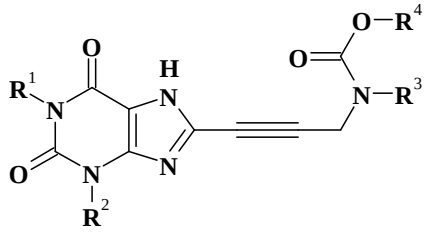
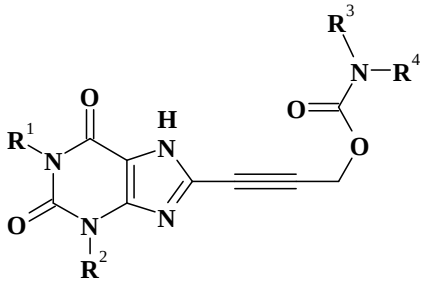
WHAT IS CLAIMED IS:

1. A compound of Formula I or II or a stereoisomer or pharmaceutically acceptable salt thereof:



I



II

wherein:

R^1 is selected from: C_{1-5} alkyl, -C_{2-5} alkylene–OH, -C_{2-5} alkylene-O-C_{1-5} alkyl, C_{3-6} cycloalkyl, -C_{1-3} alkylene-C_{3-6} cycloalkyl, -CH_2-C_{2-4} alkenyl, -CH_2-C_{2-4} alkynyl, and -C_{3-6} cycloalkylene-O-C_{1-3} alkyl;

R^2 is selected from: C_{1-5} alkyl, -C_{2-5} alkylene–OH, -C_{2-5} alkylene-O-C_{1-5} alkyl, C_{3-6} cycloalkyl, -C_{1-3} alkylene-C_{3-6} cycloalkyl, -CH_2-C_{2-4} alkenyl, -CH_2-C_{2-4} alkynyl, and -C_{3-6} cycloalkylene-O-C_{1-3} alkyl;

R^3 is selected from: C_{1-6} alkyl, -C_{2-5} alkylene-O-C_{1-5} alkyl, -C_{2-5} alkylene-S-C_{1-5} alkyl, -C_{2-5} alkylene-NR^aR^b, -C_{2-5} alkylene-OH, -C_{2-5} alkylene-SH, -C_{2-5} alkylene-NR^aR^b, C_{3-6} cycloalkyl, and, -C_{1-3} alkylene-C_{3-6} cycloalkyl;

R^4 is selected from: phenyl and 5-6 membered heteroaryl;

the phenyl and heteroaryl groups of R^4 are optionally substituted with 1-3 groups independently selected from: C_{1-4} alkyl, C_{3-6} cycloalkyl, -C_{1-3} alkylene-C_{3-6} cycloalkyl, F, Cl, Br, I, -CN, OR^a, SR^a, NR^aR^b, CF_3, OCF_3, COR^a, CO_2R^a, $C(O)NR^aR^b$, $OC(O)R^a$, OCO_2R^a, $OC(O)NR^aR^b$, NR^bCOR^a, $NR^bCO_2R^a$, $NR^bC(O)NR^aR^b$, and $S(O)_pNR^aR^b$;

each R^a is independently selected from: H, C_{1-8} alkyl, C_{3-6} cycloalkyl, and -C_{1-3} alkylene-C_{3-6} cycloalkyl;

each R^b is independently selected from: H, C_{1-8} alkyl, C_{3-6} cycloalkyl, and -C_{1-3} alkylene-C_{3-6} cycloalkyl;

alternatively, each NR^aR^b group is optionally selected from a 3-6 membered cyclic amine; and,

p is independently selected from: 0, 1, and 2.

2. A compound of Claim 1, wherein the compound is of Formula I or a stereoisomer or pharmaceutically acceptable salt thereof.

3. A compound of Claim 2, wherein:

R^1 is selected from: C_{1-3} alkyl and C_{3-6} cycloalkyl;

R^2 is selected from: C_{1-3} alkyl and C_{3-6} cycloalkyl;

R^3 is selected from: C_{1-6} alkyl and -C_{1-3} alkylene-C_{3-6} cycloalkyl;

R^4 is selected from: phenyl and 5-6 membered heteroaryl;

the phenyl and heteroaryl groups of R^4 are optionally substituted with 1-2 groups independently selected from: C_{1-4} alkyl, C_{3-6} cycloalkyl, -C_{1-3} alkylene-C_{3-6} cycloalkyl, F, Cl, Br, I, -CN, OR^a, SR^a, NR^aR^b, CF_3, OCF_3, COR^a, CO_2R^a, $C(O)NR^aR^b$, $OC(O)R^a$, OCO_2R^a, $OC(O)NR^aR^b$, NR^bCOR^a, $NR^bCO_2R^a$, $NR^bC(O)NR^aR^b$, and $S(O)_pNR^aR^b$;

each R^a is independently selected from: H, C_{1-4} alkyl, C_{3-6} cycloalkyl, and -C_{1-3} alkylene-C_{3-6} cycloalkyl;

each R^b is independently selected from: H, C_{1-4} alkyl, C_{3-6} cycloalkyl, and -C_{1-3} alkylene-C_{3-6} cycloalkyl; and,

p is independently selected from: 0, 1, and 2.

