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(54) Title: COMPOUNDS AND USES THEREOF

(57) Abstract: The present invention relates to compositions and methods for the treatment of BAF-related disorders, such as cancers and viral infections.



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COMPOUNDS AND USES THEREOF

Background

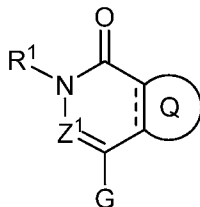
Disorders can be affected by the BAF complex. BRD9 is a component of the BAF complex. The present invention relates to useful compositions and methods for the treatment of BAF complex-related disorders, such as cancer and infection.

Summary

Bromodomain-containing protein 9 (BRD9) is a protein encoded by the BRD9 gene on chromosome 5. BRD9 is a component of the BAF (BRG1- or BRM-associated factors) complex, a SWI/SNF ATPase chromatin remodeling complex, and belongs to family IV of the bromodomain-containing proteins. BRD9 is present in several SWI/SNF ATPase chromatin remodeling complexes and is upregulated in multiple cancer cell lines. Accordingly, agents that reduce the levels and/or activity of BRD9 may provide new methods for the treatment of disease and disorders, such as cancer and infection. The inventors have found that depleting BRD9 in cells results in the depletion of the SS18-SSX fusion protein in those cells. The SS18-SSX fusion protein has been detected in more than 95% of synovial sarcoma tumors and is often the only cytogenetic abnormality in synovial sarcoma. Additionally, evidence suggests that the BAF complex is involved in cellular antiviral activities. Thus, agents that degrade BRD9 (e.g., compounds) are useful in the treatment of disorders (e.g., cancers or infections) related to BAF, BRD9, and/or SS18-SSX.

The present disclosure features compounds and methods useful for treating BAF-related disorders (e.g., cancer or infection).

In an aspect, the disclosure features a compound having the structure of **Formula I**:



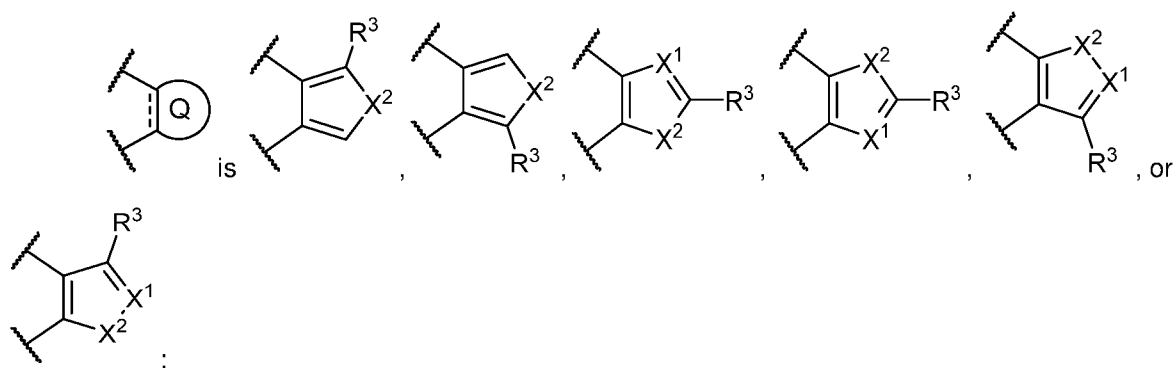
Formula I,

where

R¹ is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₁₀ carbocyclyl;

Z¹ is CR² or N;

R² is H, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, or optionally substituted C₂-C₉ heteroaryl;



