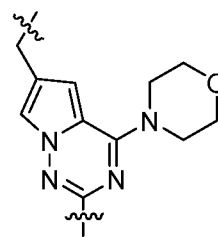
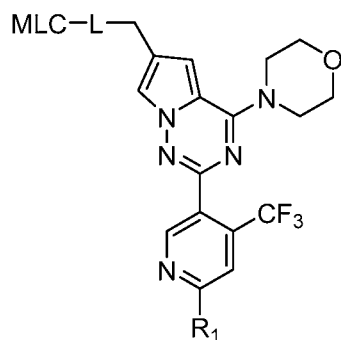


CLAIMS

1. A therapeutic conjugate that forms a covalent bond with a kinase or pseudokinase.
2. The therapeutic conjugate of claim 1, wherein the kinase is PI3-kinase (PI3K).
3. The therapeutic conjugate of claim 1 or claim 2, wherein the therapeutic conjugate has a structure of (FCB)_a-(L)_b-(CLM)_c, wherein a and c are, independently, integers between 1 and 5, b is an integer between 0 and 5, and wherein the FCB moiety comprises a PI3K inhibitor, or a fragment, analog or derivative thereof.

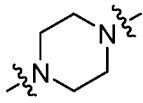
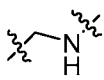


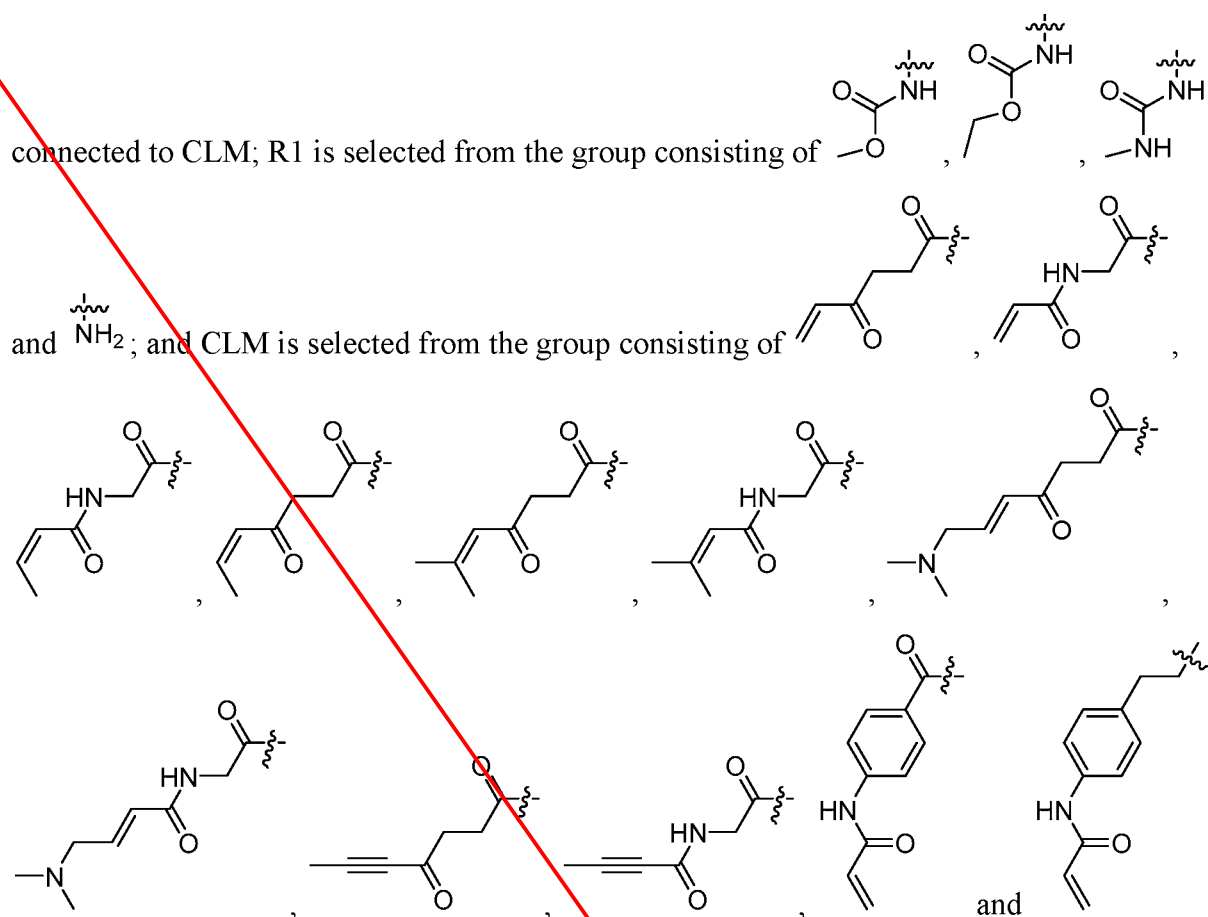
4. The therapeutic conjugate of claim 3, wherein the FCB comprises
5. The therapeutic conjugate of claim 4, wherein the therapeutic conjugate comprises a structure selected from the group consisting of Compound 1-101 to Compound 1-172.
6. The therapeutic conjugate of claim 1 or claim 2 having a structure of



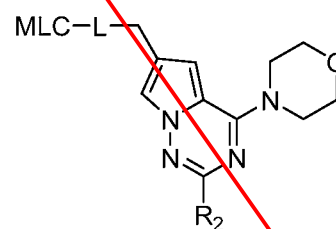
Formula 1-50

or a pharmaceutically acceptable salt thereof, wherein L is

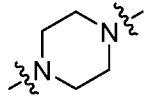
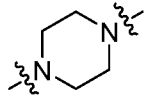
selected from the group consisting of  and  wherein either end can be