4. A compound of Claim 3, wherein:

ring R^4 is selected from phenyl, pyridyl, thienyl, furanyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrimidyl, and pyridazinyl.

5. A compound of Claim 4, wherein:

ring R^4 is selected from phenyl and pyridyl.

6. A compound of Claim 5, wherein:

R^1 is selected from: methyl, ethyl, and cyclopropyl;

R^2 is selected from: methyl, ethyl, and cyclopropyl;

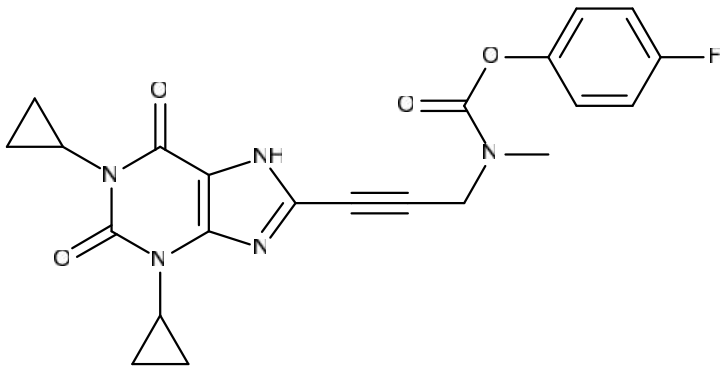
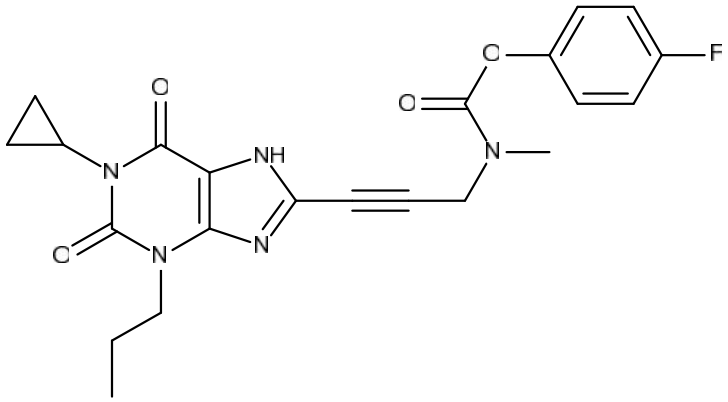
R^3 is selected from: methyl, ethyl, and –methylene-cyclopropyl;

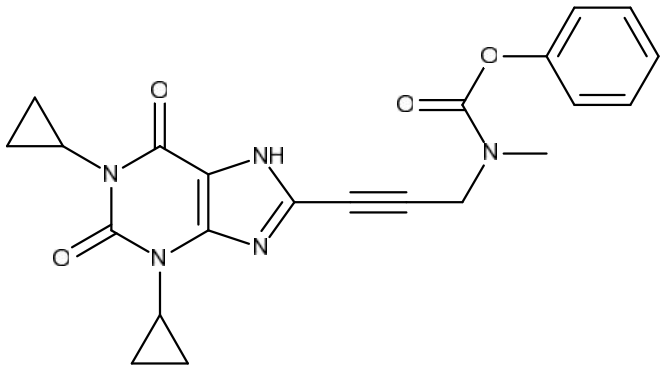
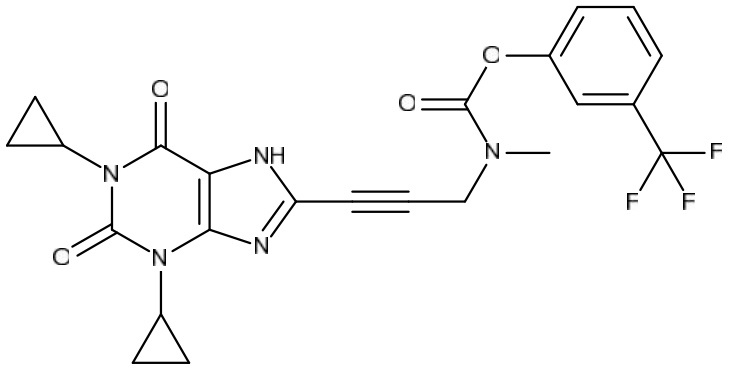
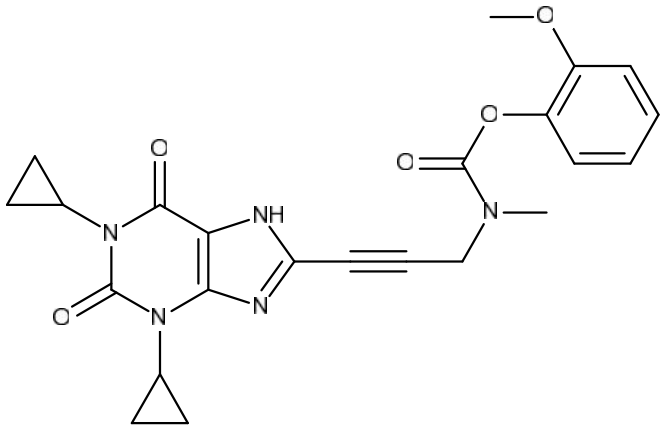
R^4 is phenyl optionally substituted with 1-2 groups independently selected from: C_{1-4} alkyl, C_{3-6} cycloalkyl, -C_{1-3} alkylene-C_{3-6} cycloalkyl, F, Cl, -CN, OR^a, NR^aR^b, CF_3, and OCF_3;

