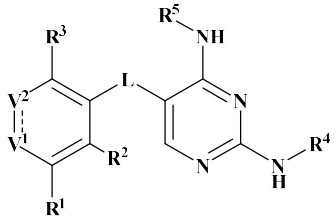
WHAT IS CLAIMED IS:

[Claim 1]. Use of a compound of Formula (I) or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound, metabolite or prodrug thereof in the manufacture of a medicament for treating, suppressing or alleviating cough or cough impulse:



Formula (I)

wherein:

L is selected from the group consisting of C(=O), CRR', NR, O, S, S=O and $S(=O)_2$;

V^1 is selected from the group consisting of N,  and NR;

V^2 is selected from the group consisting of CR^6 and C(=O);

--- represents either a single bond or a double bond, provided that when --- is a single bond, V^1 is NR and V^2 is C(=O);

R and R' are each independently selected from the group consisting of H, halogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, saturated or partially unsaturated C_{3-10} cyclic hydrocarbyl, saturated or partially unsaturated 3- to 10-membered heterocyclyl, C_{6-10} aryl, 5- to 14-membered heteroaryl and C_{6-12} aralkyl, and at most 2 ring members in the cyclic hydrocarbyl and heterocyclyl are C(=O);

R^1, R^2, R^3 and R^6 are each independently selected from the group consisting of H, halogen, -CN, $-NO_2$, $-NH_2$, -OH, -SH, -Se-R, $-Si(R)_3$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, saturated or partially unsaturated C_{3-10} cyclic hydrocarbyl, saturated or partially unsaturated 3- to 10-membered heterocyclyl, C_{6-10} aryl, 5- to 14-membered heteroaryl, C_{6-12} aralkyl, C_{1-6} haloalkyl, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)OR^a$, $-OR^a$, $-SR^a$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^b$, $-S(=O)(=NR)R^a$, $-NR^aR^b$, $-C(=O)NR^aR^b$, $-C(=S)NR^aR^b$, $-C(=NR)NR^aR^b$, $-NR^a-C(=O)R^b$, $-NR^a-C(=O)OR^b$, $-NR^a-S(=O)_2-R^b$, $-NR^a-C(=O)-NR^aR^b$, $-C_{1-6}$ alkylene-NR^aR^b, $-C_{1-6}$ alkylene-OR^a, $-C_{1-6}$ alkylene-C(=O)R, $-C_{1-6}$ alkenylene-OR^a, -O-C_{1-6} alkylene-NR^aR^b and $-P(=O)R^aR^b$;

R^4 and R^5 are each independently selected from the group consisting of H, $-C(=O)OR^a$, $-NR^aR^b$, $-NR^a-C(=O)R^b$, $-NR^a-C(=O)OR^b$, $-C_{1-6}$ alkylene-NR^aR^b, $-C_{1-6}$ alkylene-OR^a, $-C_{1-6}$ alkylene-O-C_{1-6} alkylene-OR^a, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, saturated or partially unsaturated C_{3-10} cyclic hydrocarbyl, saturated or partially unsaturated 3- to 10-membered heterocyclyl, C_{6-10} aryl, 5- to 14-membered heteroaryl and C_{6-12} aralkyl;

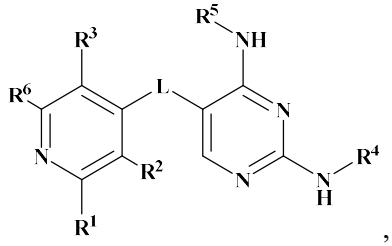
alternatively, R^1 and R^4 together form -NH-(C_{1-6} alkylene)-L-(C_{1-6} alkylene)-, preferably $-NHCH_2CH_2-O-CH_2CH_2-$;

the above alkyl, alkylene, alkenyl, alkynyl, cyclic hydrocarbyl, heterocyclyl, aryl, heteroaryl and aralkyl, at each occurrence, are each optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxyl, oxo, amino, cyano, nitro, $-Si(R)_3$, C_{1-6} alkyl, saturated or partially unsaturated C_{3-6} cyclic hydrocarbyl, saturated or partially unsaturated 3- to 10-membered heterocyclyl, C_{6-10} aryl, 5- to 14-membered heteroaryl, C_{6-12} aralkyl, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)OR^a$, $-OR^a$, $-SR^a$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2NR^aR^b$, $-NR^aR^b$, $-C(=O)NR^aR^b$, $-NR^a-C(=O)R^b$, $-NR^a-C(=O)OR^b$, $-NR^a-S(=O)_2-R^b$, $-NR^a-C(=O)-NR^aR^b$, $-C_{1-6}$ alkylene-NR^aR^b, $-C_{1-6}$ alkylene-OR^a, $-C_{1-6}$ alkenylene-OR^a and -O-C_{1-6} alkylene-NR^aR^b, the alkyl, cyclic hydrocarbyl, heterocyclyl, aryl, heteroaryl and aralkyl are further optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxyl, oxo, amino, cyano, nitro, $-NR^aR^b$, C_{1-6} alkyl, -O-C_{1-6} alkyl, saturated or partially unsaturated C_{3-6} cyclic hydrocarbyl, saturated or partially unsaturated 3- to 10-membered heterocyclyl, C_{6-10} aryl, 5- to 14-membered heteroaryl and C_{6-12} aralkyl; and

R^a and R^b, at each occurrence, are each independently selected from the group consisting of H, -OH, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, saturated or partially unsaturated C_{3-10} cyclic hydrocarbyl, saturated or partially unsaturated 3- to 10-membered heterocyclyl, C_{6-10} aryl, 5- to 14-membered heteroaryl and C_{6-12} aralkyl; alternatively, R^a and R^b together with the atom to which they are attached form a 3- to 12-membered heterocycle or heteroaromatic ring, the above groups are further optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxyl, oxo, amino, cyano, nitro, C_{1-6} alkyl, -O-C_{1-6} alkyl, saturated or partially unsaturated C_{3-6} cyclic hydrocarbyl,

saturated or partially unsaturated 3- to 10-membered heterocyclyl, C_{6-10} aryl, 5- to 14-membered heteroaryl and C_{6-12} aralkyl.

~~[~~Claim 2~~]~~. The use according to claim 1, wherein the compound has the structure of any of the following formulae: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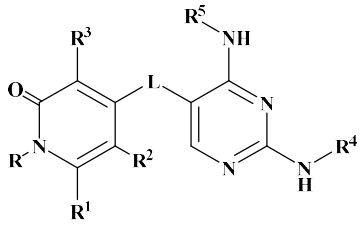
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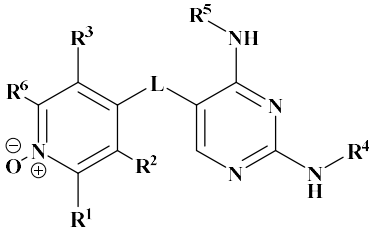
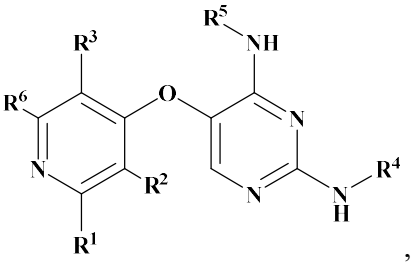


(II) (III) (IV);