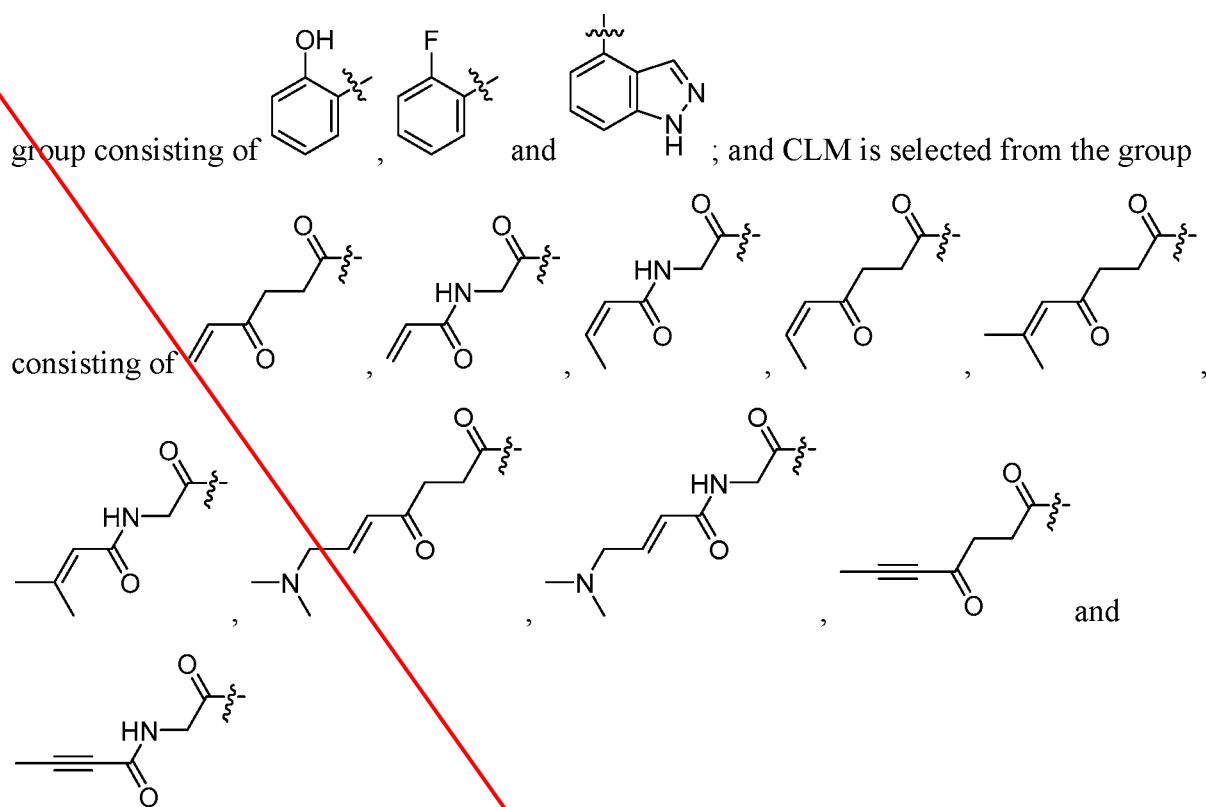


7. The therapeutic conjugate of claim 6 selected from the group consisting of compounds 1-101, 1-102, 1-103, 1-104, 1-105, 1-106, 1-107, 1-108, 1-109, 1-110, 1-111, 1-112, 1-113, 1-114, 1-115, 1-116, 1-117, 1-118, 1-119, 1-120, 1-121, 1-122, 1-123, 1-124, 1-125, 1-126, 1-127, 1-128, 1-129, 1-130, 1-137, 1-138, 1-145, 1-146, 1-153, 1-154, 1-161, 1-162, 1-169, 1-170, 1-171 and 1-172.



Formula 1-51

8. The therapeutic conjugate of claim 1 having a structure of  or a pharmaceutically acceptable salt thereof, wherein L is ; R2 is selected from the



9. The therapeutic conjugate of claim 8 selected from the group consisting of compounds 1-131, 1-132, 1-133, 1-134, 1-135, 1-136, 1-139, 1-140, 1-141, 1-142, 1-143, 1-144, 1-147, 1-148, 1-149, 1-150, 1-151, 1-152, 1-155, 1-156, 1-157, 1-158, 1-159, 1-160, 1-163, 1-164, 1-165, 1-166, 1-167 and 1-168.

10. A therapeutic conjugate comprising a structure selected from Compound 1-101 to Compound 1-172, or a pharmaceutical acceptable salt thereof.

11. A therapeutic conjugate comprising a structure selected from Compound 1-1 to Compound 1-11, or a pharmaceutical acceptable salt thereof.

12. A pharmaceutical composition comprising the therapeutic conjugate of any one of claims 1-11 and at least one pharmaceutically acceptable excipient.

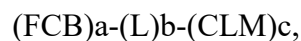
13. A method of regulating the activity of a kinase or pseudokinase, comprising administering the therapeutic conjugate of any one of claims 1-11.

14. The method of claim 13, wherein the activity of the kinase or pseudokinase is inhibited.

15. The method of claim 13, wherein the kinase is PI3K.
16. A method of treating a subject in need thereof comprising administering a therapeutically effective amount of the pharmaceutical composition of claim 12.
17. The method of claim 16, wherein the subject has a therapeutic condition selected from the group consisting of cancer, neurodegenerative disease, autoimmune disorder and aging.
18. The method of claim 17, wherein the subject has cancer.
19. The method of claim 18, wherein the subject has cancer with a mutation in the PIK3CA gene.

CLAIMS

1. A compound having the formula:



or a pharmaceutically acceptable salt thereof,

wherein:

CLM is a covalent linking modality;

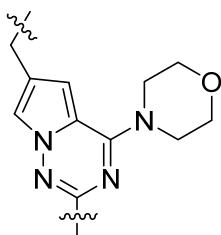
L is a linker;

a and c are, independently, integers between 1 and 5,

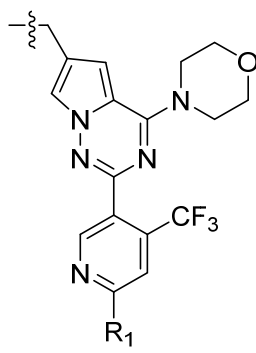
b is an integer between 0 and 5, and

wherein the FCB moiety comprises a PI3K inhibitor, or a fragment, analog or derivative thereof.

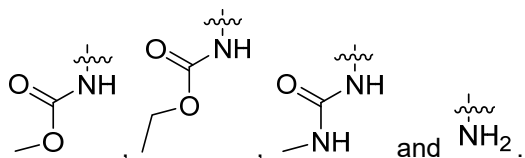
2. The compound of claim 1, wherein the FCB comprises



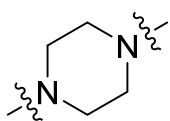
3. The compound of claim 2, wherein FCB has the structure:



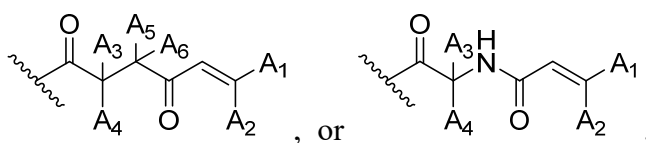
wherein R₁ is selected from the group consisting of:



4. The compound of any one of claims 1-3, wherein a, b, and c are 1.
5. The compound of any one of claims 1-4, wherein L is a substituted or unsubstituted C₃-C₁₀ heterocycloalkyl.
6. The compound of claim 5, wherein L is an unsubstituted C₅-C₆ heterocycloalkyl.
7. The compound of claim 6, wherein L is:

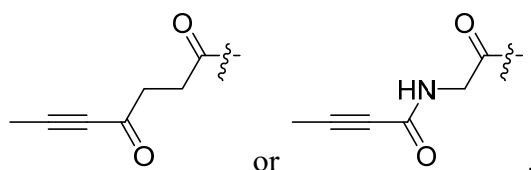


8. The compound of any one of claims 1-7, wherein CLM is



wherein A₁, A₂, A₃, A₄, A₅ and A₆ are each independently selected from the group consisting of H, halogen, CF₃, -OH, -NH₂, -SH, -SCH₃, -CN, -NO₂, -CH₂(NH₂), -C(O)OH, -S(O)₂NH₂, -C(O)NH₂, -C(O)CH₃, NHC(O)-C₁₋₆ alkyl, N(C₁₋₃ alkyl)C(O)-C₁₋₆ alkyl, OC(O)NH₂, OC(O)NH(CH₃), OC(O)N(CH₃)₂, optionally substituted C₁₋₆ alkyl, optionally substituted C₂₋₆ alkenyl, and optionally substituted C₂₋₆ alkynyl.

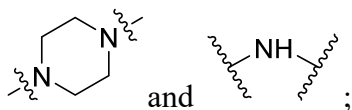
9. The compound of claim 8, wherein A₁, A₂, A₃, A₄, A₅ and A₆ are each independently H or optionally substituted C₁₋₆ alkyl.
10. The compound of claim 9, wherein A₁, A₂, A₃, A₄, A₅ and A₆ are H or unsubstituted C₁₋₆ alkyl.
11. The compound of any one of claims 1-7, wherein CLM is:



C=CC(=O)CC(=O)O*, C=CC(=O)NCOC(=O)O*, CC(=C)C(=O)CC(=O)O*, CC(=C)C(=O)NCOC(=O)O*, CN(C)CC=CC(=O)CC(=O)O*, or

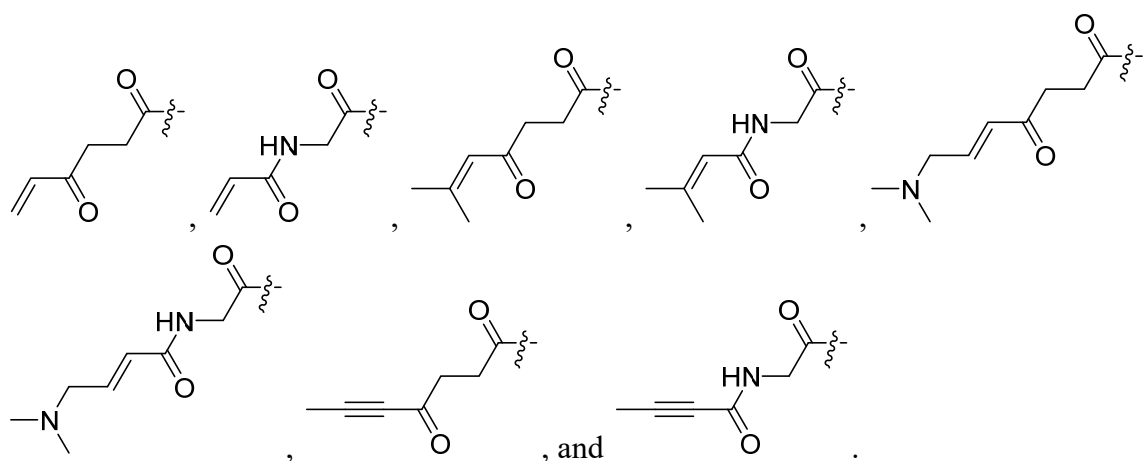
*CC1=CC=C2N=CN=C(C2=C1C3=CC=CC(=C3)C(F)(F)F)N4CCOCC4

or a pharmaceutically acceptable salt thereof,
wherein L is selected from the group consisting of:

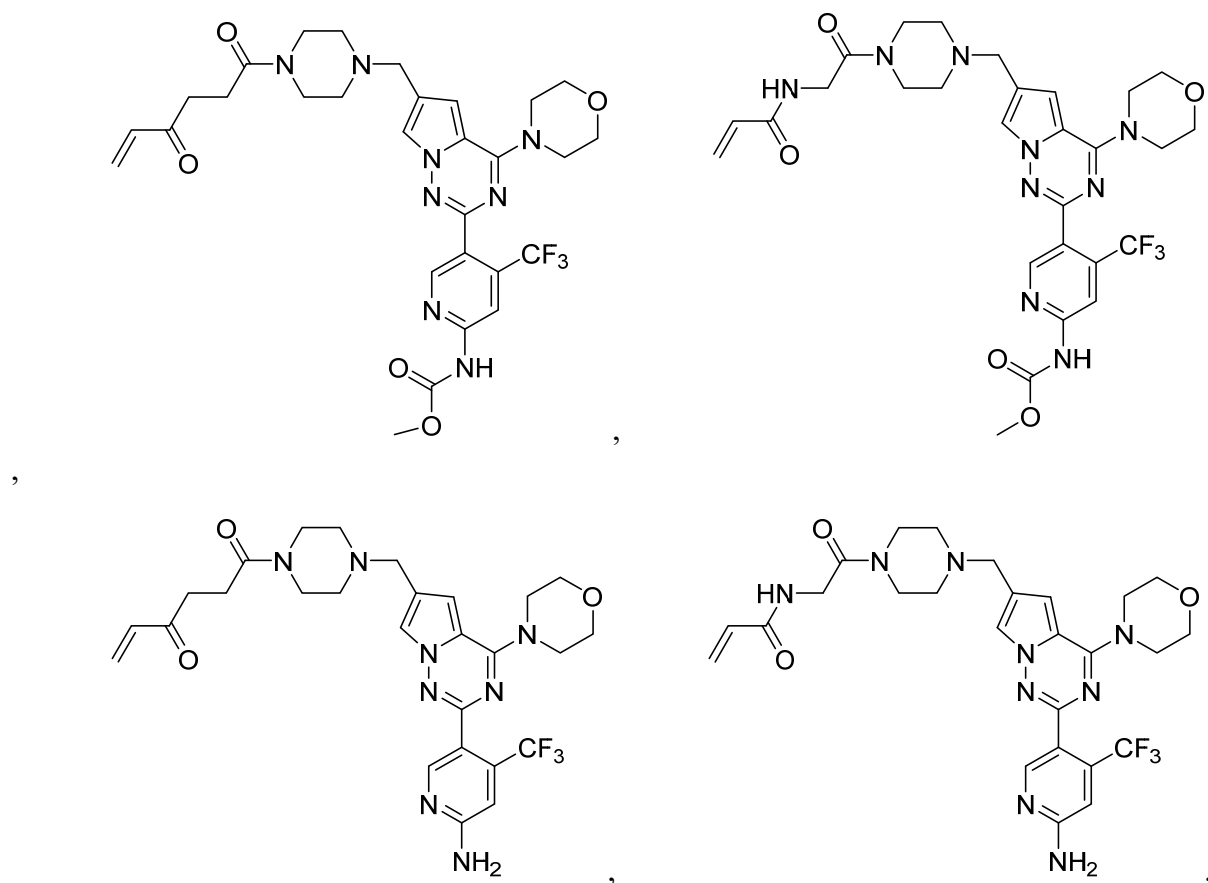


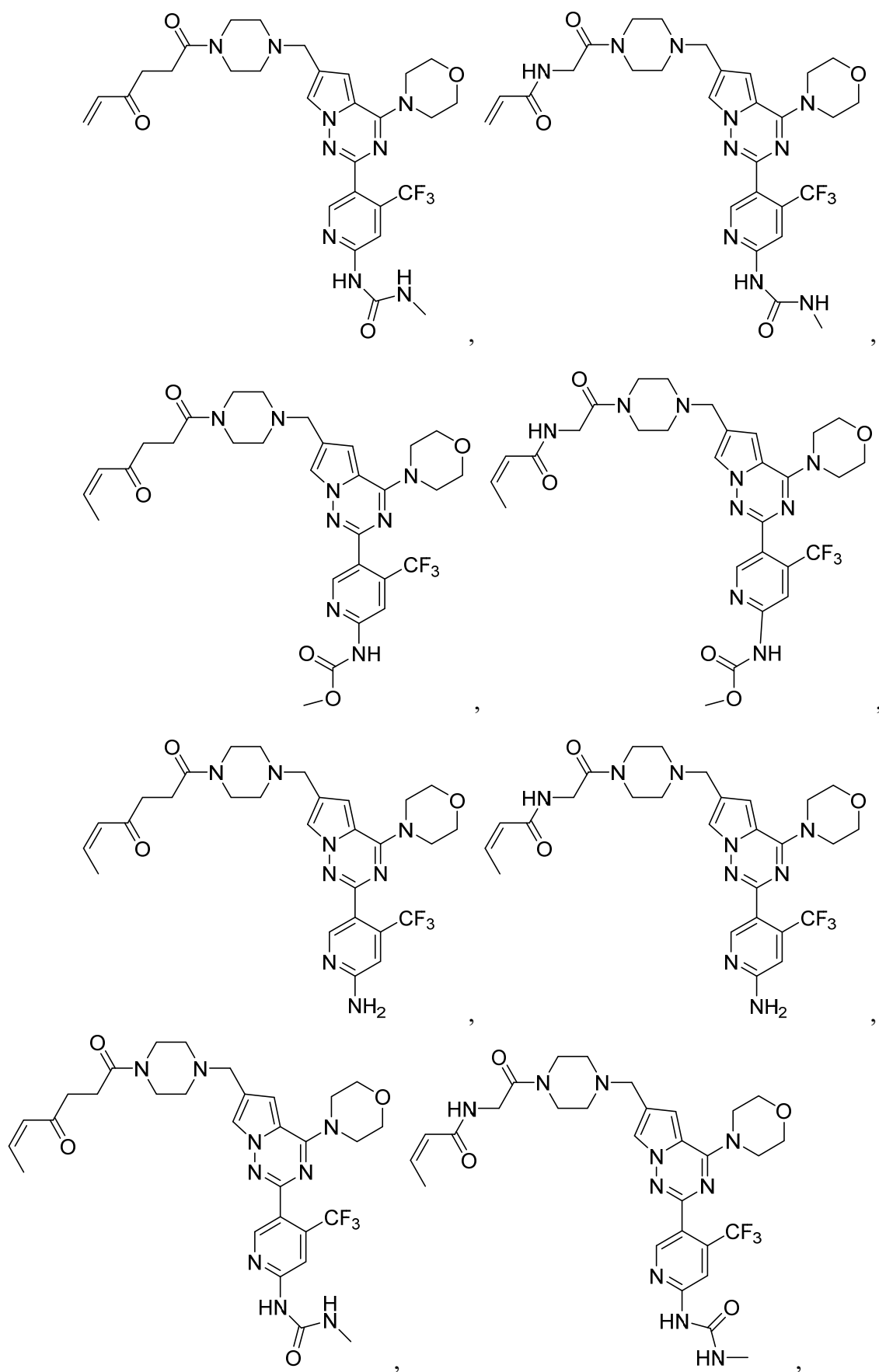
$\text{O}=\text{C}-\text{NH}-$, $\text{O}=\text{C}-\text{NH}-$, $\text{O}=\text{C}-\text{NH}-$ and NH_2 ; and