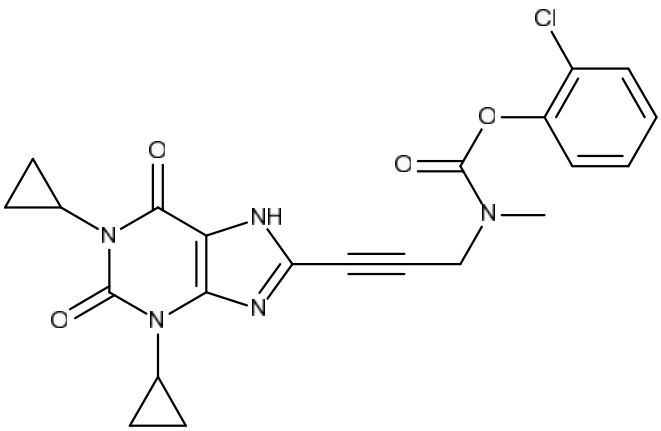
each R^a is independently selected from: H, methyl, and ethyl; and,

each R^b is independently selected from: H, methyl, and ethyl.

7. A compound of Claim 1, wherein the compound is selected from compounds 1-6:

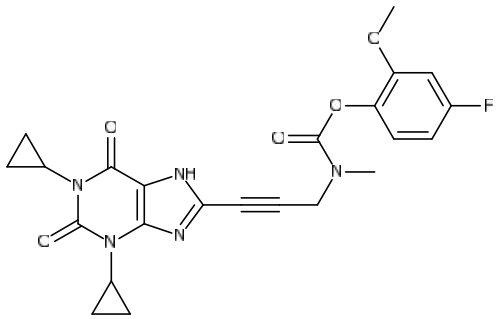
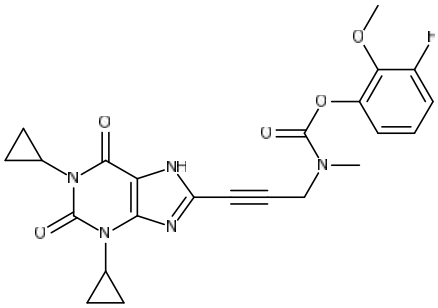
1	
2	

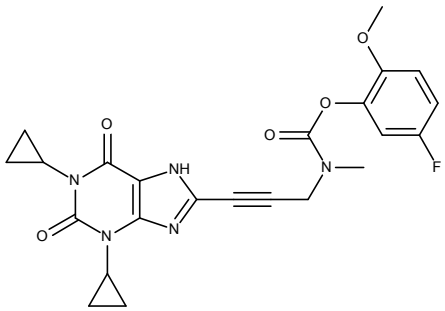
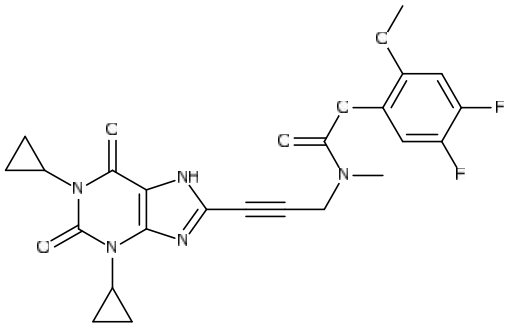
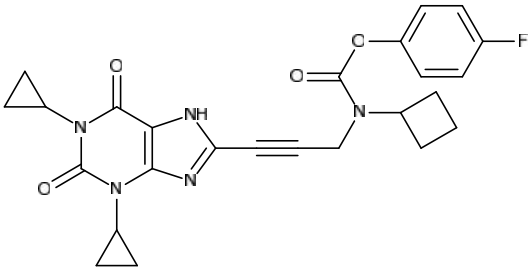
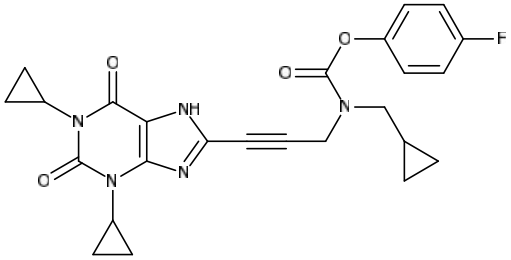
3	
4	
5	