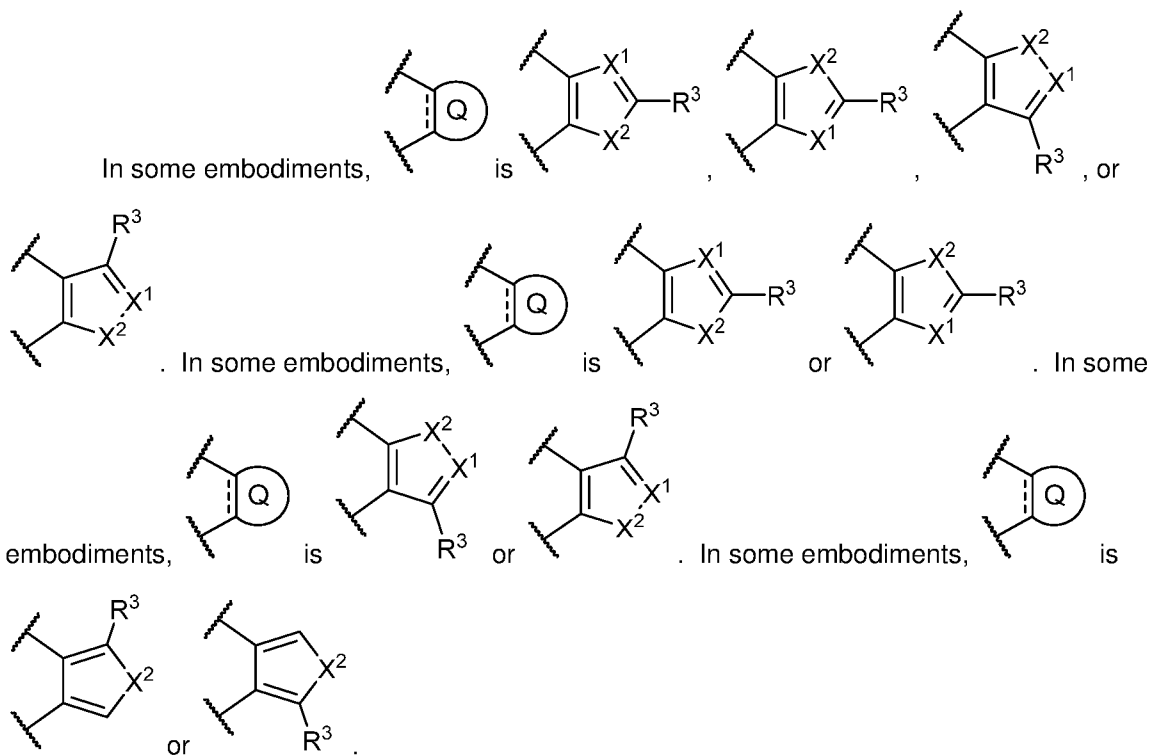
X¹ is CR^{X1} or N;

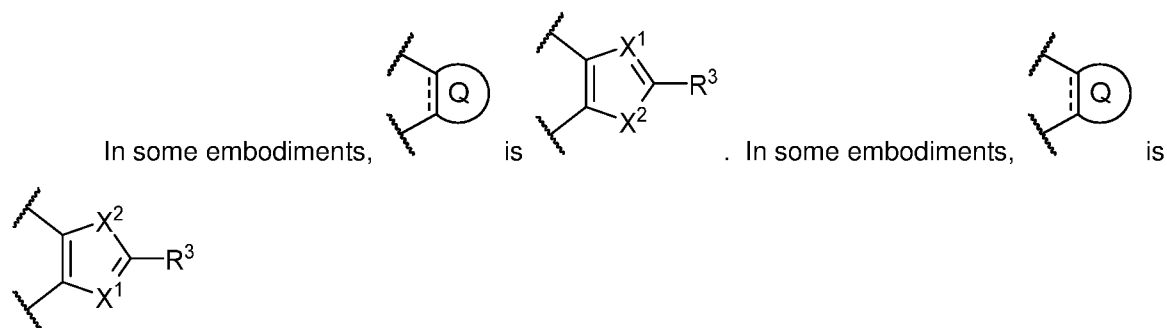
X² is O or S;

5 R^{X1} is H or optionally substituted C₁-C₆ alkyl;

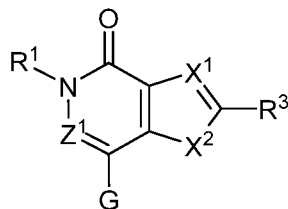
R³ is H, cyano, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₁-C₆ alkoxy, optionally substituted amino, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₃-C₁₀ heterocyclyl, or optionally substituted C₂-C₉ heteroaryl; and

10 G is optionally substituted C₃-C₁₀ carbocyclyl, C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, or optionally substituted C₂-C₉ heteroaryl, or a pharmaceutically acceptable salt thereof.





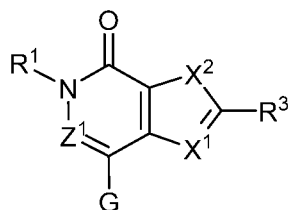
In some embodiments, the compound of **Formula I** has the structure of **Formula IA**:



Formula IA,

or a pharmaceutically acceptable salt thereof.

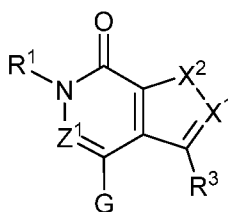
In some embodiments, the compound of **Formula I** has the structure of **Formula IB**:



Formula IB,

or a pharmaceutically acceptable salt thereof.

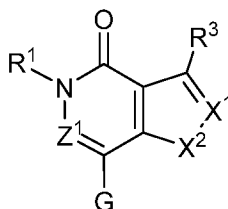
In some embodiments, the compound of **Formula I** has the structure of **Formula IC**:



Formula IC,

or a pharmaceutically acceptable salt thereof.