Claim 3. The use according to claim 1 or 2, wherein the compound~~preferably~~ has the structure of any of the following formulae: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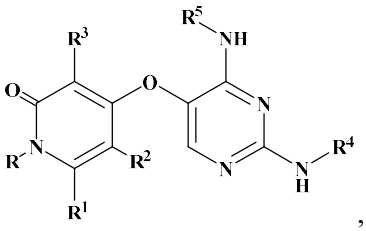
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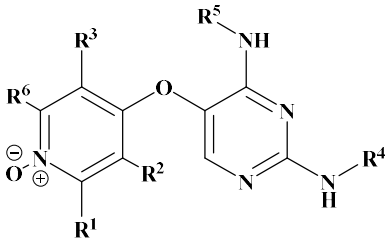
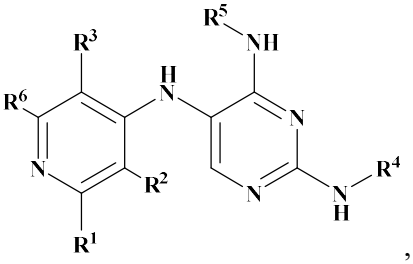


(II') (III') (IV')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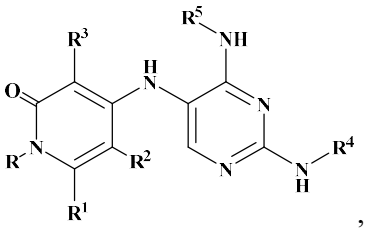
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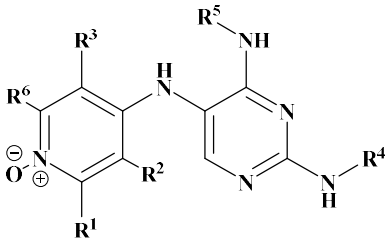
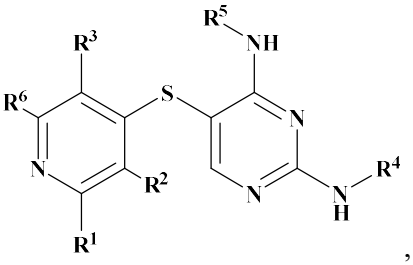


(II'') (III'') (IV'')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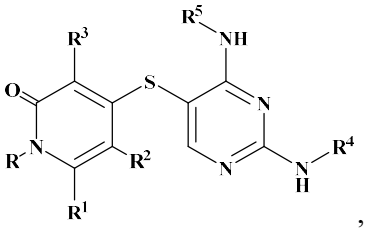
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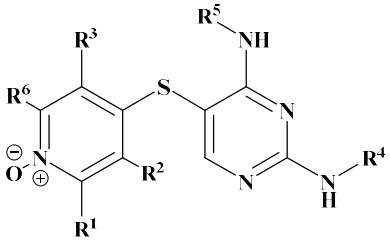
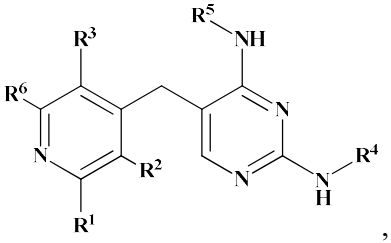


(II''') (III''') (IV''')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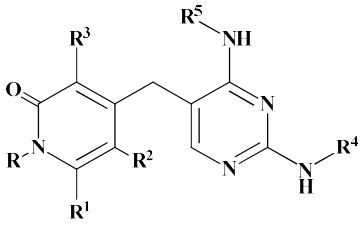
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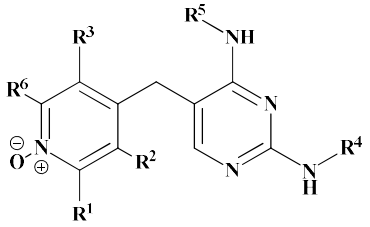
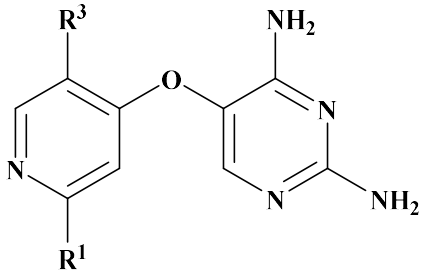


(II'''') (III'''') (IV'''');

Claim 4. The use according to any one of claims 1 to 3, wherein ~~more preferably,~~ the compound of Formula (I) has the structure of any of the following formulae:



(II'-1)

wherein:

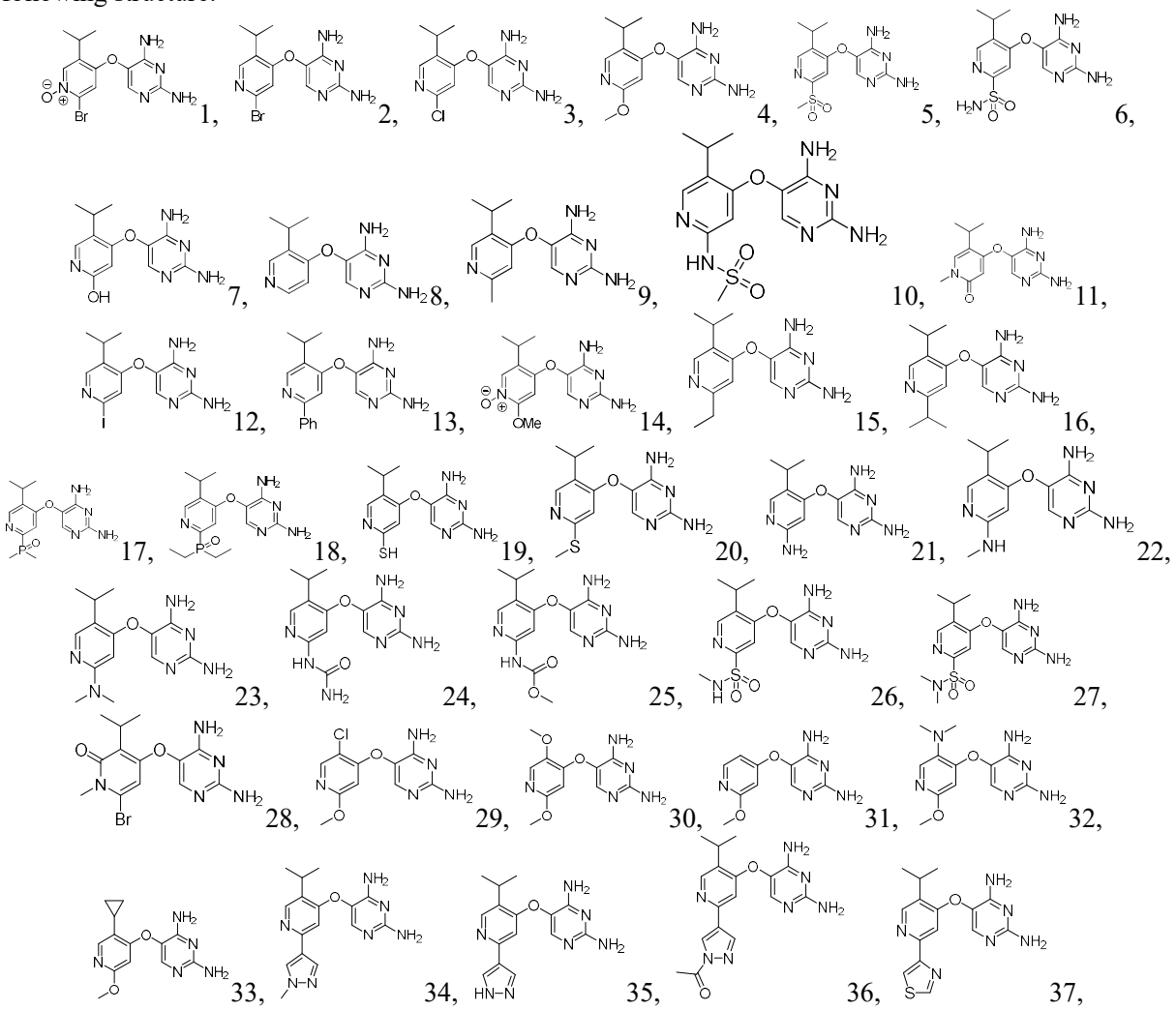
R^1 is selected from the group consisting of F, Cl, Br, I and C_{2-6} alkynyl~~, preferably Br or ethynyl~~; and