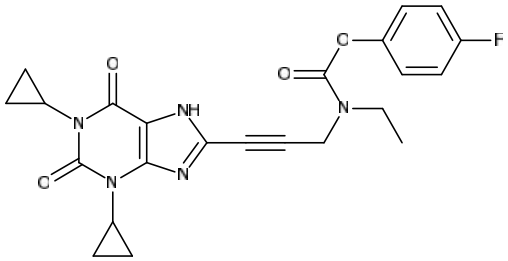
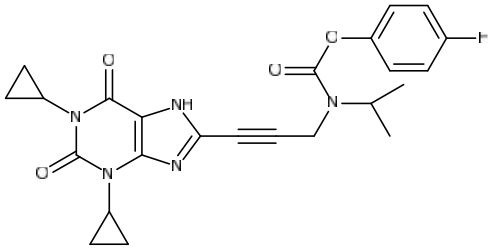
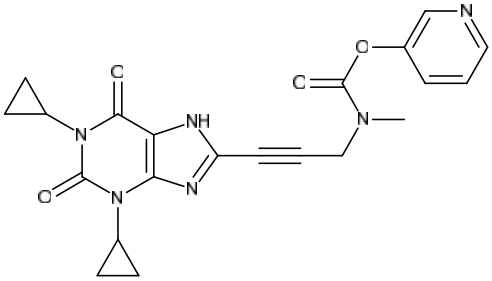
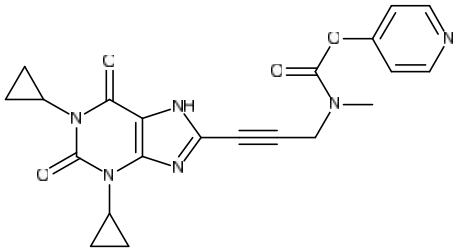
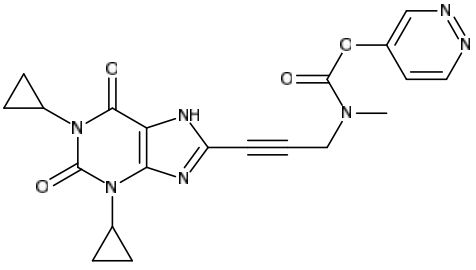
6	

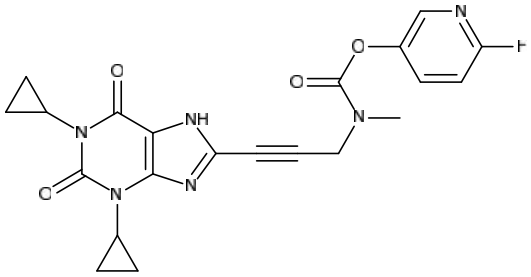
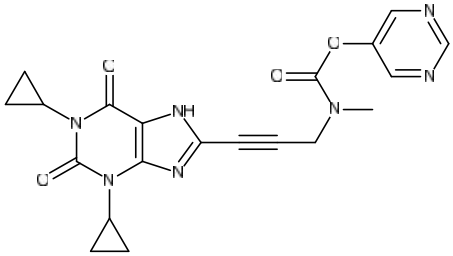
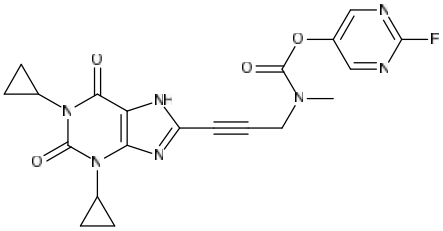
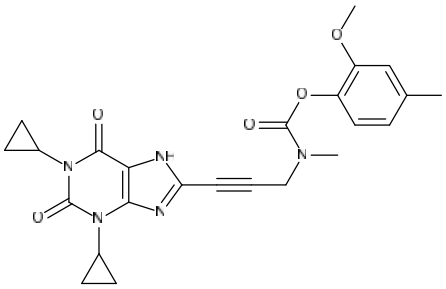
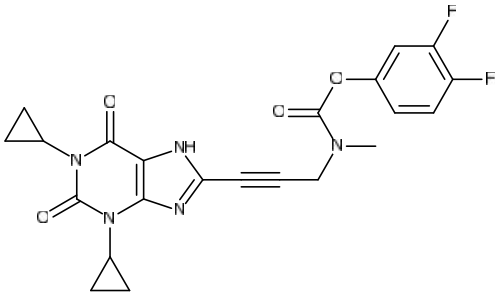
or a pharmaceutically acceptable salt thereof.