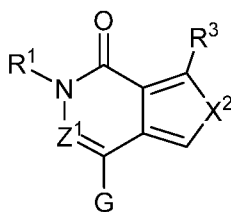
In some embodiments, the compound of **Formula I** has the structure of **Formula ID**:



Formula ID,

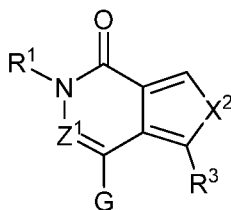
or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound of **Formula I** has the structure of **Formula IE**:

**Formula IE,**

or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound of **Formula I** has the structure of **Formula IF**:

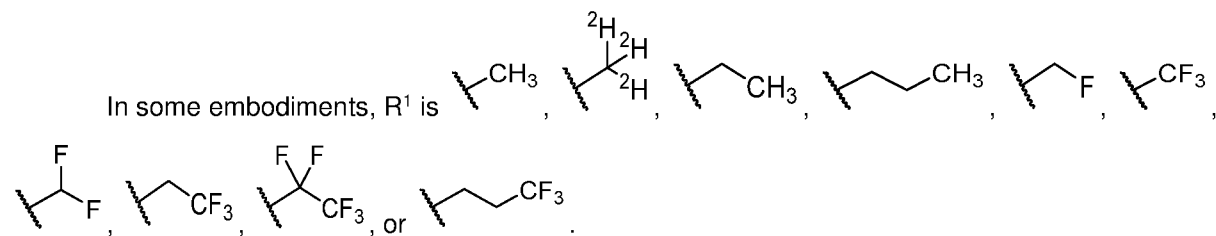
**Formula IF,**

or a pharmaceutically acceptable salt thereof.

In some embodiments, R¹ is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₁₀ carbocyclyl. In some embodiments, R¹ is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₂-C₆ alkenyl, or optionally substituted C₃-C₁₀ carbocyclyl. In some embodiments, R¹ is H, optionally substituted C₁-C₆ alkyl, or optionally substituted C₃-C₁₀ carbocyclyl.

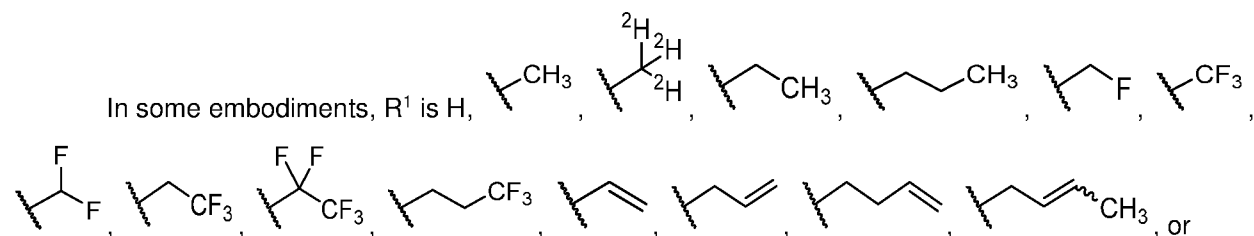
In some embodiments, R¹ is H. In some embodiments, R¹ is optionally substituted C₁-C₆ alkyl. In some embodiments, R¹ is optionally substituted C₂-C₆ alkenyl. In some embodiments, R¹ is optionally substituted C₃-C₁₀ carbocyclyl.

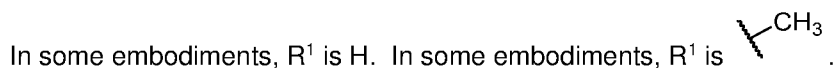
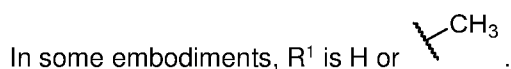
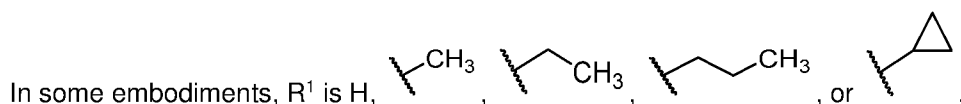
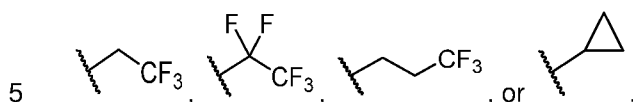
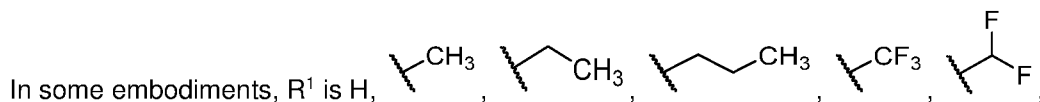
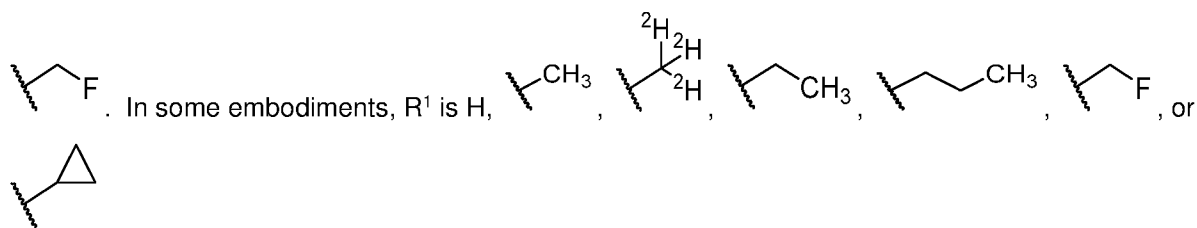
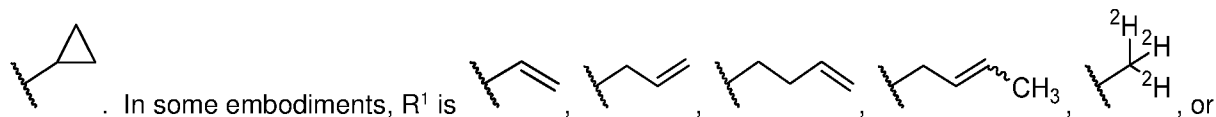
In some embodiments, optionally substituted C₁-C₆ alkyl is C₁-C₆ perfluoroalkyl.



