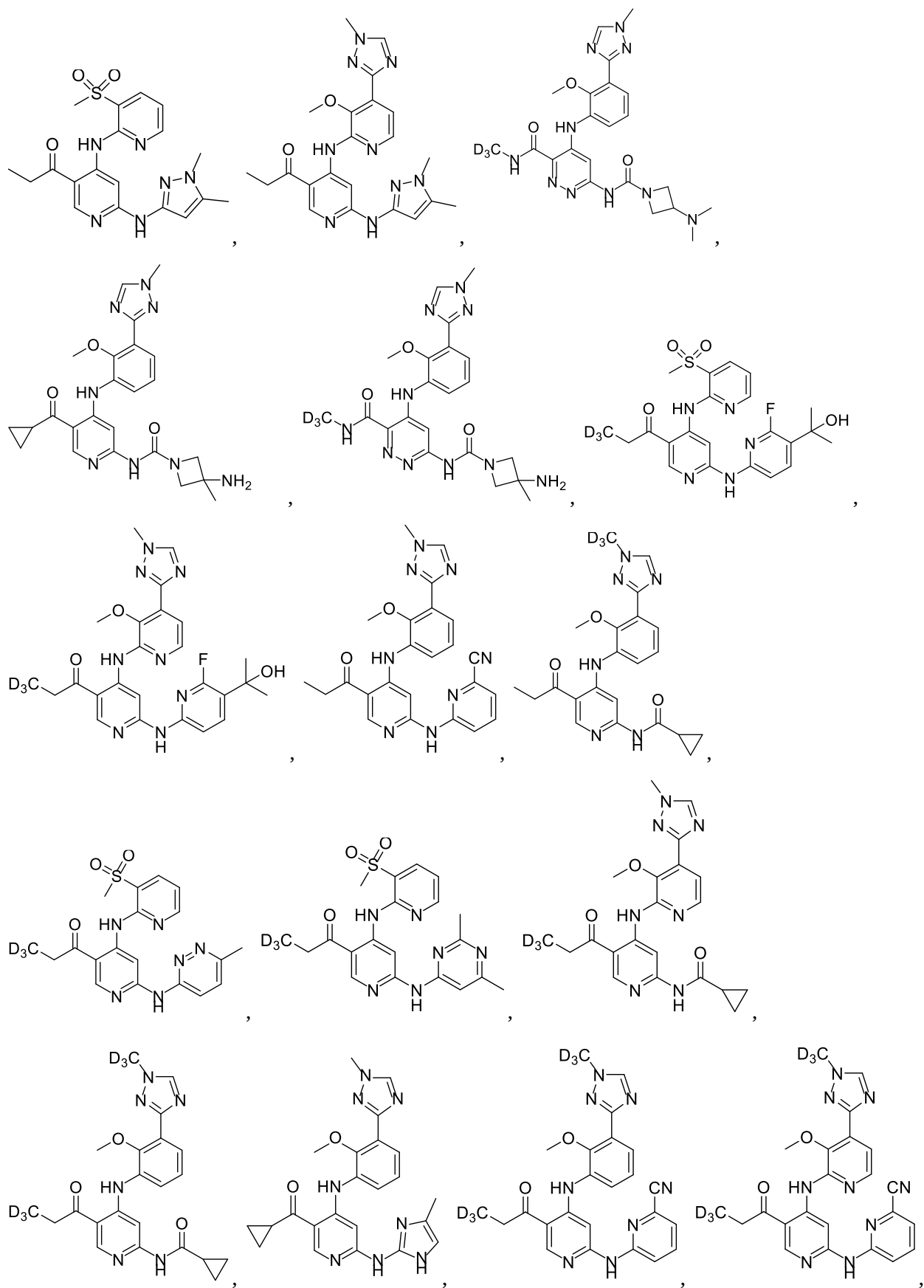




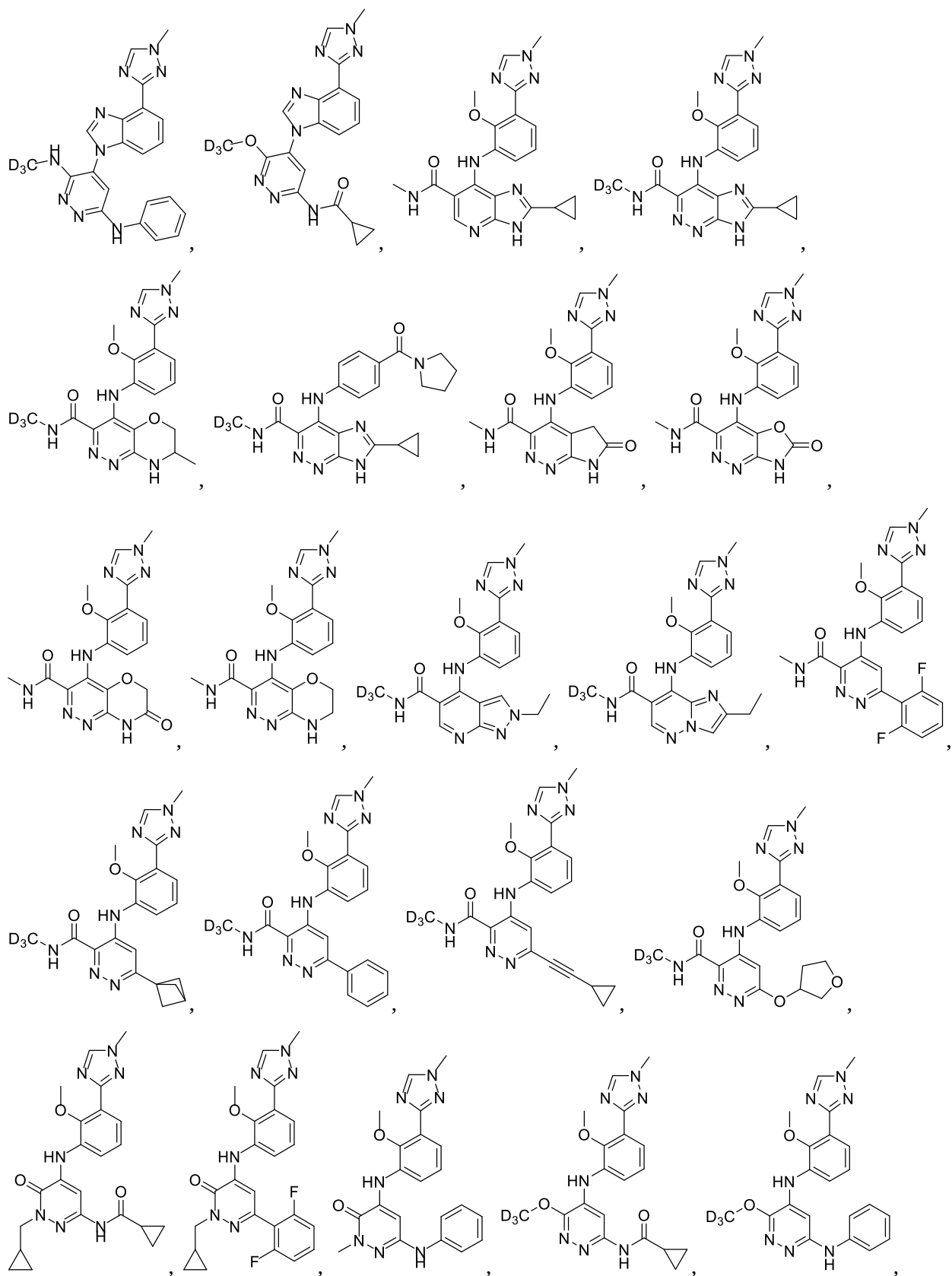


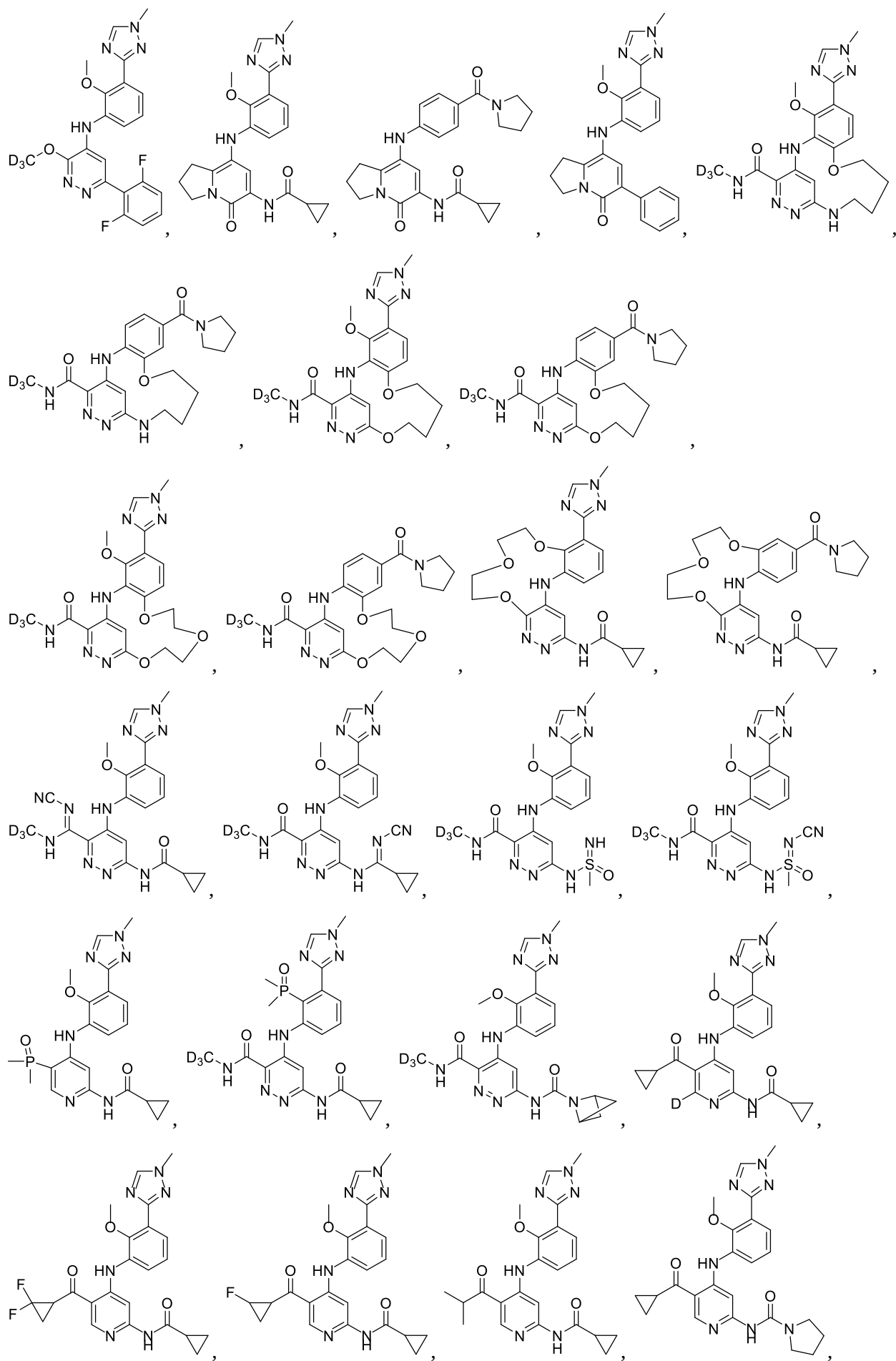


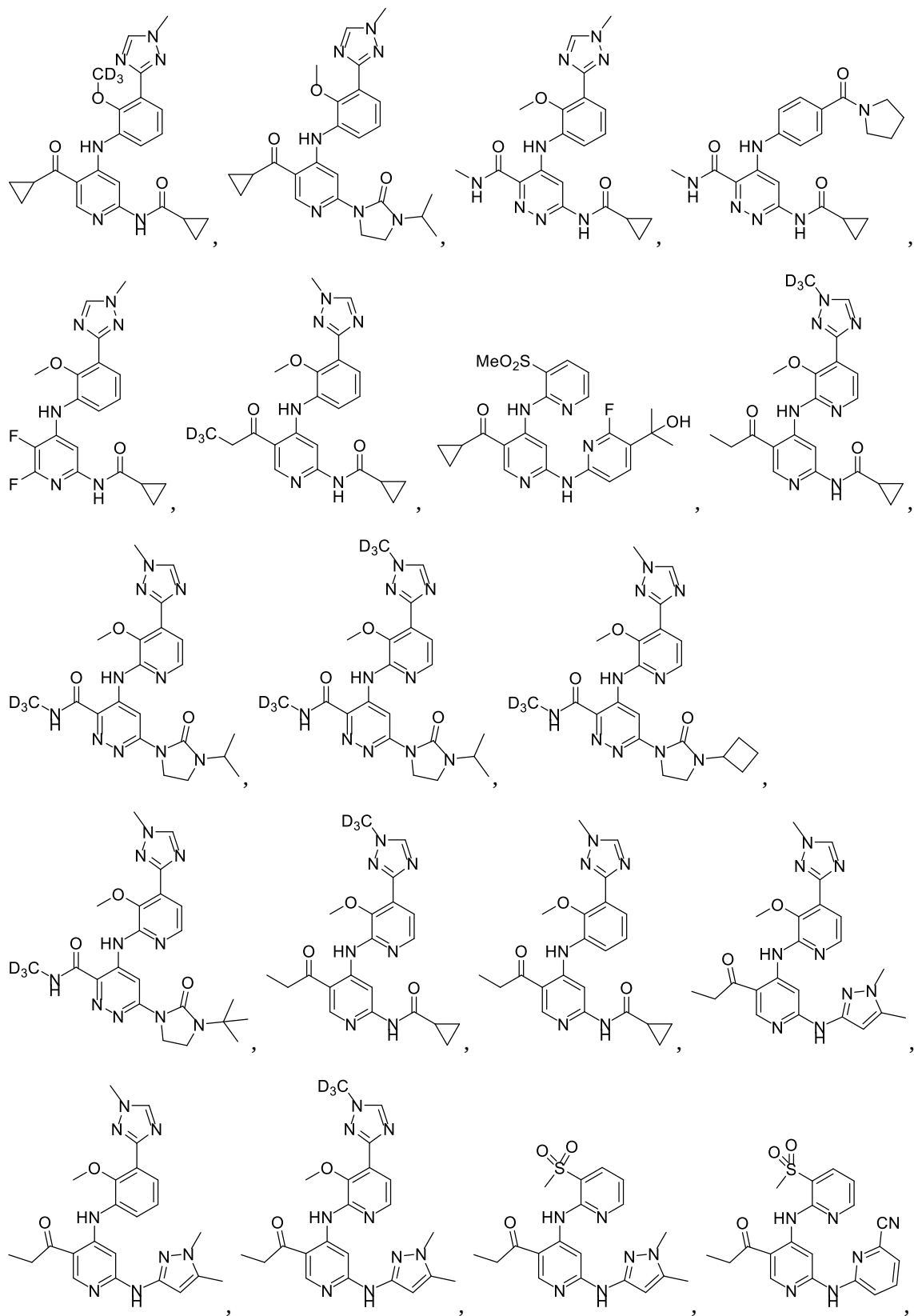


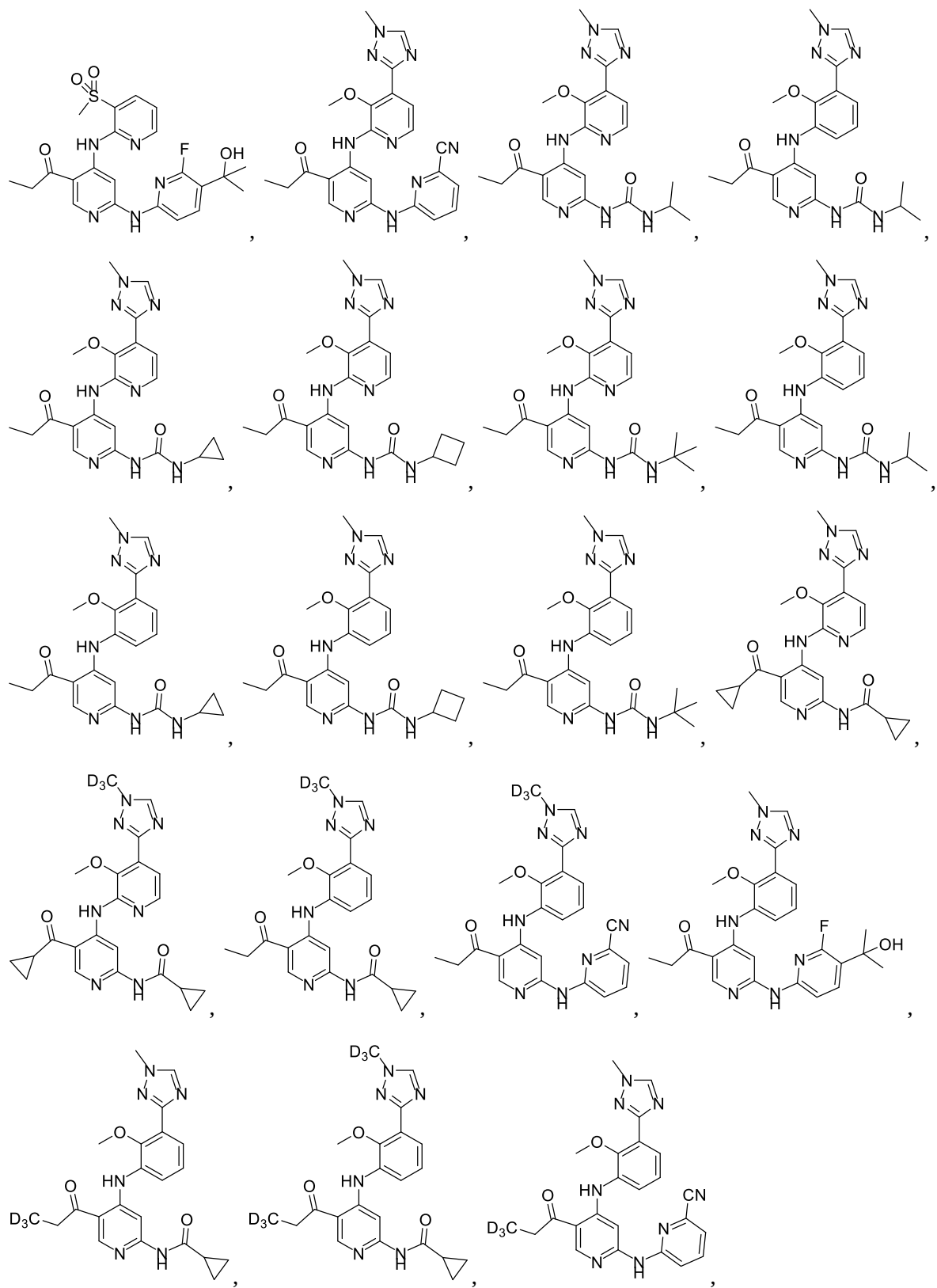


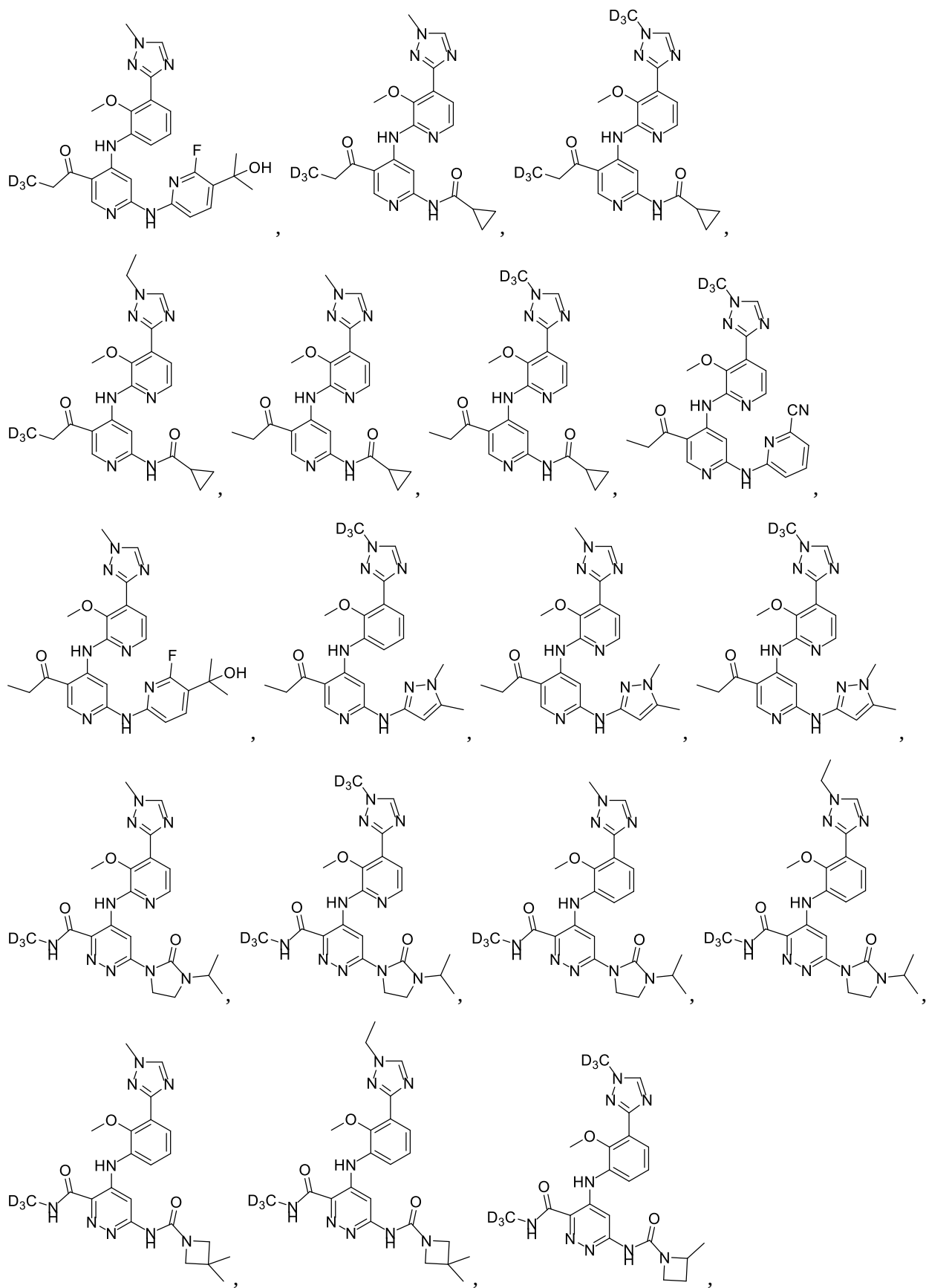


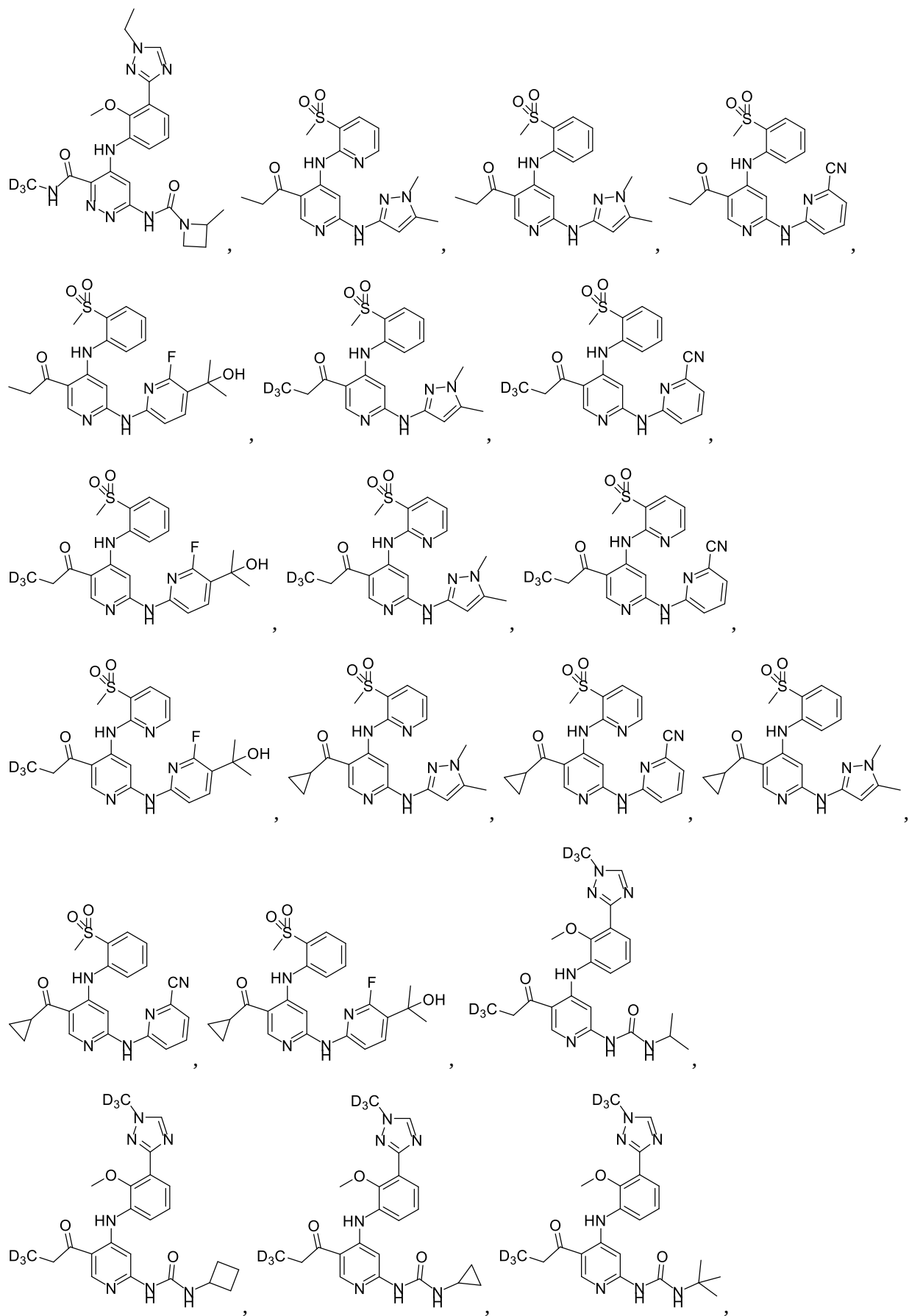