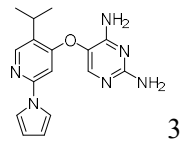
R^3 is C_{1-6} alkyl, preferably isopropyl.

Claim 5. The use according to any one of claims 1 to 4, wherein R^1 is Br or ethynyl.

Claim 6. The use according to any one of claims 1 to 5, wherein R^3 is isopropyl.

Claim ~~3~~7. The ~~method~~ use according to any one of claims 1 to~~r~~ ~~2~~6, wherein the compound has the following structure:

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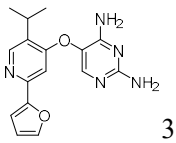
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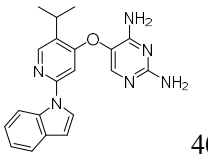
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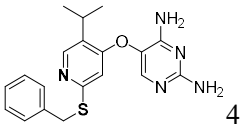
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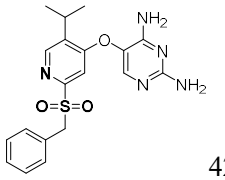
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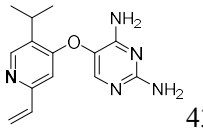
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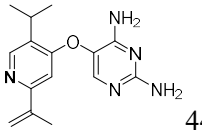
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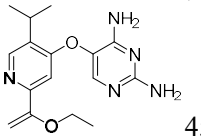
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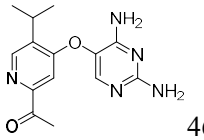
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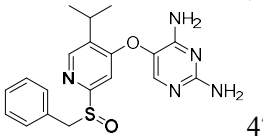
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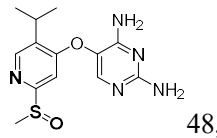
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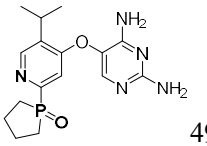
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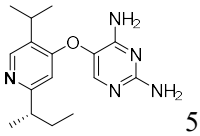
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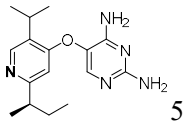
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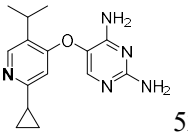
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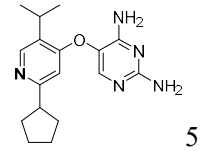
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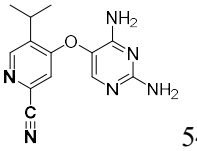
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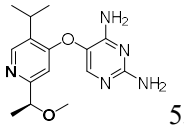
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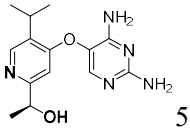
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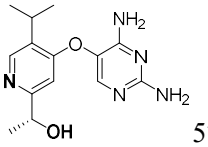
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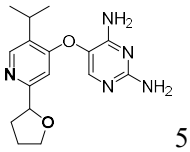
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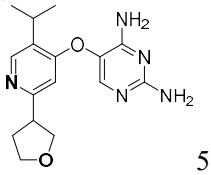
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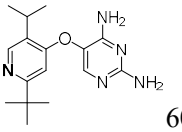
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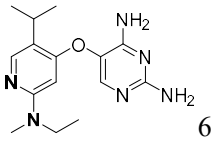
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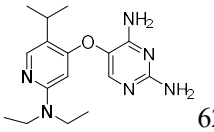
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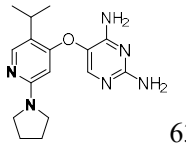
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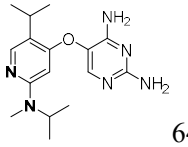
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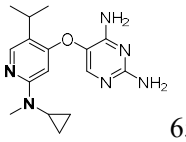
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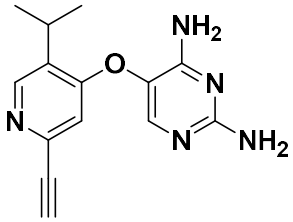
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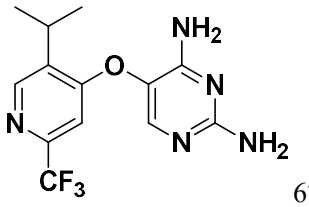
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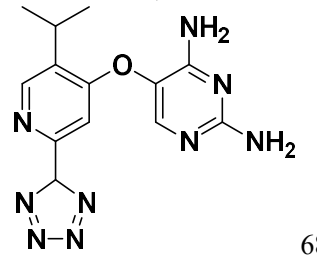
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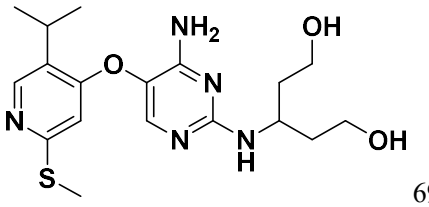
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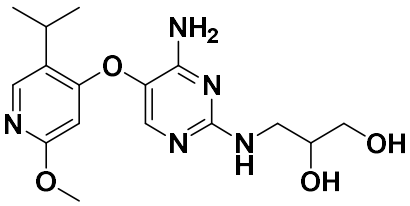
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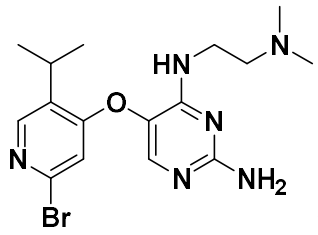
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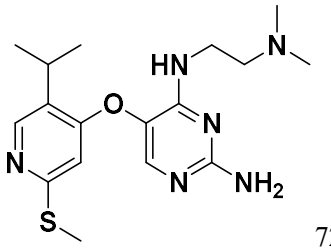
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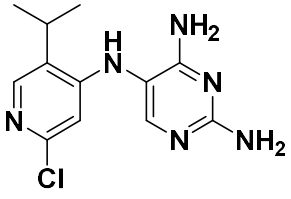
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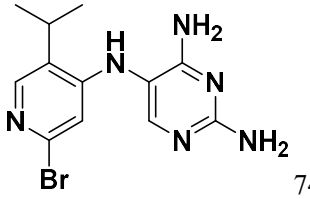
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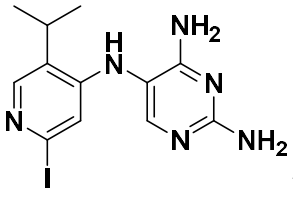
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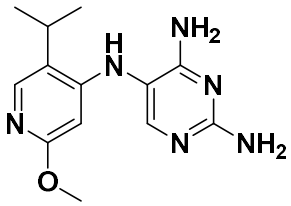