In some embodiments, R¹ is , or .

In some embodiments, R¹ is .





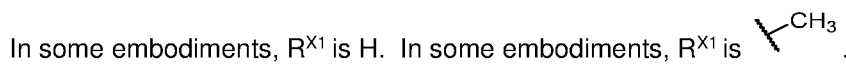
In some embodiments, Z¹ is CR². In some embodiments, Z¹ is N.

10 In some embodiments, R² is H, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₃-C₁₀ carbocyclyl, or optionally substituted C₆-C₁₀ aryl.

In some embodiments, R² is H, halogen, or optionally substituted C₁-C₆ alkyl.



In some embodiments, R² is H. In some embodiments, R² is F. In some embodiments, R² is



In some embodiments, X¹ is CH or N. In some embodiments, X¹ is CH. In some embodiments, X¹ is N.

In some embodiments, X² is O. In some embodiments, X² is S.

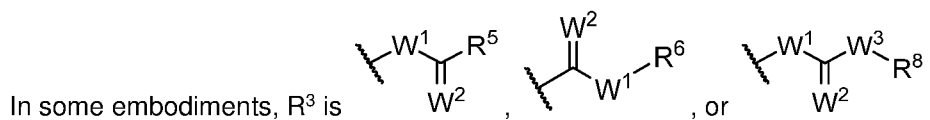
20 In some embodiments, R³ is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₂-C₉ heteroaryl, or optionally substituted C₁-C₆ heteroalkyl.

In some embodiments, R³ is H, cyano, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₁-C₆ alkoxy, optionally substituted amino, optionally substituted C₃-C₁₀ heterocyclyl, or optionally substituted C₂-C₉ heteroaryl. In some embodiments, R³ is optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₁₀ heterocyclyl. In some embodiments, R³ is cyano, optionally substituted C₁-C₆ alkoxy, or optionally substituted amino.

25

In some embodiments, R^3 is H, optionally substituted C_1 - C_6 alkyl, or optionally substituted C_1 - C_6 heteroalkyl. In some embodiments, R^3 is H or optionally substituted C_1 - C_6 alkyl. In some embodiments, R^3 is H. In some embodiments, R^3 is optionally substituted C_1 - C_6 alkyl.

In some embodiments, R^3 is optionally substituted C_2 - C_9 heteroaryl or optionally substituted C_1 - C_6 heteroalkyl. In some embodiments, R^3 is optionally substituted C_1 - C_6 heteroalkyl.



where

W^1 is NR^4 or O;

W^2 is NH, O, or S;

10 W^3 is NR^7 or O;

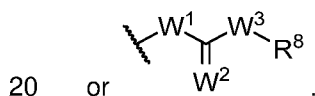
R^4 is H or optionally substituted C_1 - C_6 alkyl;

R^5 is optionally substituted C_1 - C_6 alkyl, optionally substituted C_3 - C_{10} carbocyclyl, or optionally substituted C_2 - C_9 heterocyclyl;

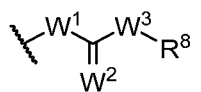
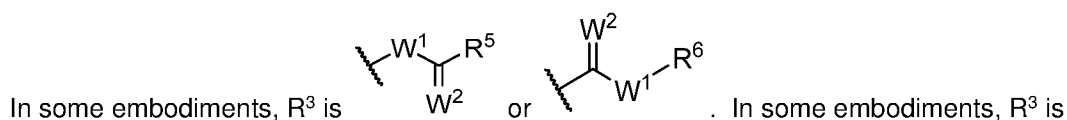
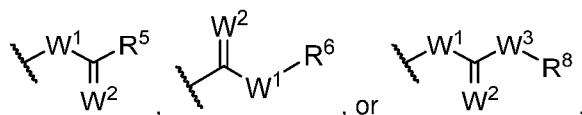
15 R^6 is H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_3 - C_{10} carbocyclyl, or optionally substituted C_2 - C_9 heterocyclyl;

R^7 is H or optionally substituted C_1 - C_6 alkyl; and

R^8 is H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_3 - C_{10} carbocyclyl, or optionally substituted C_2 - C_9 heterocyclyl.