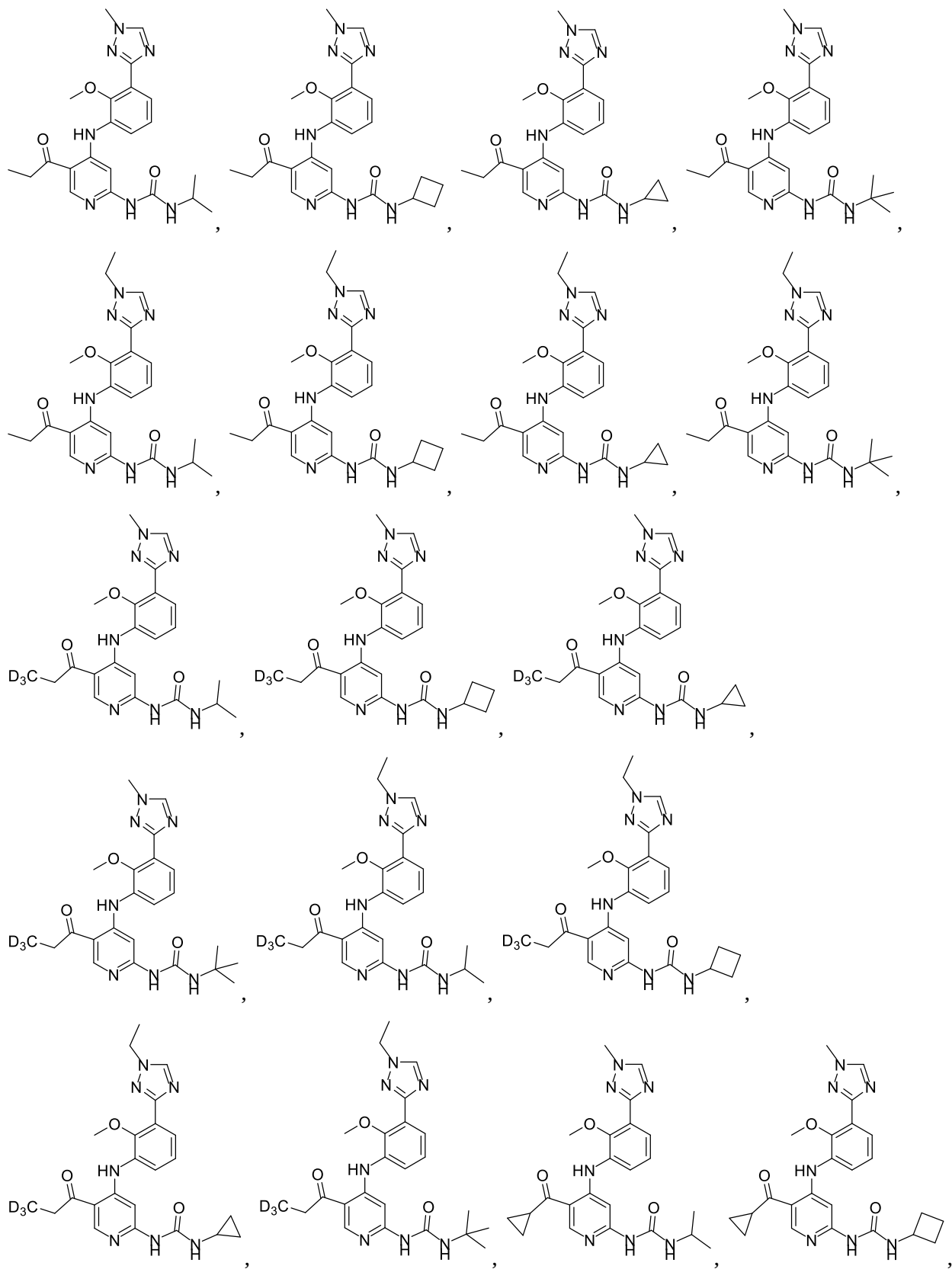


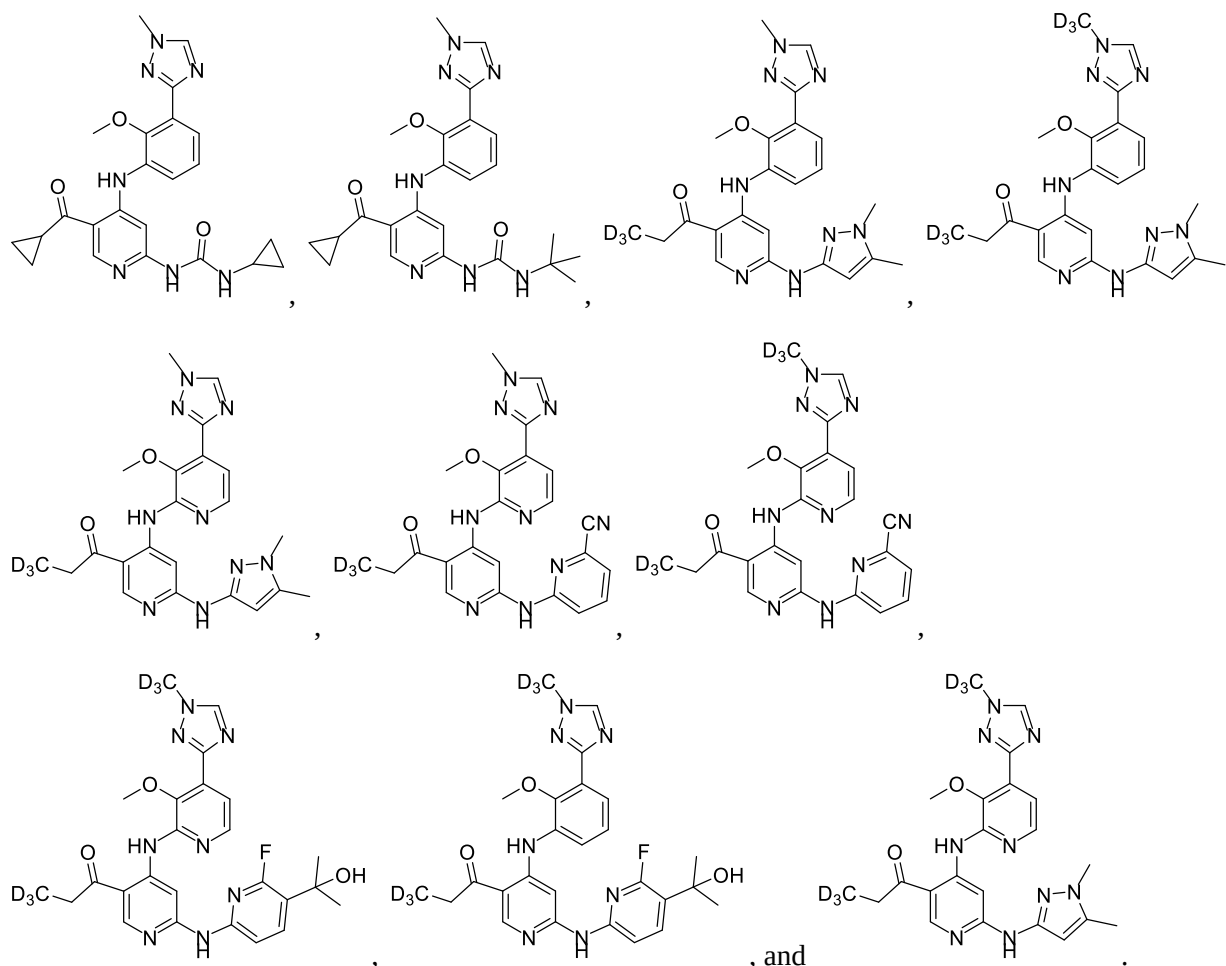












41. A pharmaceutical composition comprising a therapeutically effective amount of the compound of any one of claims 1-40, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, and a pharmaceutically acceptable excipient.