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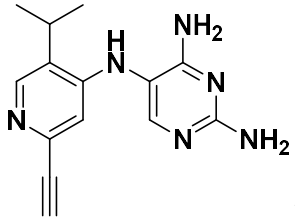
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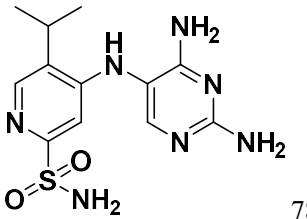
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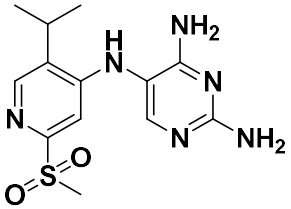
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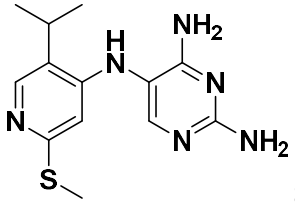
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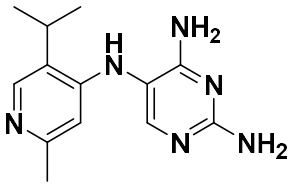
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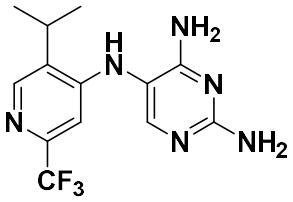
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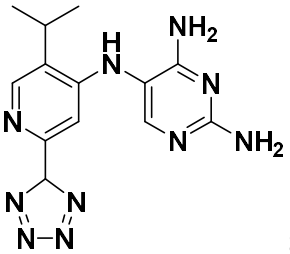
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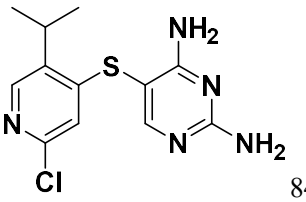
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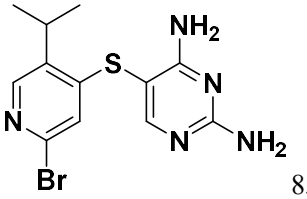
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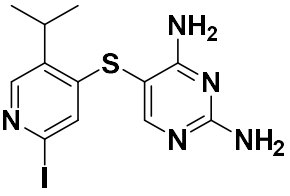
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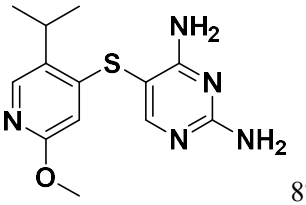
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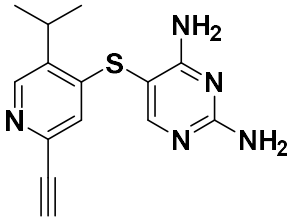
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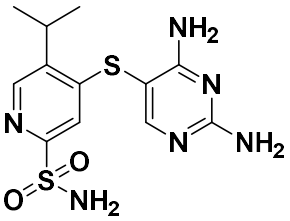
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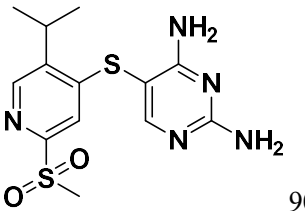
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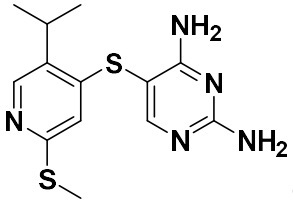
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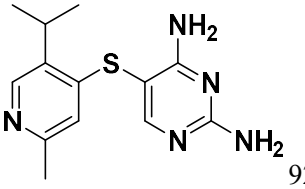
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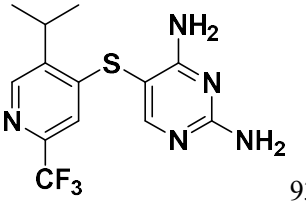
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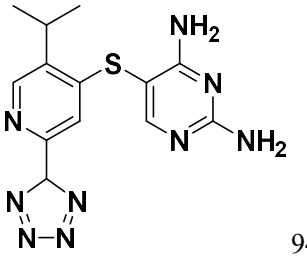
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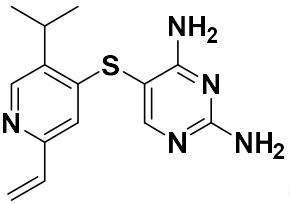
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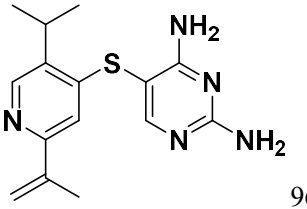
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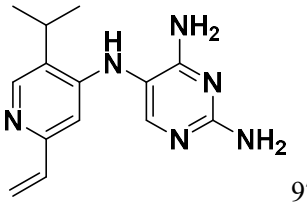
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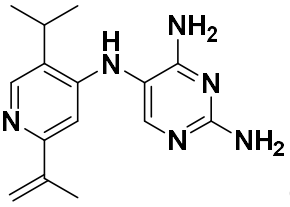
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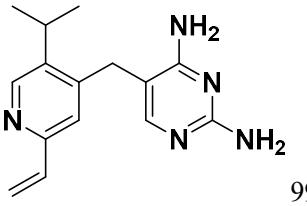
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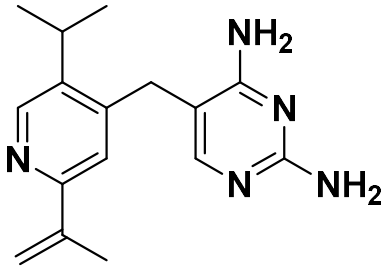
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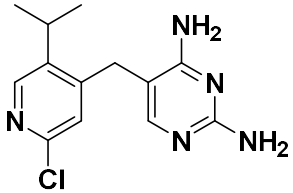
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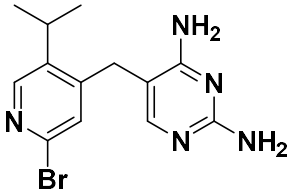
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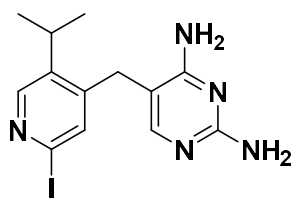
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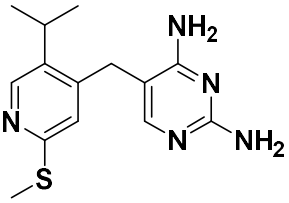
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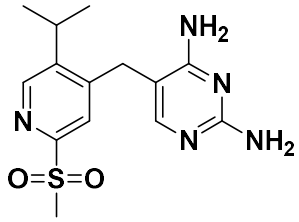
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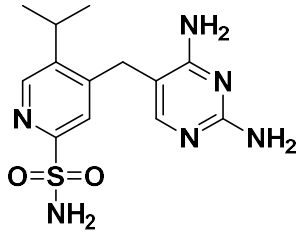
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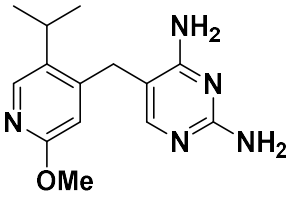
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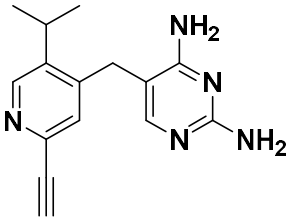
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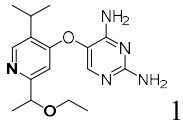
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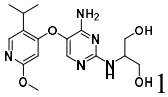
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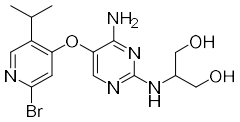
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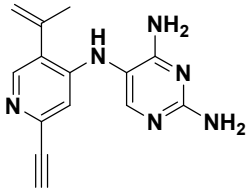
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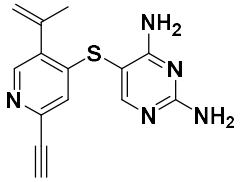
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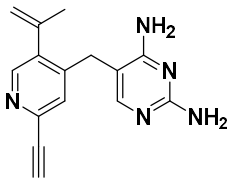
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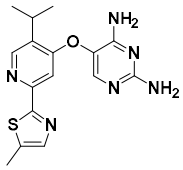
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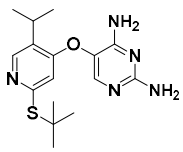
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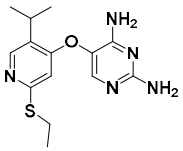
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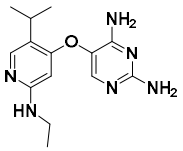
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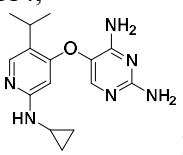