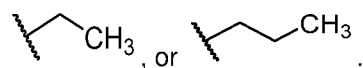
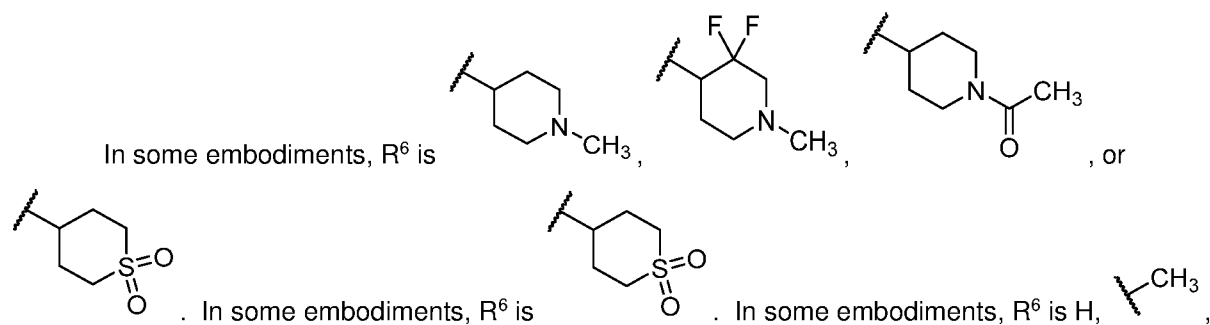
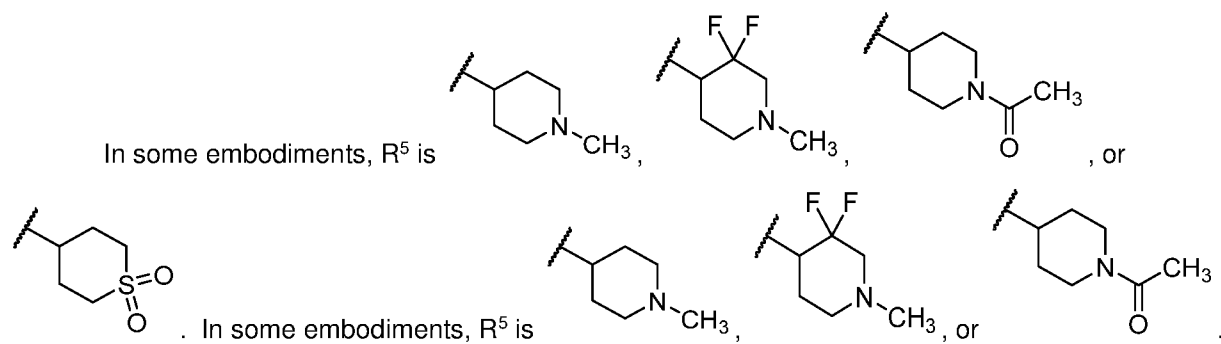
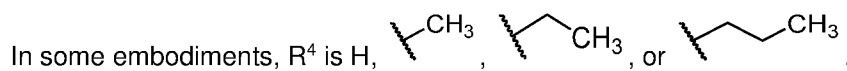
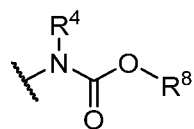
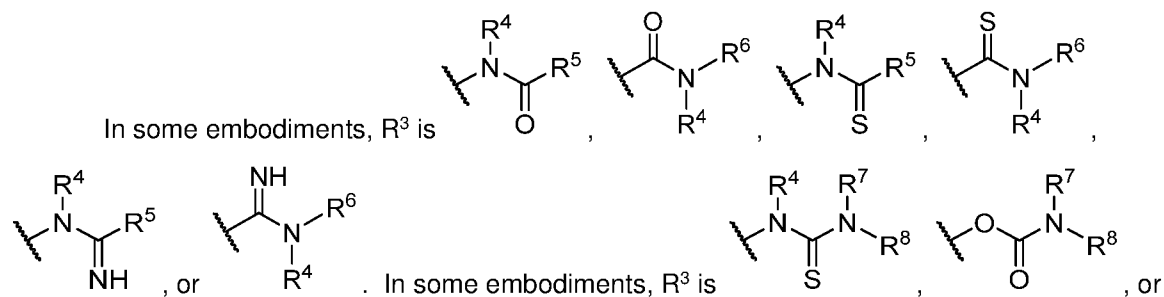
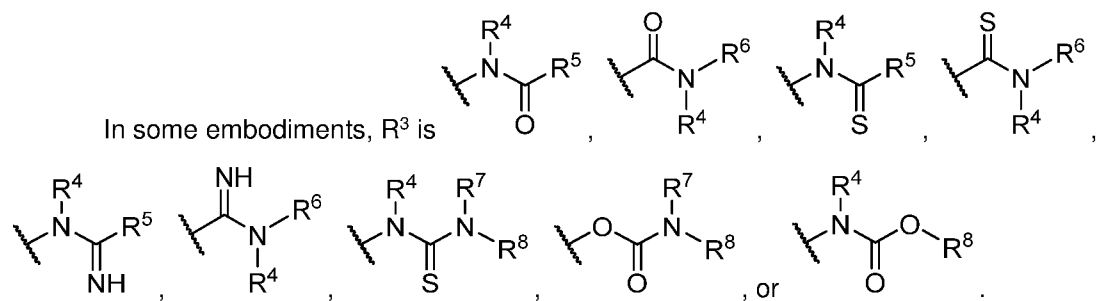
In some embodiments, R^3 is optionally substituted C_2 - C_9 heteroaryl. In some embodiments, R^3 is