42. A compound of any one of claims 1-40, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, for use in inhibiting a TYK2 enzyme in a patient or biological sample, or for use in treating a TYK2-mediated disorder.
43. Use of a compound of any one of claims 1-40, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, in the manufacture of a medicament for inhibiting a TYK2 enzyme in a patient or biological sample.
44. Use of a compound of any one of claims 1-40, or a pharmaceutically acceptable salt, stereoisomer, or solvate thereof, in the manufacture of a medicament for treating a TYK2-mediated disorder.
45. The compound for use of claim 42, or the use of claim 44, wherein the TYK2-mediated disorder is an autoimmune disorder, an inflammatory disorder, a proliferative disorder, an endocrine disorder, a neurological disorder, or a disorder associated with transplantation.
46. The compound for use of claim 42, or the use of claim 44, wherein the disorder is associated with type I interferon, IL-10, IL-12, or IL-23 signaling.

47. The compound for use of claim 42, or the use of claim 44, wherein the disorder is selected from Crohn's disease, rheumatoid arthritis, psoriasis, systemic lupus erythematosus, ulcerative colitis, psoriatic arthritis, and systemic sclerosis.
48. The compound for use of, or the use of claim 47, wherein the disease or disorder is rheumatoid arthritis.
49. The compound for use of, or the use of claim 47, wherein the disease is psoriasis.
50. The compound for use of, or the use of claim 47, wherein the disease or disorder is systemic lupus erythematosus.
51. The compound for use of, or the use of claim 47, wherein the disease or disorder is ulcerative colitis.
52. The compound for use of, or the use of claim 47, wherein the disease or disorder is psoriatic arthritis.
53. The compound for use of, or the use of claim 47, wherein the disease or disorder is systemic sclerosis.