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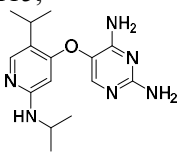
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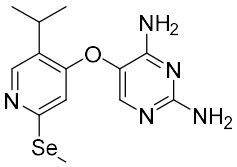
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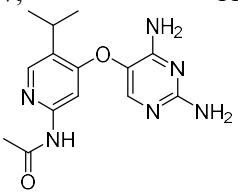
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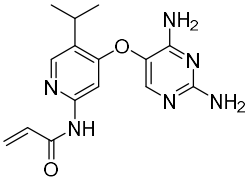
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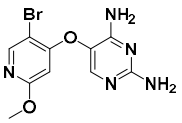
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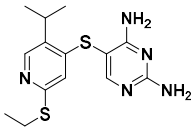
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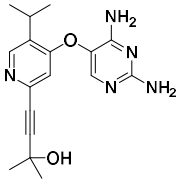
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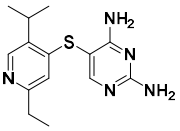
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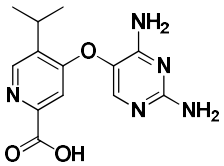
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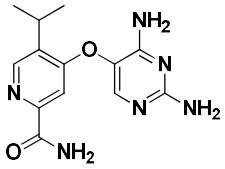
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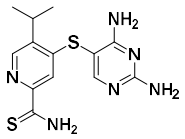
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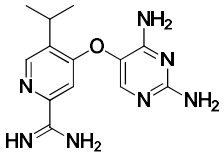
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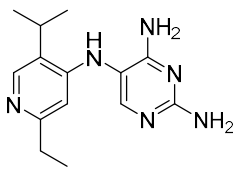
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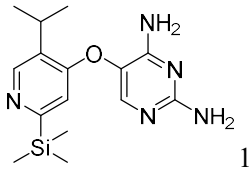
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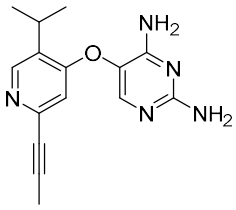
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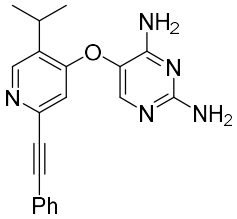
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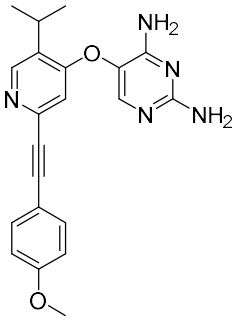
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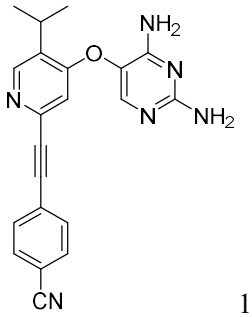
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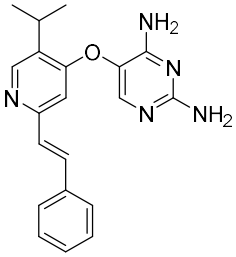
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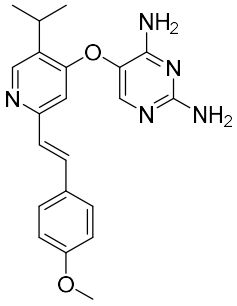
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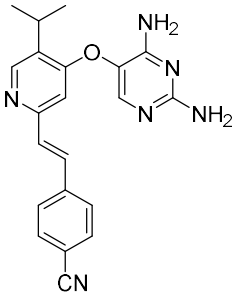
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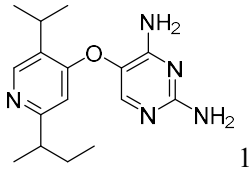
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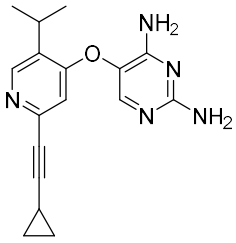
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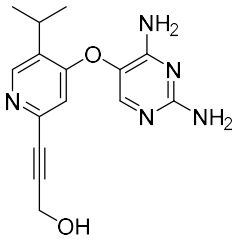
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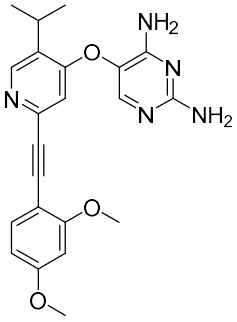
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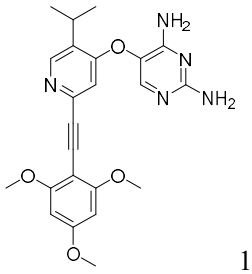
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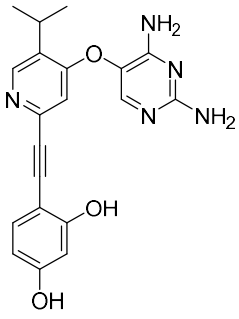
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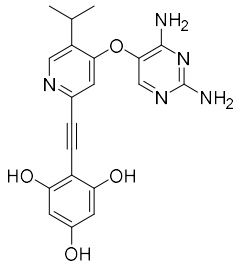
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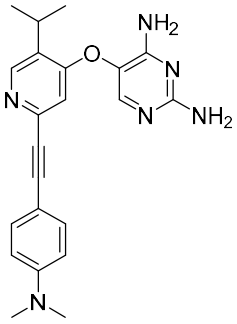
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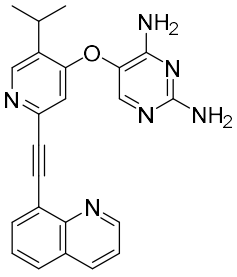
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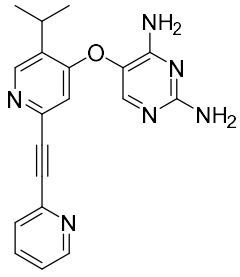
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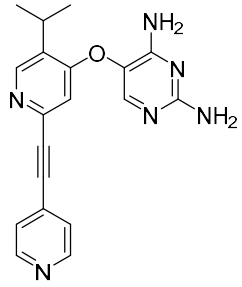
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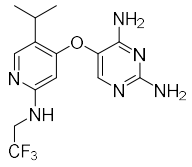
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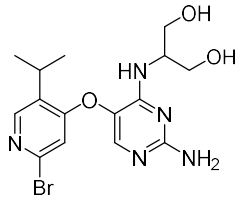
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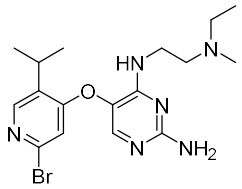
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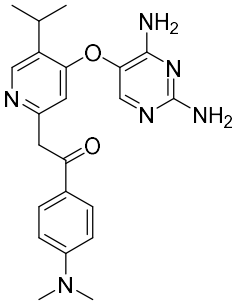
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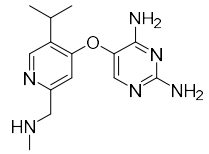
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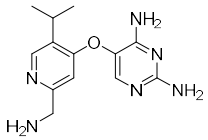
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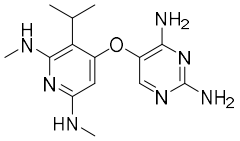
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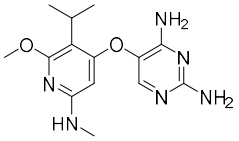
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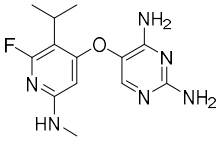
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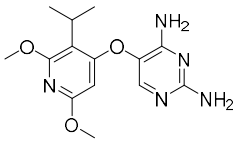