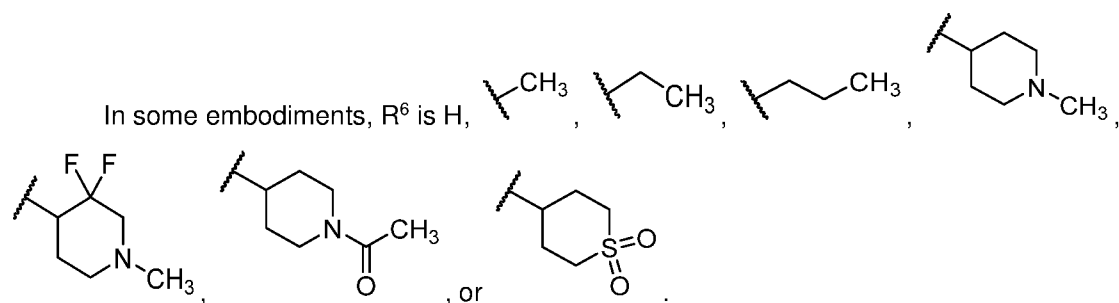


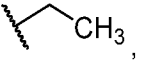
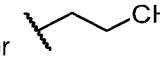
25 In some embodiments, W^1 is NR^4 . In some embodiments, W^1 is O.

In some embodiments, W^2 is NH. In some embodiments, W^2 is O. In some embodiments, W^2 is S.

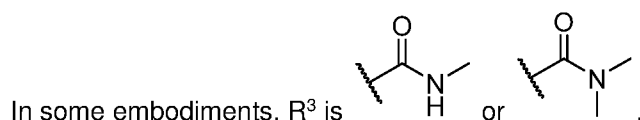
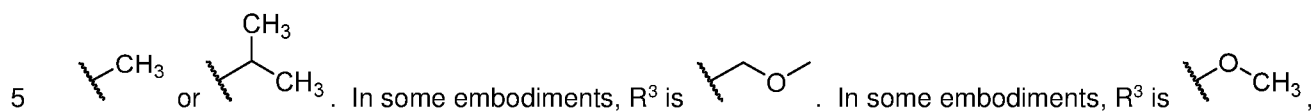
In some embodiments, W^3 is NR^7 . In some embodiments, W^3 is O.





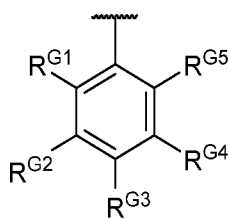
In some embodiments, R^7 is H, , , or .

In some embodiments, R^3 is H. In some embodiments, R^3 is cyano. In some embodiments, R^3 is



10 In some embodiments, G is optionally substituted C_3 - C_{10} carbocyclyl or optionally substituted C_2 - C_9 heterocyclyl. In some embodiments, G is optionally substituted C_6 - C_{10} aryl or optionally substituted C_2 - C_9 heteroaryl.

In some embodiments, G is optionally substituted C_3 - C_{10} carbocyclyl. In some embodiments, G is optionally substituted C_6 - C_{10} aryl. In some embodiments, G is optionally substituted C_2 - C_9 heterocyclyl. In some embodiments, G is optionally substituted C_2 - C_9 heteroaryl.