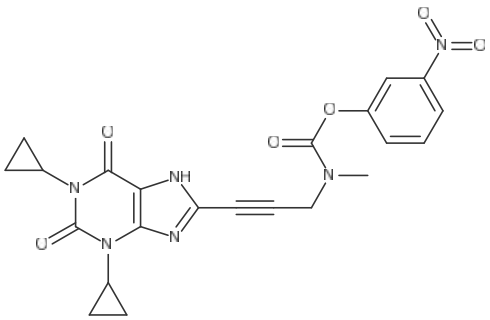
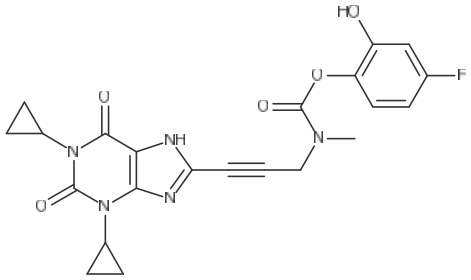
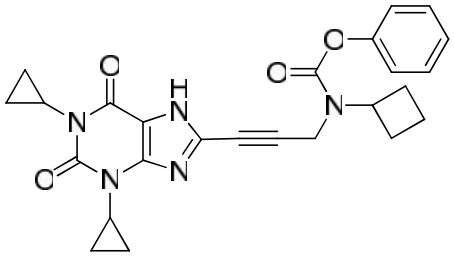
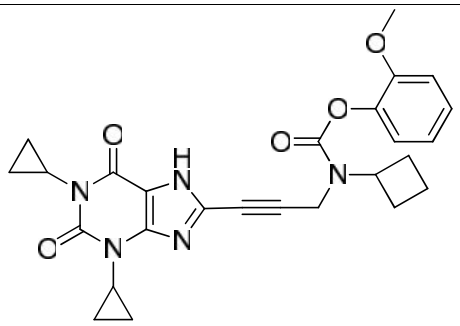
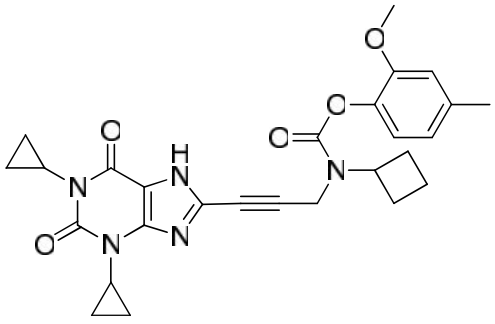
8. A compound of Claim 1, wherein the compound is selected from compounds 1-26:

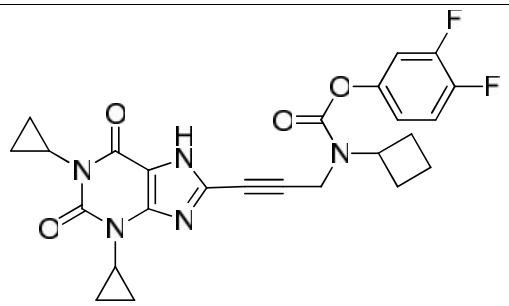
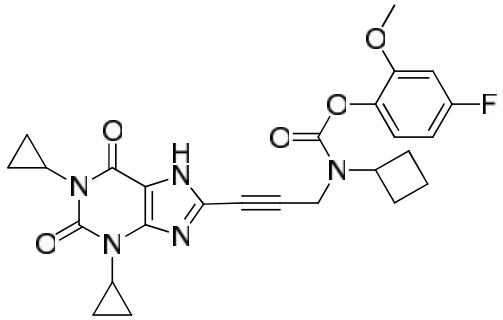
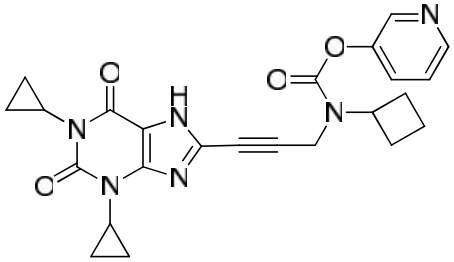
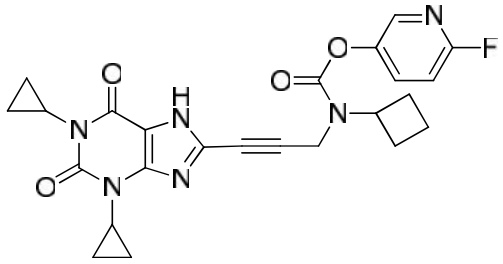
1	
2	

3	
4	
5	
6	

7	
8	
9	
10	
11	

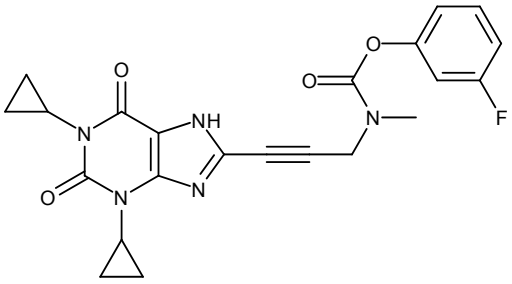
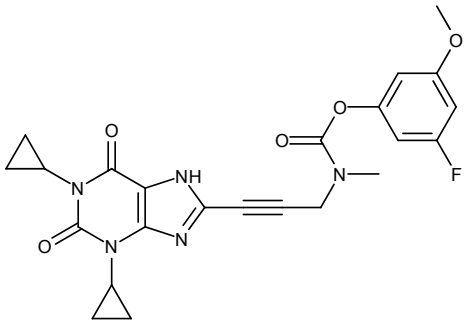
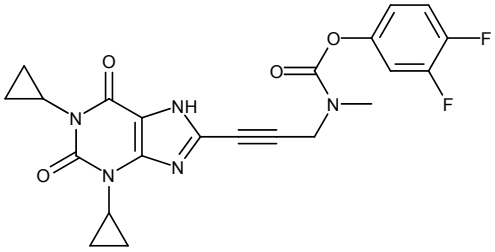
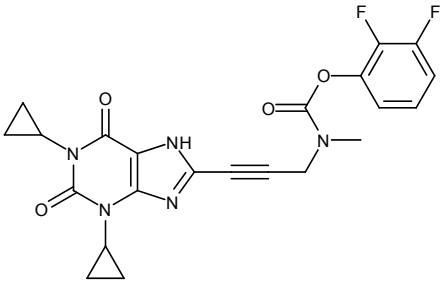
12	
13	
14	
15	
16	