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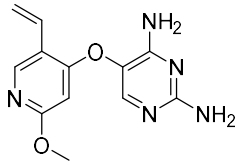
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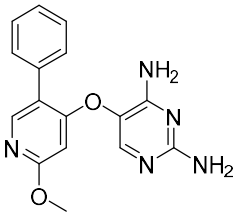
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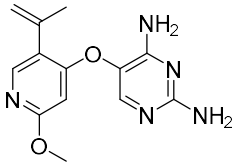
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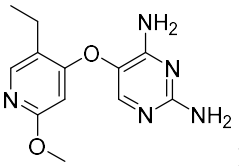
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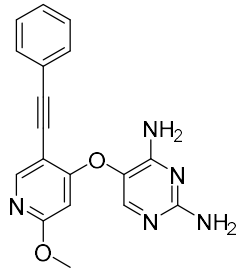
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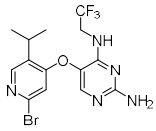
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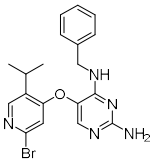
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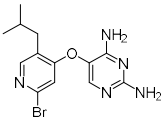
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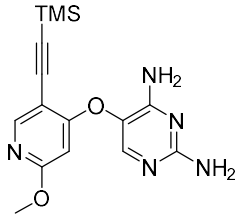
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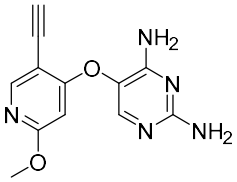
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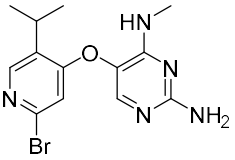
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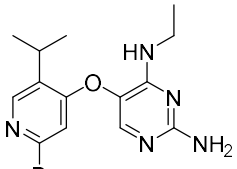
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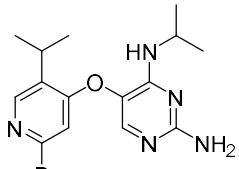
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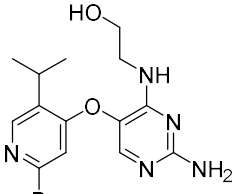
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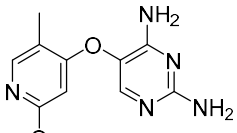
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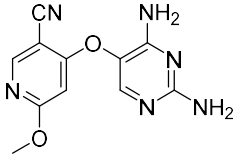
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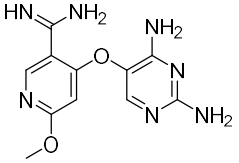
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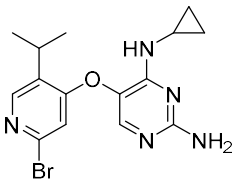
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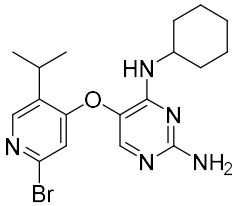
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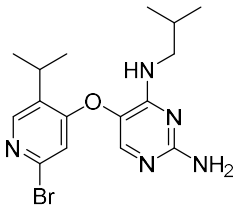
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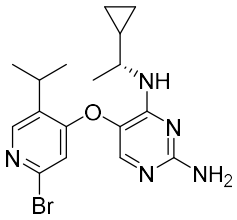
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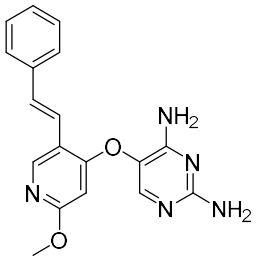
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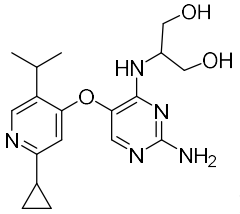
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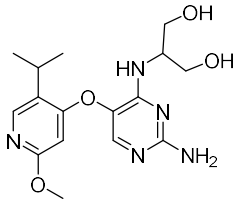
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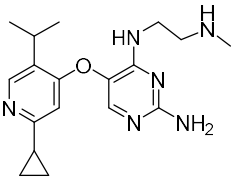
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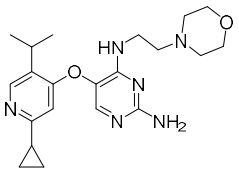
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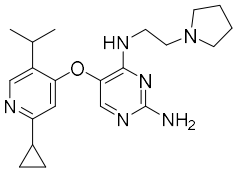
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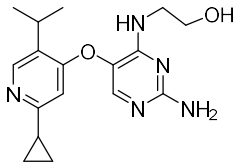
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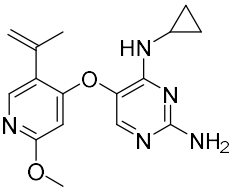
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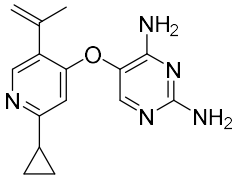
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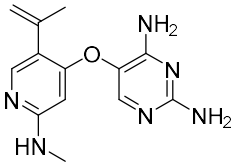
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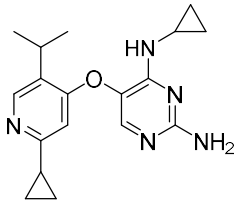
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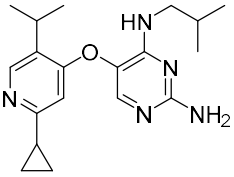
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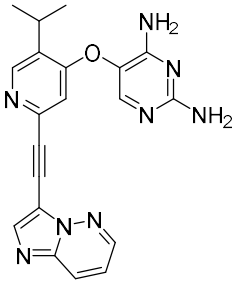
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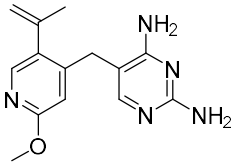
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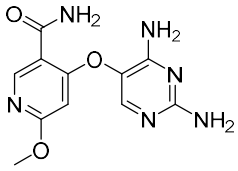
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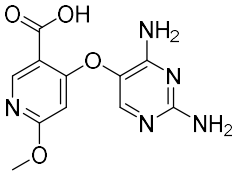
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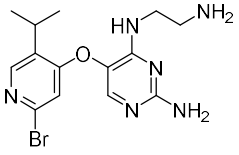
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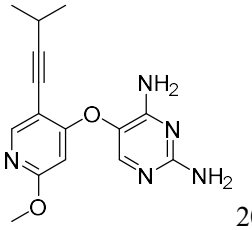
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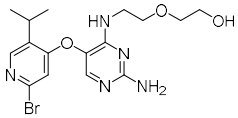
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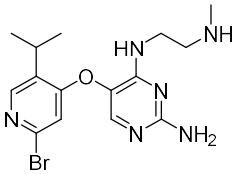
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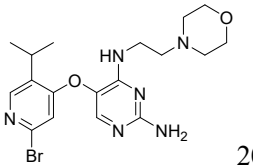
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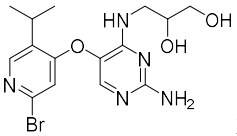