15 In some embodiments, G is where

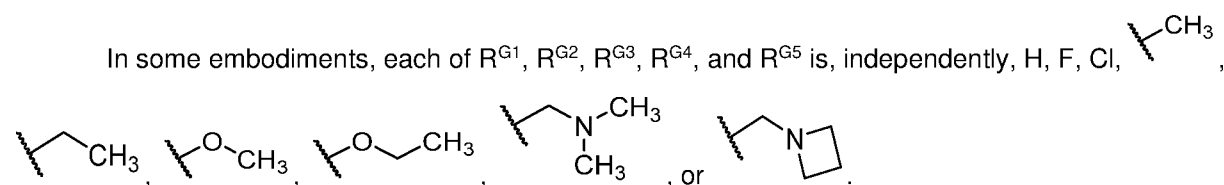
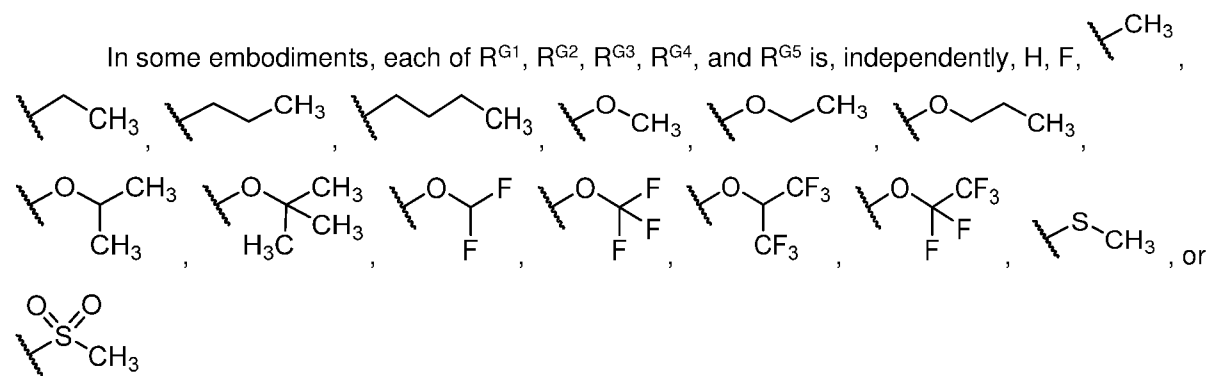
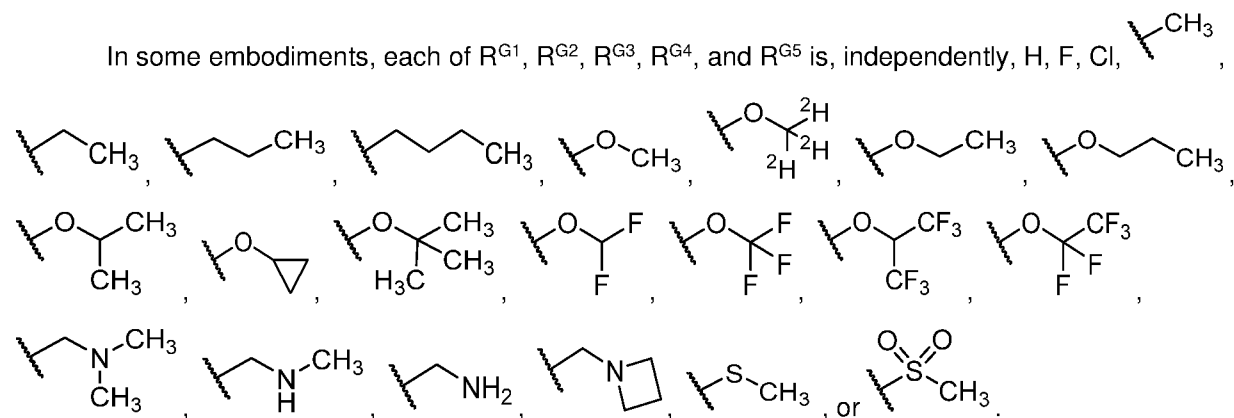
each of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, 20 optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted $-O$ - C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_2 - C_5 heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or R^{G1} and R^{G2} , R^{G2} and R^{G3} , R^{G3} and R^{G4} , and/or R^{G4} and R^{G5} , together with the carbon atoms to which each is attached,

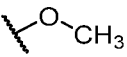
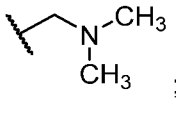
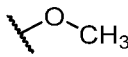
combine to form optionally substituted C₆-C₁₀ aryl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heteroaryl, or optionally substituted C₂-C₉ heterocyclyl.

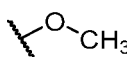
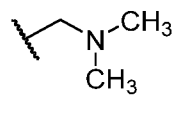
In some embodiments, each of R^{G1}, R^{G2}, R^{G3}, R^{G4}, and R^{G5} is, independently, H, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₂-C₉ heteroaryl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, optionally substituted -O-C₃-C₆ carbocyclyl, optionally substituted -C₁-C₃ alkyl-C₃-C₆ carbocyclyl, optionally substituted -C₁-C₃ alkyl-C₂-C₅ heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or R^{G1} and R^{G2}, R^{G2} and R^{G3}, R^{G3} and R^{G4}, and/or R^{G4} and R^{G5}, together with the carbon atoms to which each is attached, combine to form optionally substituted C₆-C₁₀ aryl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heteroaryl, or optionally substituted C₂-C₉ heterocyclyl.

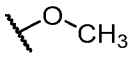
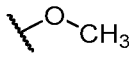
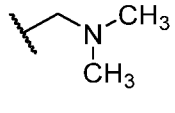
In some embodiments, each of R^{G1}, R^{G2}, R^{G3}, R^{G4}, and R^{G5} is, independently, H, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted -O-C₃-C₆ carbocyclyl, or optionally substituted -C₁-C₃ alkyl-C₂-C₅ heterocyclyl; or R^{G1} and R^{G2}, R^{G2} and R^{G3}, R^{G3} and R^{G4}, and/or R^{G4} and R^{G5}, together with the carbon atoms to which each is attached, combine to form optionally substituted C₂-C₉ heteroaryl or optionally substituted C₂-C₉ heterocyclyl.