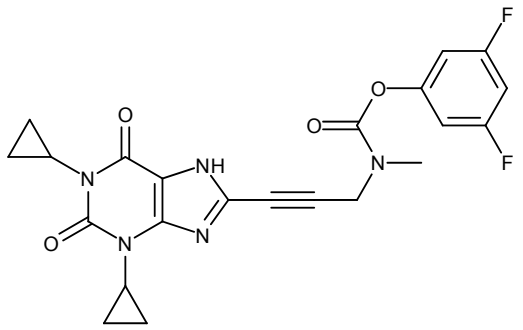
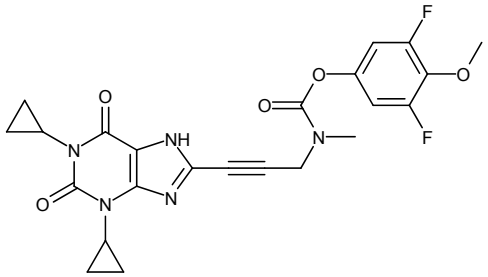
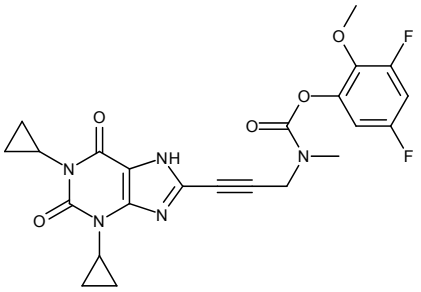
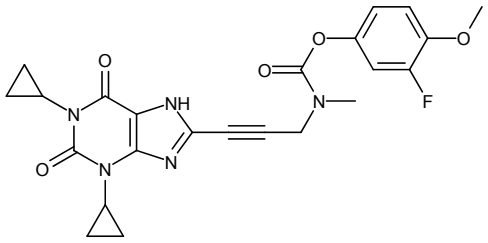
17	
18	
19	
21	
22	

23	
24	
25	
26	

or pharmaceutically acceptable salt thereof.

9. A compound of Claim 1, wherein the compound is selected from compounds 27-34:

27	
28	
29	
30	

31	
32	
33	
34	

or pharmaceutically acceptable salt thereof.

10. A compound of Claim 1, wherein the compound is of Formula II or a stereoisomer or pharmaceutically acceptable salt thereof.

11. A compound of Claim 10, wherein:

R^1 is selected from: C_{1-3} alkyl and C_{3-6} cycloalkyl;

R^2 is selected from: C_{1-3} alkyl and C_{3-6} cycloalkyl;

R^3 is selected from: C_{1-6} alkyl and -C_{1-3} alkylene-C_{3-6} cycloalkyl;

R^4 is selected from: phenyl and 5-6 membered heteroaryl;

the phenyl and heteroaryl groups of R^4 are optionally substituted with 1-2 groups independently selected from: C_{1-4} alkyl, C_{3-6} cycloalkyl, -C_{1-3} alkylene-C_{3-6} cycloalkyl, F, Cl, Br, I, -CN, OR^a, SR^a, NR^aR^b, CF_3, OCF_3, COR^a, CO_2R^a, $C(O)NR^aR^b$, $OC(O)R^a$, OCO_2R^a, $OC(O)NR^aR^b$, NR^bCOR^a, $NR^bCO_2R^a$, $NR^bC(O)NR^aR^b$, and $S(O)_pNR^aR^b$;

each R^a is independently selected from: H, C_{1-4} alkyl, C_{3-6} cycloalkyl, and -C_{1-3} alkylene-C_{3-6} cycloalkyl;

each R^b is independently selected from: H, C_{1-4} alkyl, C_{3-6} cycloalkyl, and -C_{1-3} alkylene-C_{3-6} cycloalkyl; and,

p is independently selected from: 0, 1, and 2.

12. A compound of Claim 11, wherein:

ring R^4 is selected from phenyl, pyridyl, thienyl, furanyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrimidyl, and pyridazinyl.

13. A compound of Claim 12, wherein:

ring R^4 is selected from phenyl and pyridyl.