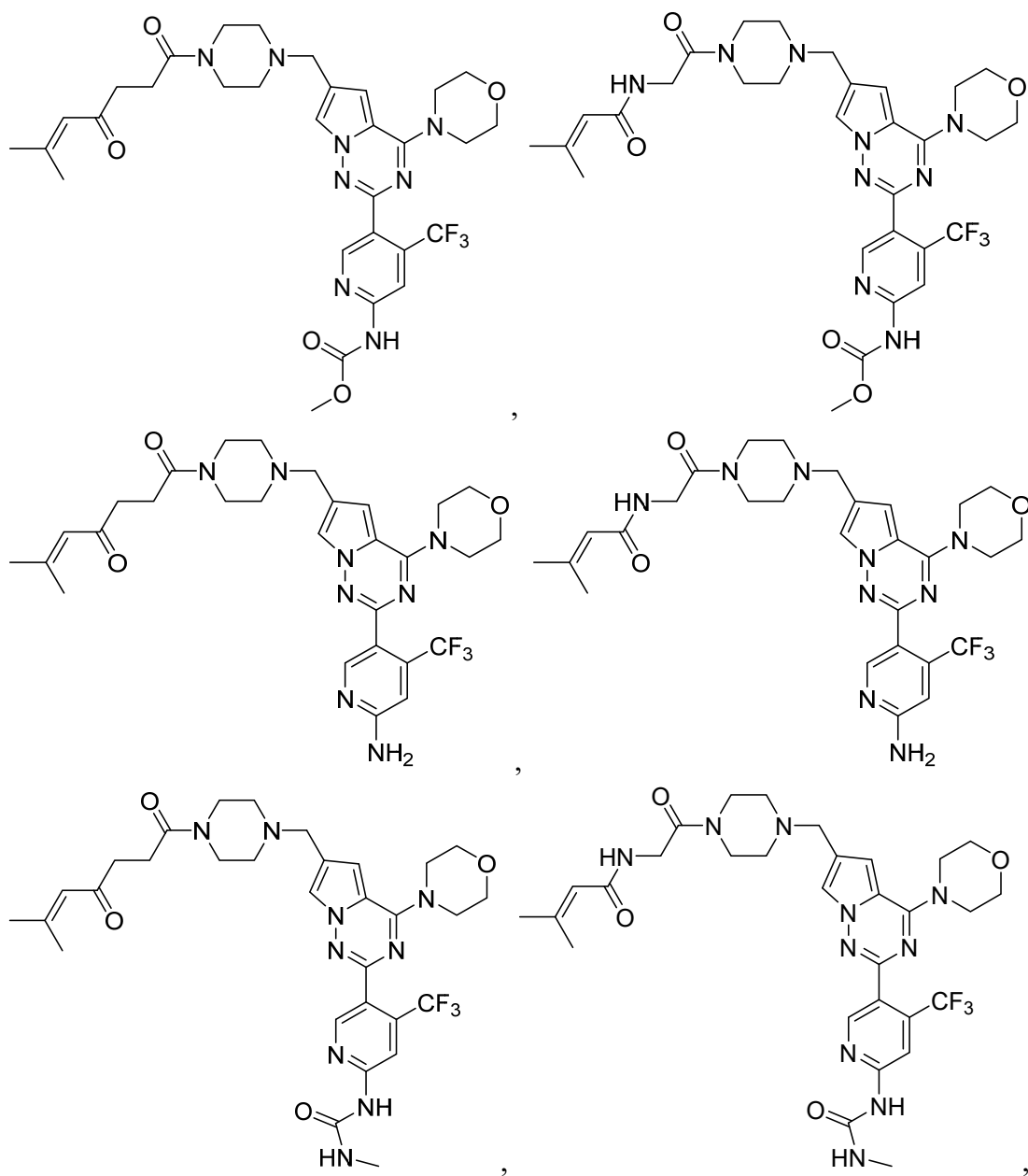
101

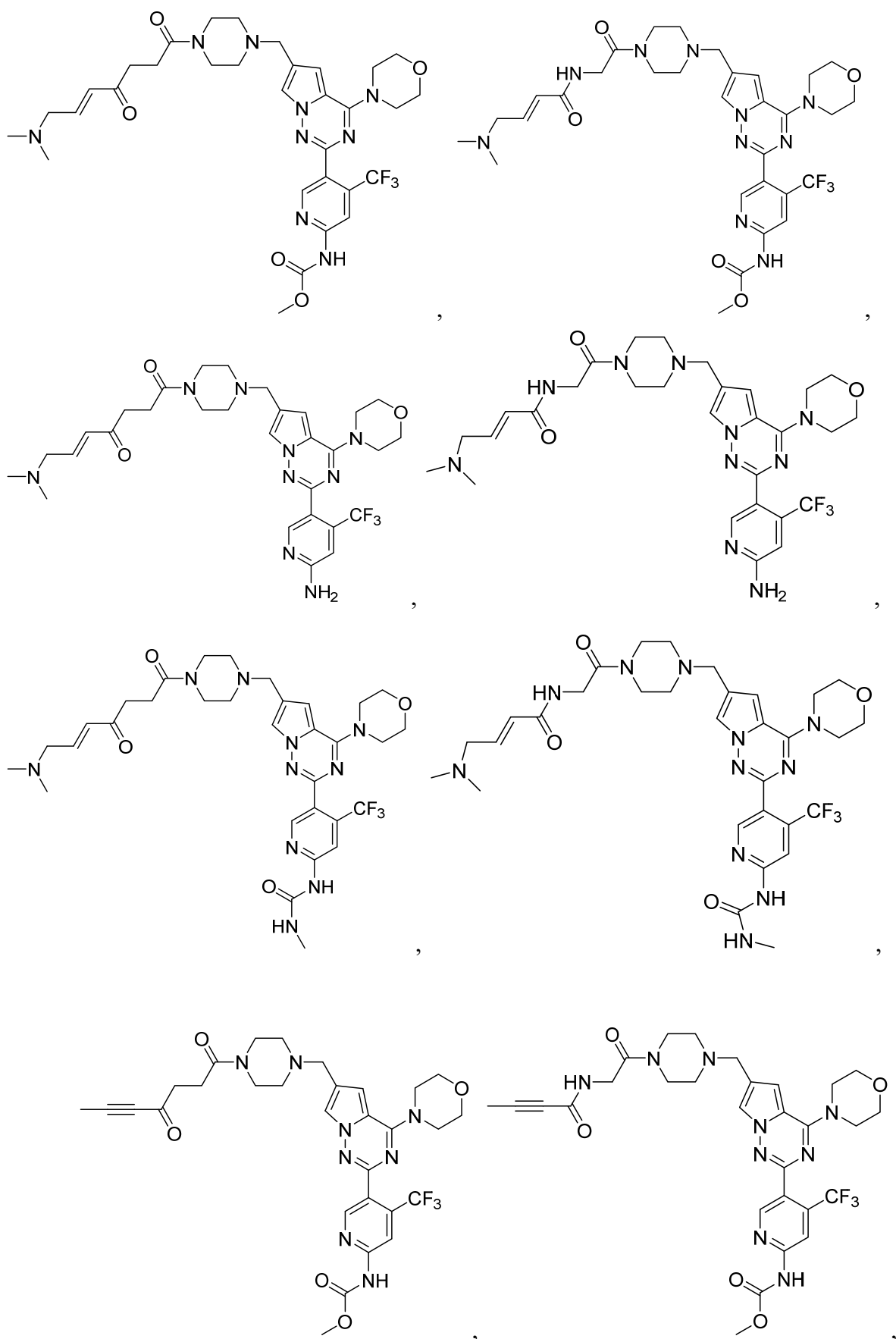


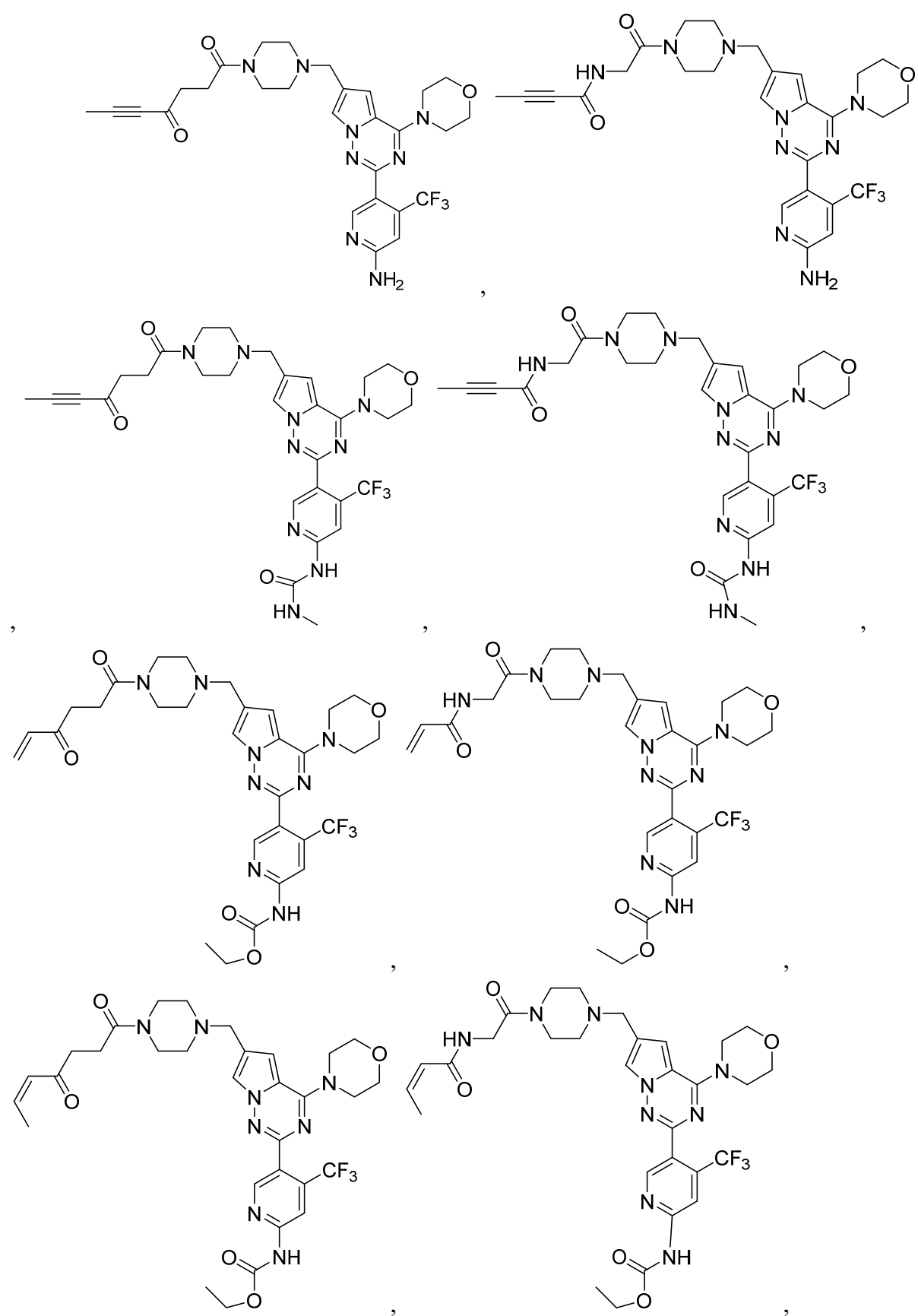
17. The compound of claim 13, wherein the compound is selected from the group consisting of:

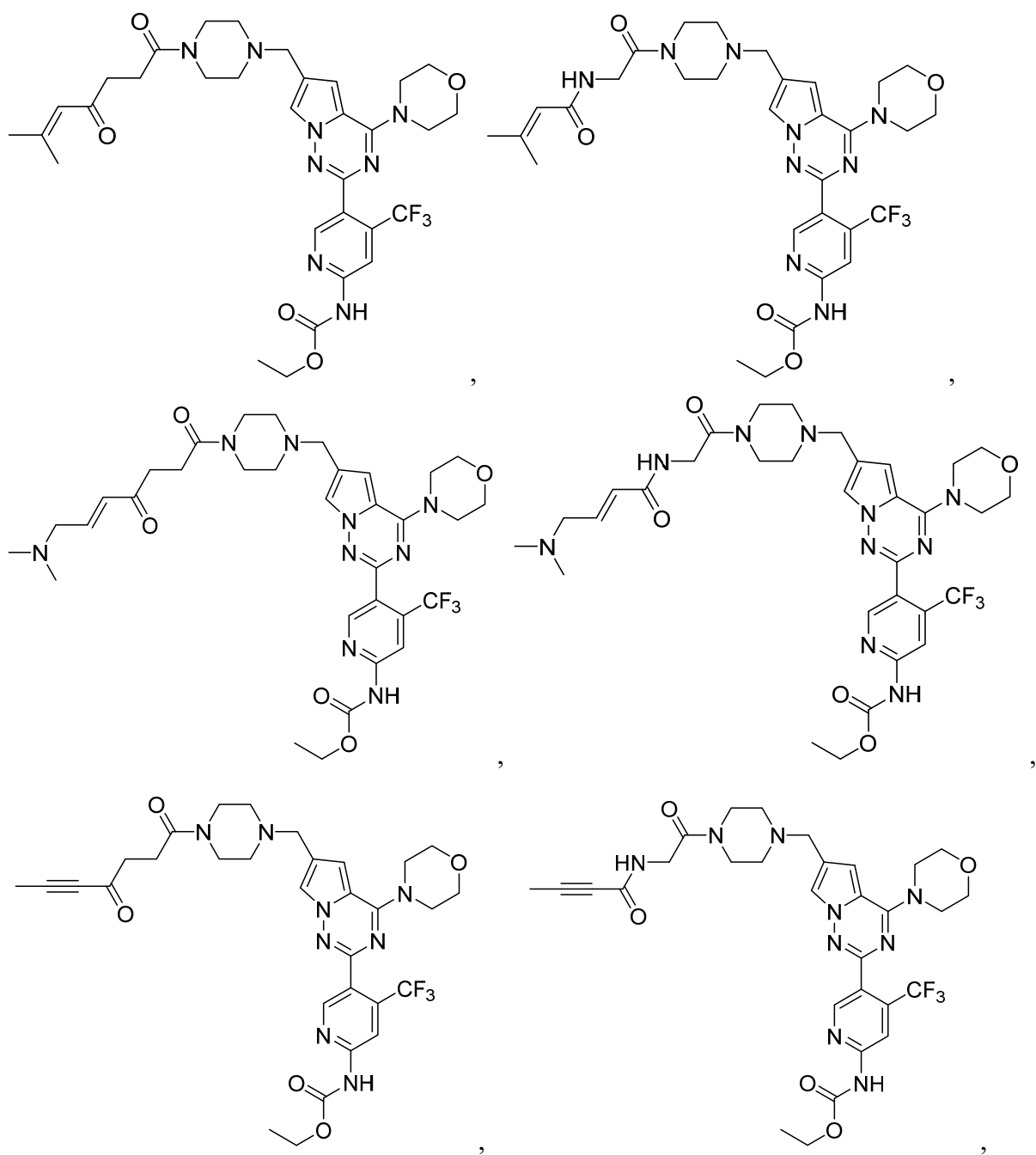


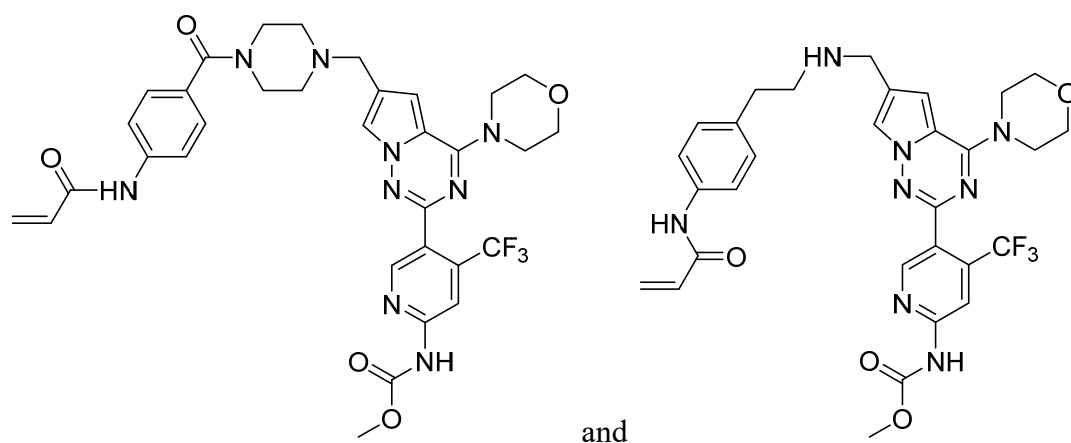




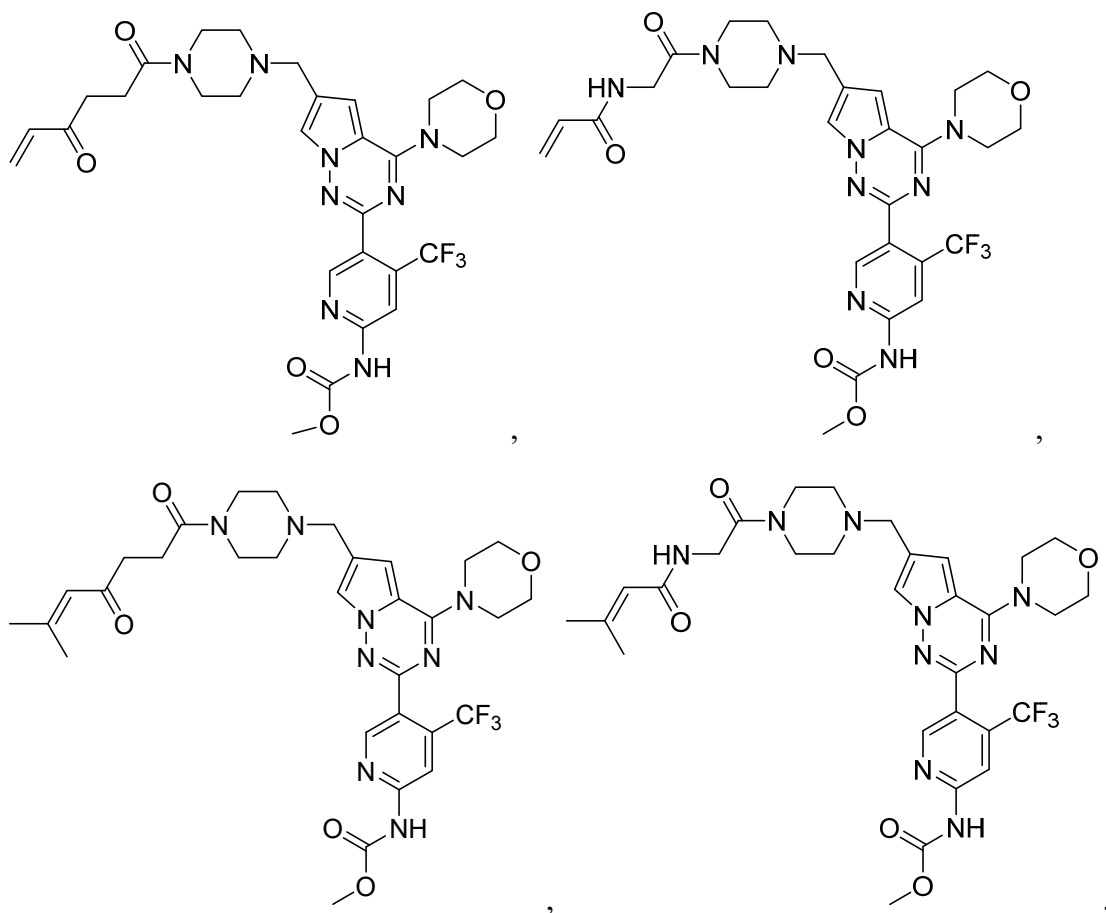


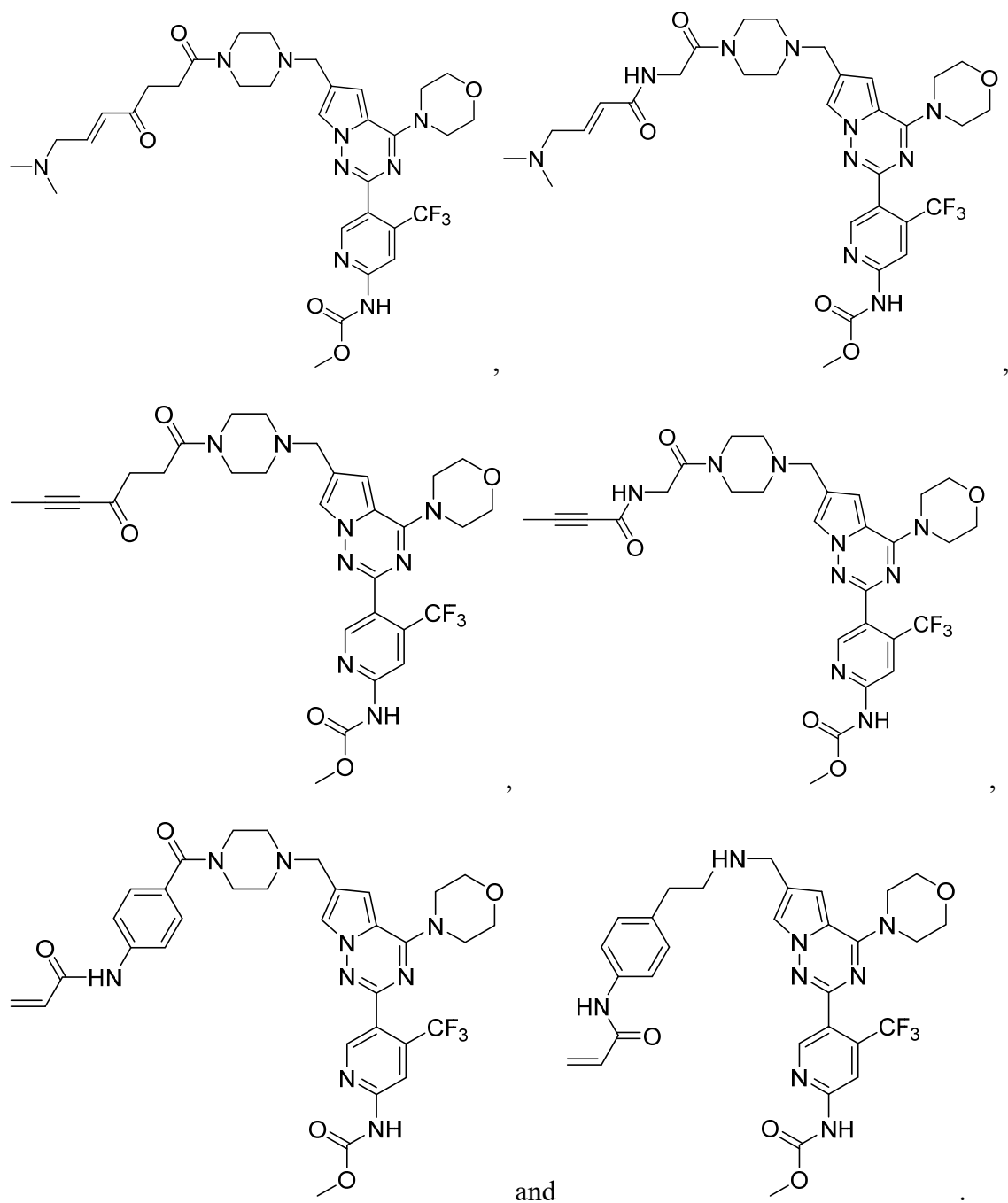




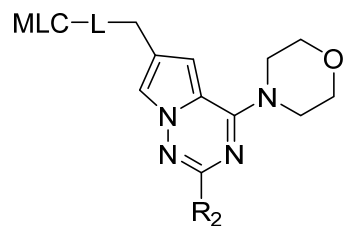


18. The compound of claim 17, wherein the compound is selected from the group consisting of:





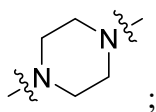
19. The compound of claim 1 having a structure of Formula (1-51):