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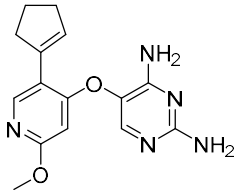
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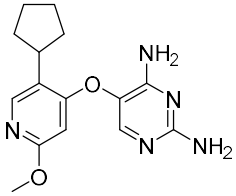
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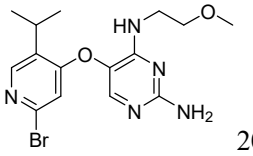
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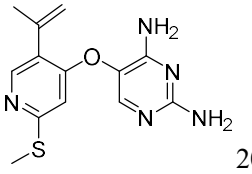
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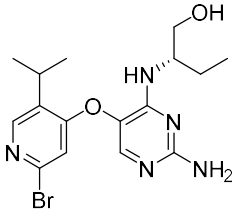
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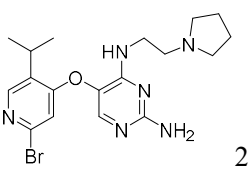
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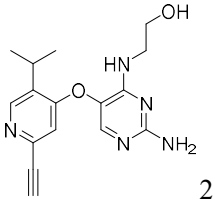
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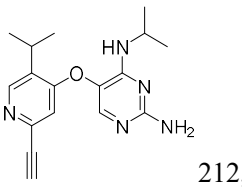
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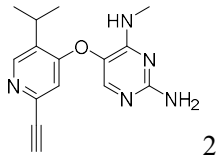
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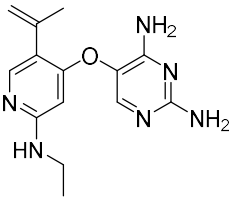
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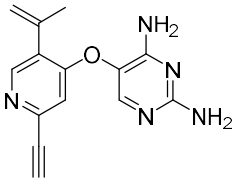
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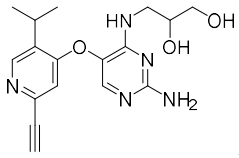
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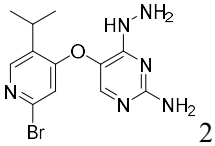
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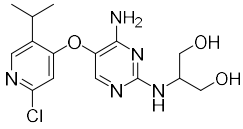
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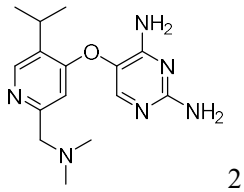
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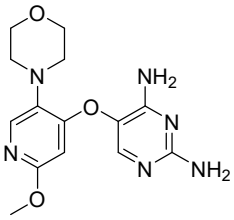
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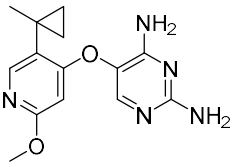
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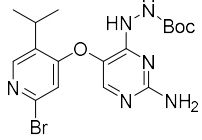
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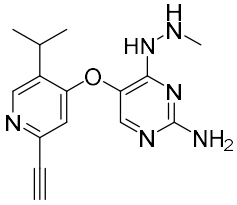
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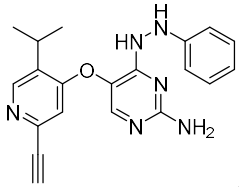
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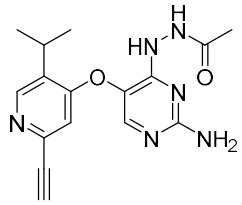
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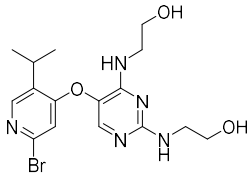
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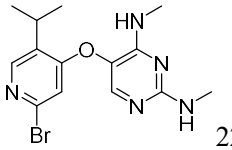
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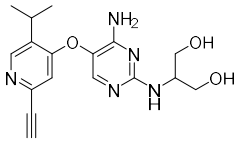
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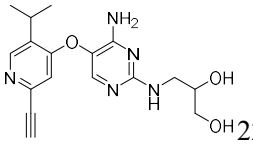
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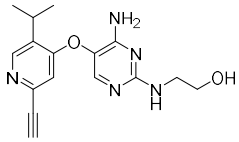
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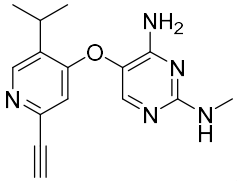
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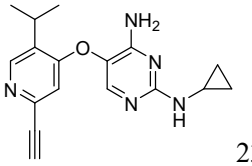
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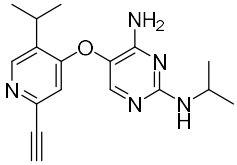
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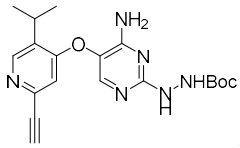
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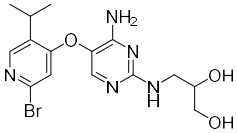
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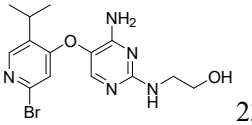
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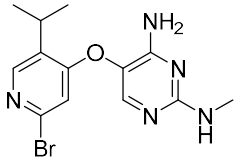
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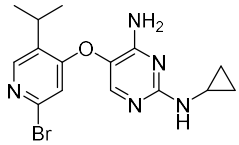
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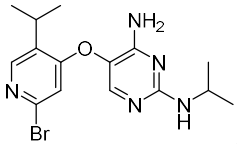
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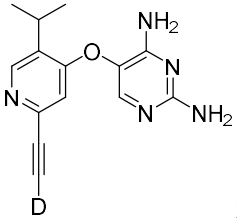
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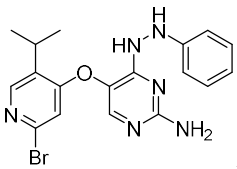
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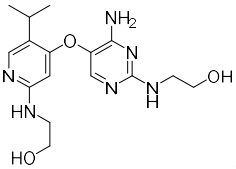
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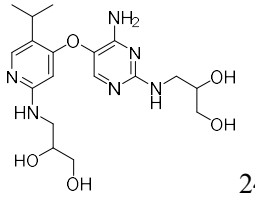
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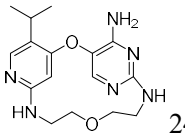
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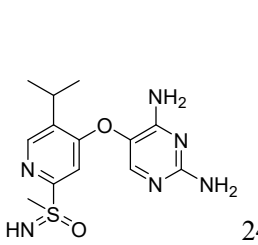
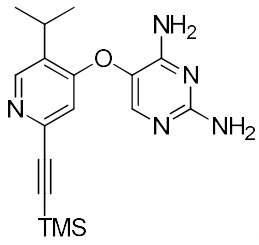
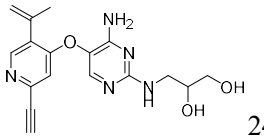
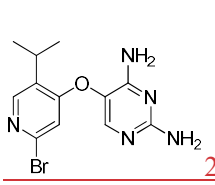