14. A compound of Claim 13, wherein:

R^1 is selected from: methyl, ethyl, and cyclopropyl;

R^2 is selected from: methyl, ethyl, and cyclopropyl;

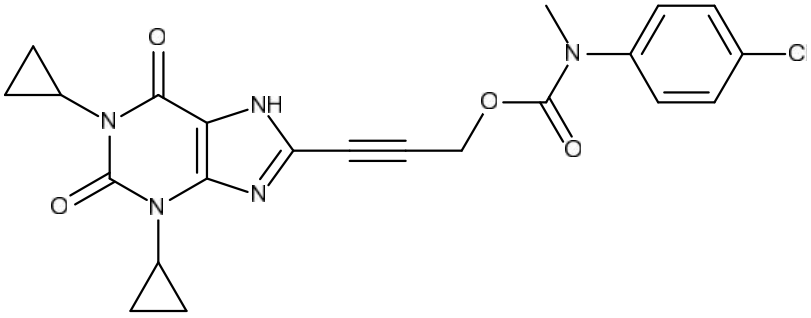
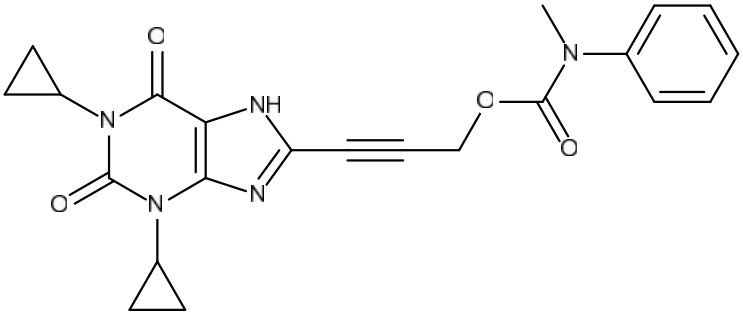
R^3 is selected from: methyl, ethyl, and –methylene-cyclopropyl;

R^4 is phenyl optionally substituted with 1-2 groups independently selected from: C_{1-4} alkyl, C_{3-6} cycloalkyl, -C_{1-3} alkylene-C_{3-6} cycloalkyl, F, Cl, -CN, OR^a, NR^aR^b, CF_3, and OCF_3;

each R^a is independently selected from: H, methyl, and ethyl; and,

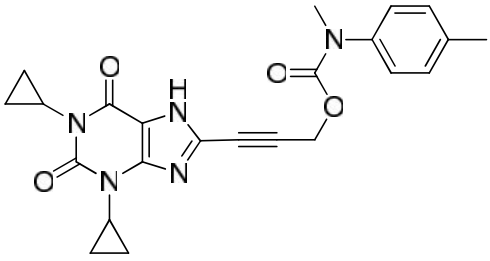
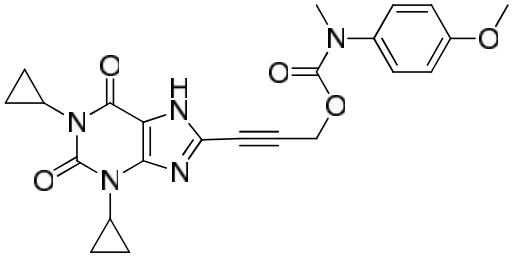
each R^b is independently selected from: H, methyl, and ethyl.

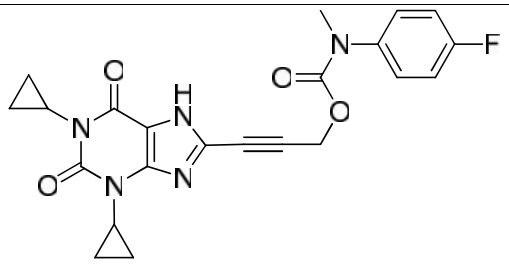
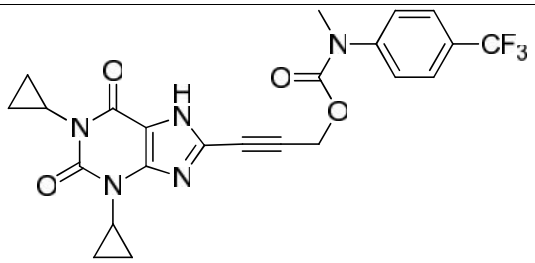
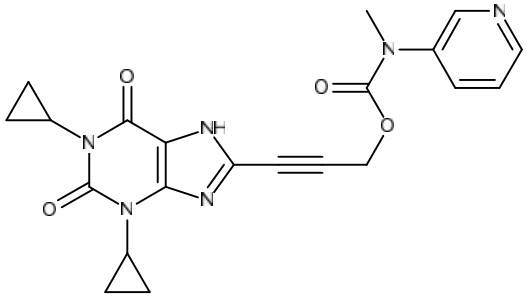
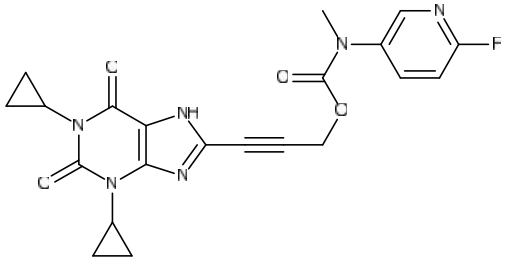
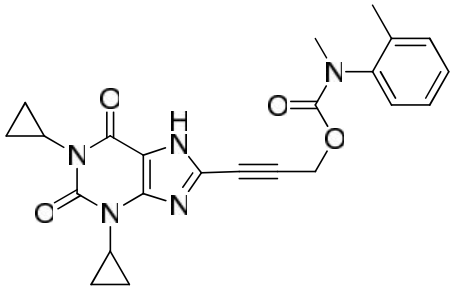
15. A compound of Claim 1, wherein the compound is selected from compounds 7-8:

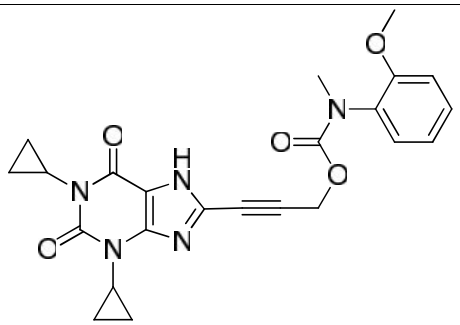
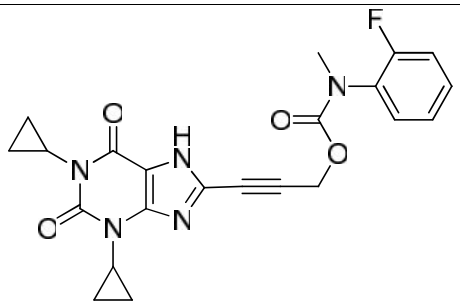
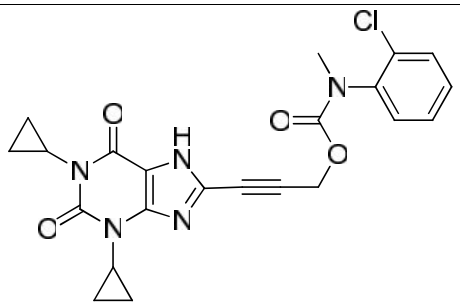
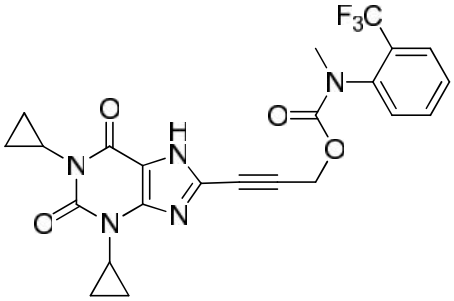
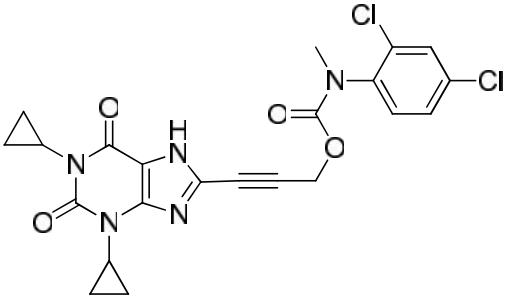
7	
8	

or a pharmaceutically acceptable salt thereof.

16. A compound of Claim 1, wherein the compound is selected from compounds 35-46:

35	
36	

37	
38	
39	
40	
41	

42	
43	
44	
45	
46	

or a pharmaceutically acceptable salt thereof.

17. A pharmaceutical composition, comprising: a compound of Claim 1 or a stereoisomer or pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

18. A method for treating an adenosine A_{2B} receptor associated state in a subject, comprising: administering to the subject an effective amount of a compound of Claims 1 or a stereoisomer or pharmaceutically acceptable salt thereof.

19. The method of Claim 18, wherein the adenosine A_{2B} receptor associated state is selected from asthma, bronchoconstriction, chronic obstructive pulmonary disorder, angiogenesis, pulmonary fibrosis, emphysema, allergies, allergic diseases, autoimmune diseases, inflammation, atherosclerosis, hypertension, congestive heart failure, retinopathy, diarrheal diseases, insulin resistance, Type 1 diabetes, Type 2 diabetes, obesity, fatty liver disease, pain, wound healing, inflammatory gastrointestinal tract disorders, sickle cell disease, cancer, heart attack, diabetic retinopathy, hyperbaric oxygen-induced retinopathy, inhibition of angiogenesis in neoplastic tissues, gastrointestinal disorders, immunological disorders, hypersensitivity disorders, neurological disorders, and cardiovascular diseases due to both cellular hyperproliferation and apoptosis.

20. The method of Claim 18, wherein the adenosine A_{2B} receptor associated state is selected from: asthma, insulin resistance, atherosclerosis, fatty liver disease, bladder cancer, and breast cancer.

21. The method of Claim 20, wherein the adenosine A_{2B} receptor associated state is human cell line MDA-MB-231 breast cancer.