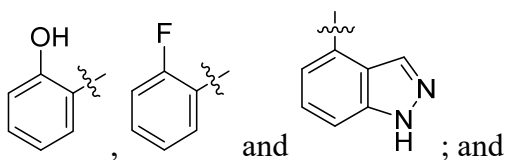
Formula 1-51

or a pharmaceutically acceptable salt thereof, wherein:

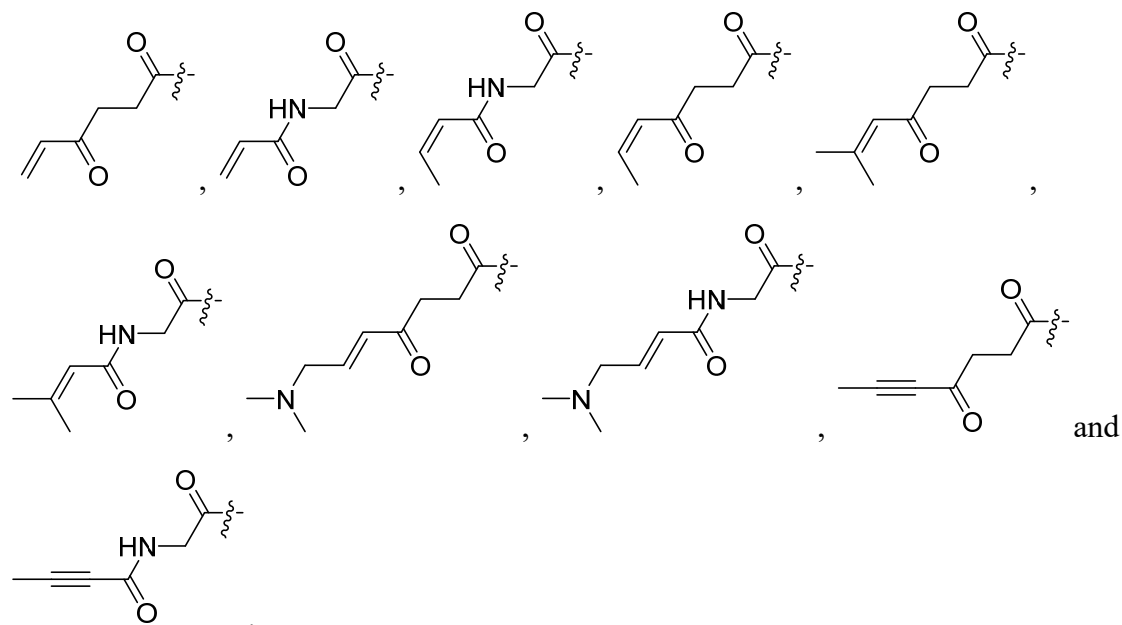
L is:



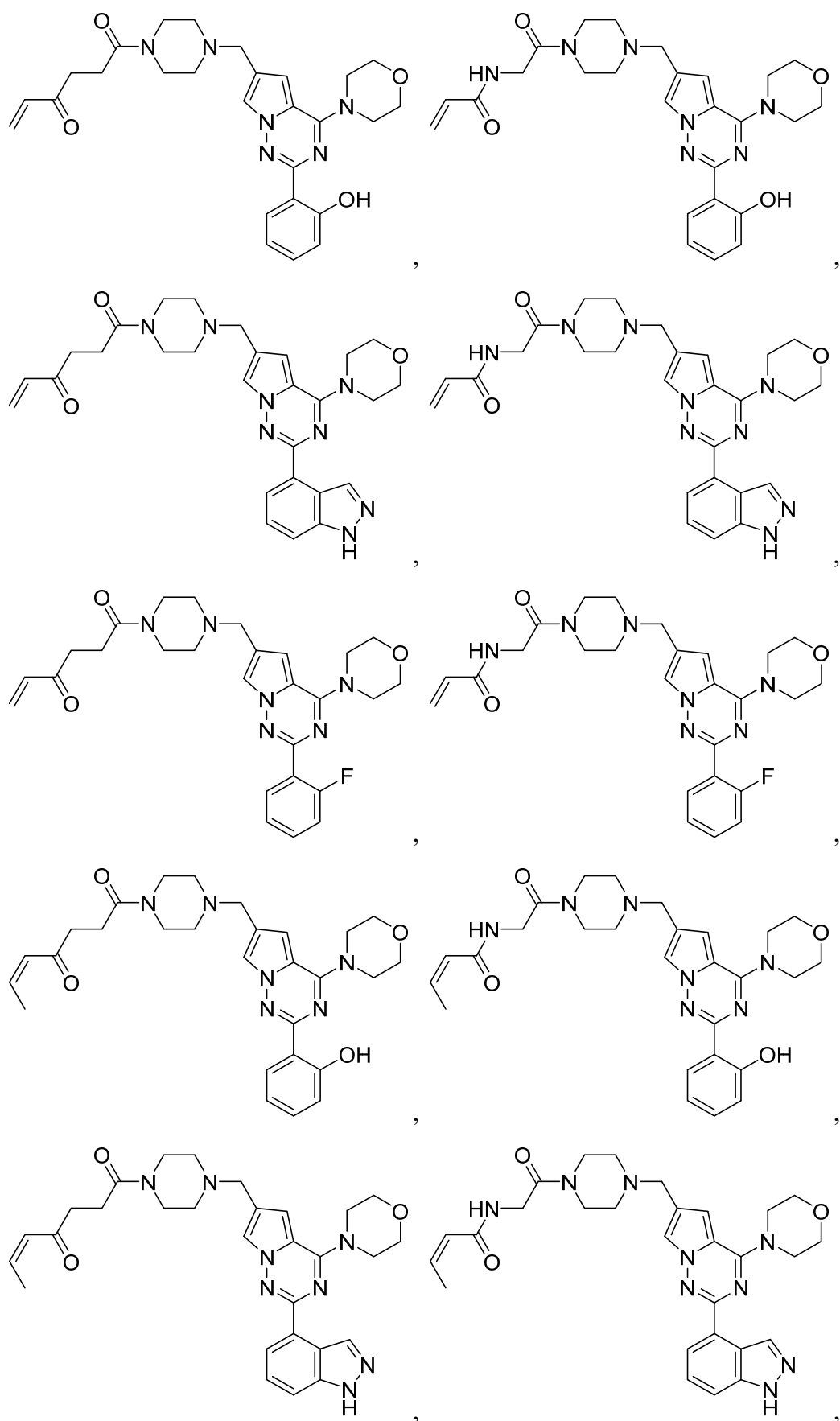
R₂ is selected from the group consisting of:

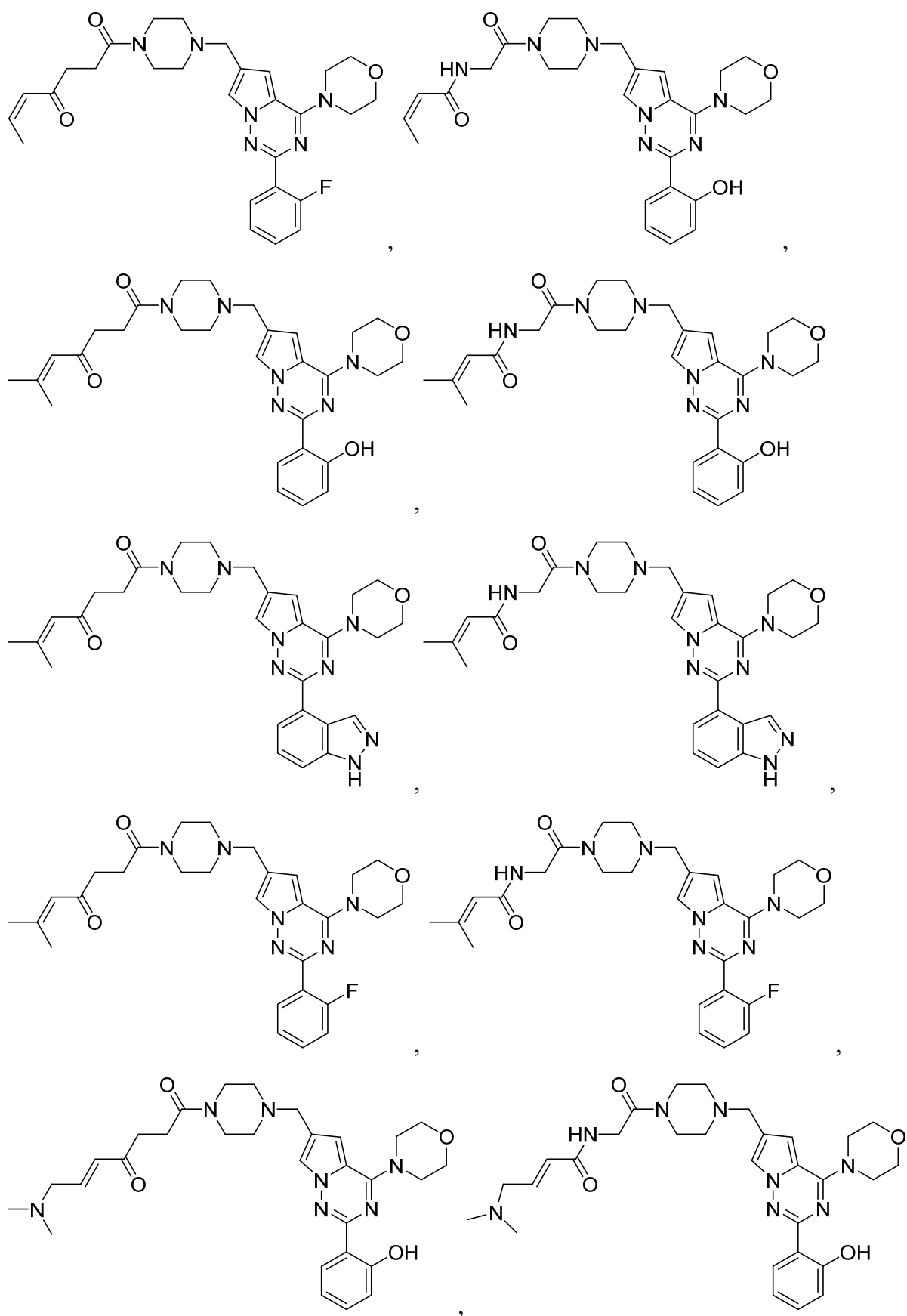


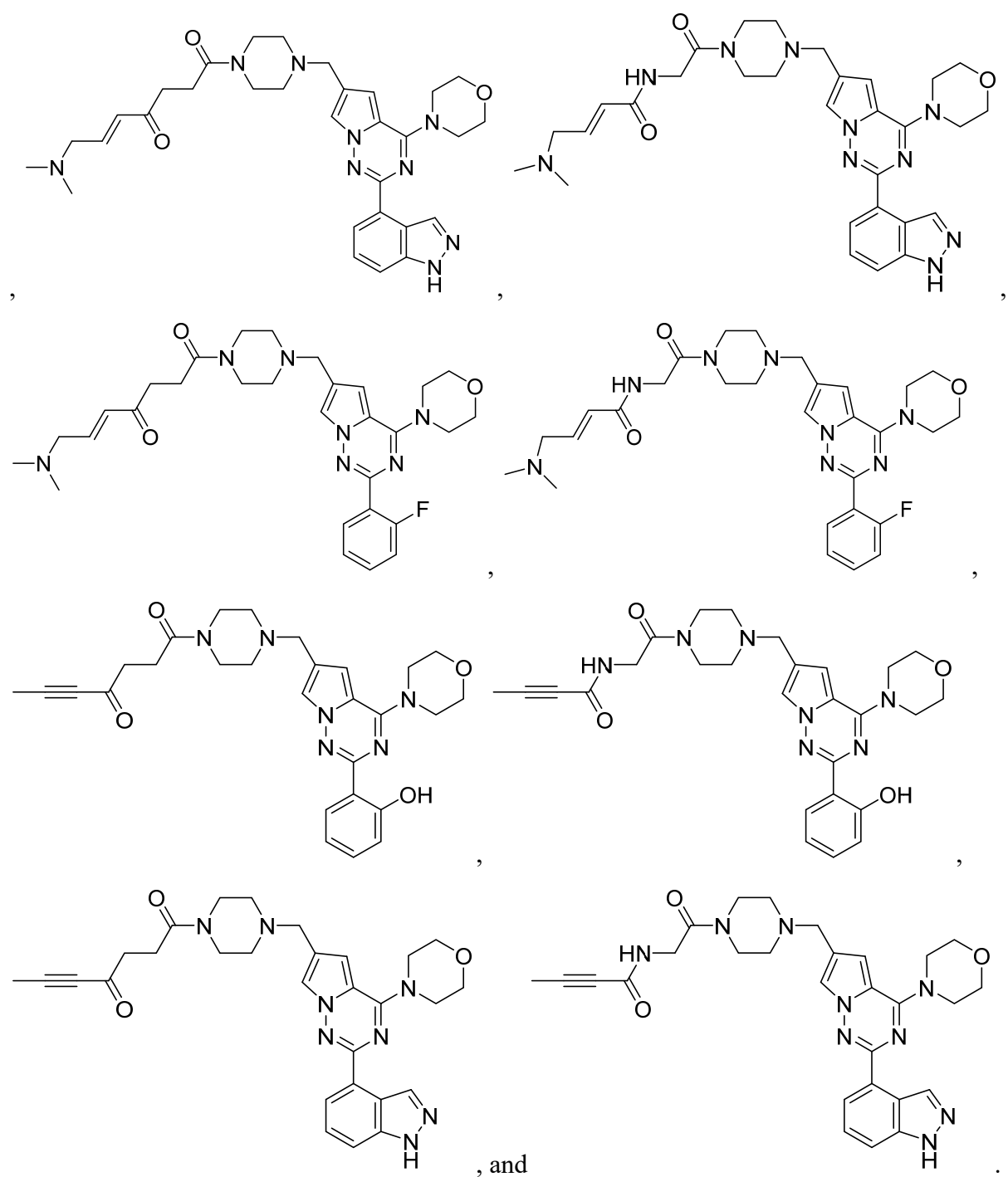
CLM is selected from the group consisting of:



20. The compound of claim 1 selected from the group consisting of:







21. A pharmaceutical composition comprising a compound of any one of claims 1-20 and at least one pharmaceutically acceptable excipient.

22. Use of the compound of any one of claims 1-20 in the manufacture of a medicament for the regulation of the activity of a kinase or pseudokinase in a subject.

23. The use of claim 22, wherein the activity of the kinase or pseudokinase is inhibited.
24. The use of claim 22, wherein the kinase is PI3K.
25. Use of the compound of any one of claims 1-20, or the pharmaceutical composition of claim 21, in the manufacture of a medicament for the treatment of a therapeutic condition in a subject, wherein the compound or the pharmaceutical composition is to be administered to the subject, and wherein the therapeutic condition is selected from the group consisting of cancer, neurodegenerative disease, autoimmune disorder and aging.
26. The use of claim 25 wherein the subject has cancer.
27. The use of claim 25, wherein the subject has cancer with a mutation in the PIK3CA gene.