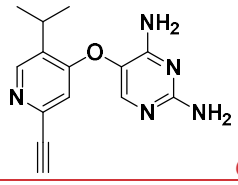
245,


246 or


247.

Claim 8. The use according to any one of claims 1 to 7, wherein the compound has the following structure:



2, or


66.

[Claim 94]. The use according to any one of claims 1 to 38, wherein the compound of Formula (I) or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound, metabolite or prodrug thereof is to be administered in an amount of about 0.005 mg/day to about 5000 mg/day, e.g., in an amount of about 0.005, 0.05, 0.5, 5, 10, 20, 30, 40, 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1500, 2000, 2500, 3000, 3500, 4000, 4500 or 5000 mg/day.

[Claim 105]. The use according to any one of claims 1 to 38, wherein the compound of Formula (I) or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound, metabolite or prodrug thereof is to be administered in an amount of about 1 ng/kg to about 200 mg/kg, about 1 μg/kg to about 100 mg/kg or about 1 mg/kg to about 50 mg/kg per day, e.g., is to be administered in an amount of about 1 μg/kg, about 10 μg/kg, about 25 μg/kg, about 50 μg/kg, about 75 μg/kg, about 100 μg/kg, about 125 μg/kg, about 150 μg/kg, about 175 μg/kg, about 200 μg/kg, about 225 μg/kg, about 250 μg/kg, about 275 μg/kg, about 300 μg/kg, about 325 μg/kg, about 350 μg/kg, about 375 μg/kg, about 400 μg/kg, about 425 μg/kg, about 450 μg/kg, about 475 μg/kg, about 500 μg/kg, about 525 μg/kg, about 550 μg/kg, about 575 μg/kg, about 600 μg/kg, about 625 μg/kg, about 650 μg/kg, about 675 μg/kg, about 700 μg/kg, about 725 μg/kg, about 750 μg/kg, about 775 μg/kg, about 800 μg/kg, about 825 μg/kg, about 850 μg/kg, about 875 μg/kg, about 900 μg/kg, about 925 μg/kg, about 950 μg/kg, about 975 μg/kg, about 1 mg/kg, about 5 mg/kg, about 10 mg/kg, about 15 mg/kg, about 20 mg/kg, about 25 mg/kg, about 30 mg/kg, about 35 mg/kg, about 40 mg/kg, about 45 mg/kg, about 50 mg/kg, about 60 mg/kg, about 70 mg/kg, about 80 mg/kg, about 90 mg/kg, about 100 mg/kg, about 125 mg/kg, about 150 mg/kg, about 175 mg/kg, about 200 mg/kg body weight per unit dose.

[Claim 116]. The use according to any one of claims 1 to 510, wherein the daily dose of the compound of Formula (I) or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound, metabolite or prodrug thereof is to be administered at one time or is to be administered in two, three or four doses.

[Claim 127]. The use according to any one of claims 1 to 611, wherein the compound of Formula (I) or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound, metabolite or prodrug thereof is to be administered continuously for at least 3 days, at least 4 days, at least 5 days, at least 6 days, at least 7 days, at least 8 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, at least 15 days, at least 16 days, at least 17 days, at least 18 days, at least 19 days, at least 20 days, at least 21 days, at least 22 days, at least 23 days, at least 24 days, at least 25 days, at least 30 days, at least 35 days, at least 40 days, at least 45 days, at least 50 days, at least half a year, at least 1 year, at least 2 years, at least 3 years, at least 4 years, or at least 5 years.

[Claim 138]. The use according to any one of claims 1 to 712, wherein the compound of Formula (I) or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically

labeled compound~~, metabolite or prodrug~~ thereof is to be administered for one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) courses of treatment, wherein each course of treatment lasts for at least 3 days, at least 4 days, at least 5 days, at least 6 days, at least 7 days, at least 8 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, at least 15 days, at least 16 days, at least 17 days, at least 18 days, at least 19 days, at least 20 days, at least 21 days, at least 22 days, at least 23 days, at least 24 days, at least 25 days, at least 30 days, at least 35 days, at least 40 days, at least 45 days or at least 50 days; and the interval between every two courses of treatment is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 days, two weeks, three weeks, or four weeks.

~~[~~Claim 149~~]~~. The use according to any one of claims 1 to ~~8~~13, wherein the compound of Formula (I) or a

pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound~~, metabolite or prodrug~~ thereof is to be administered through injection (e.g., intravenous, intraarterial, subcutaneous, intraperitoneal, intramuscular injection, including dripping), or transdermal administration, or is to be administered via oral, buccal, nasal, transmucosal, or topical route, as an ophthalmic formulation, or via inhalation.

~~[~~Claim 15~~10]~~. The use according to any one of claims 1 to ~~9~~14, wherein the compound of Formula (I) or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound~~, metabolite or prodrug~~ thereof is to be administered in a dosage form selected from the group consisting of tablet, capsule, lozenge, hard candy, powder, spray, emulsion, cream, salve, suppository, gel, paste, lotion, injection, nanoformulation, patch, aqueous suspension, solution, elixir, and syrup.

~~[~~Claim 16~~11]~~. The ~~method~~ use according to any one of claims 1 to ~~10~~15, wherein the cough is selected from the group consisting of acute cough, sub-acute cough, chronic cough, treatment-resistant cough, treatment-resistant chronic cough, idiopathic chronic cough, post-viral cough, iatrogenic cough, cough associated with post-nasal drip, cough associated with cold, upper respiratory infection, asthma, lung cancer and/or chronic obstructive pulmonary disease (COPD), cough associated with interstitial disease, cough associated with pulmonary fibrosis, cough associated with gastroesophageal reflux disease (GERD), cough associated with smoking or a form of bronchitis, and neuronal hypersensitivity underlying acute, sub-acute or chronic cough.~~; preferably,~~

Claim 17. The use according to any one of claims 1 to 16, wherein the cough is selected from the group consisting of chronic cough, treatment-resistant cough, treatment-resistant chronic cough, and cough associated with pulmonary fibrosis.