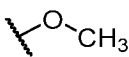
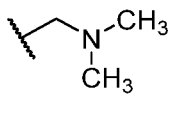
In some embodiments, each of R^{G1}, R^{G2}, R^{G3}, R^{G4}, and R^{G5} is, independently, H, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted -O-C₃-C₆ carbocyclyl, or optionally substituted -C₁-C₃ alkyl-C₂-C₅ heterocyclyl.

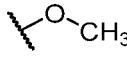
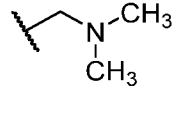
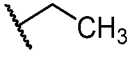


In some embodiments, R^{G1} is H; R^{G2} is ; R^{G3} is ; R^{G4} is ; and

R^{G5} is H. In some embodiments, R^{G1} is H; R^{G2} is ; R^{G3} is ; R^{G4} is H; and R^{G5} is

. In some embodiments, R^{G1} is H; R^{G2} is ; R^{G3} is ; R^{G4} is Cl or F; and

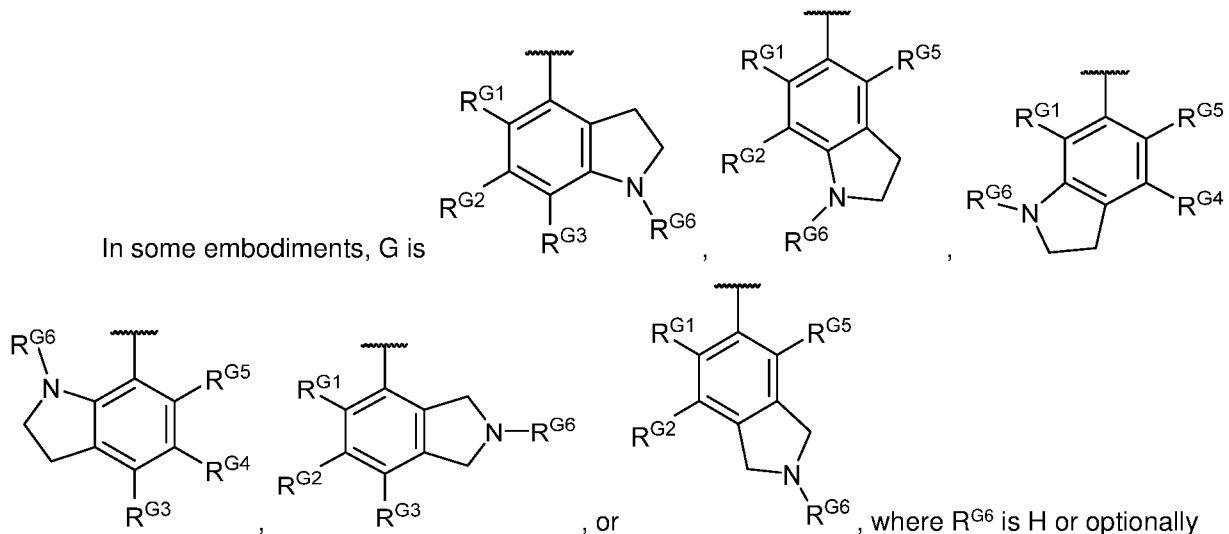
R^{G5} is H. In some embodiments, R^{G1} is H; R^{G2} is ; R^{G3} is ; R^{G4} is H; and

5 R^{G5} is H. In some embodiments, R^{G1} is H; R^{G2} is ; R^{G3} is ; R^{G4} is ; and R^{G5} is H.

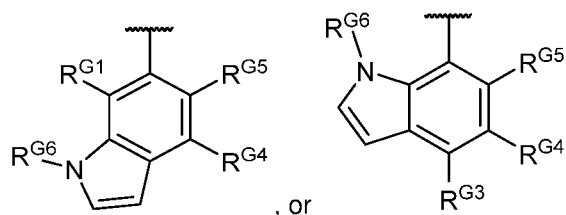
In some embodiments, R^{G1} and R^{G2} , R^{G2} and R^{G3} , R^{G3} and R^{G4} , and/or R^{G4} and R^{G5} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_2 - C_9 heteroaryl or optionally substituted C_2 - C_9 heterocyclyl.

10 In some embodiments, R^{G1} and R^{G2} , R^{G2} and R^{G3} , R^{G3} and R^{G4} , and/or R^{G4} and R^{G5} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_2 - C_9 heterocyclyl. In some embodiments, R^{G1} and R^{G2} , R^{G2} and R^{G3} , R^{G3} and R^{G4} , and/or R^{G4} and R^{G5} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_2 - C_9 heteroaryl.

In some embodiments, G is



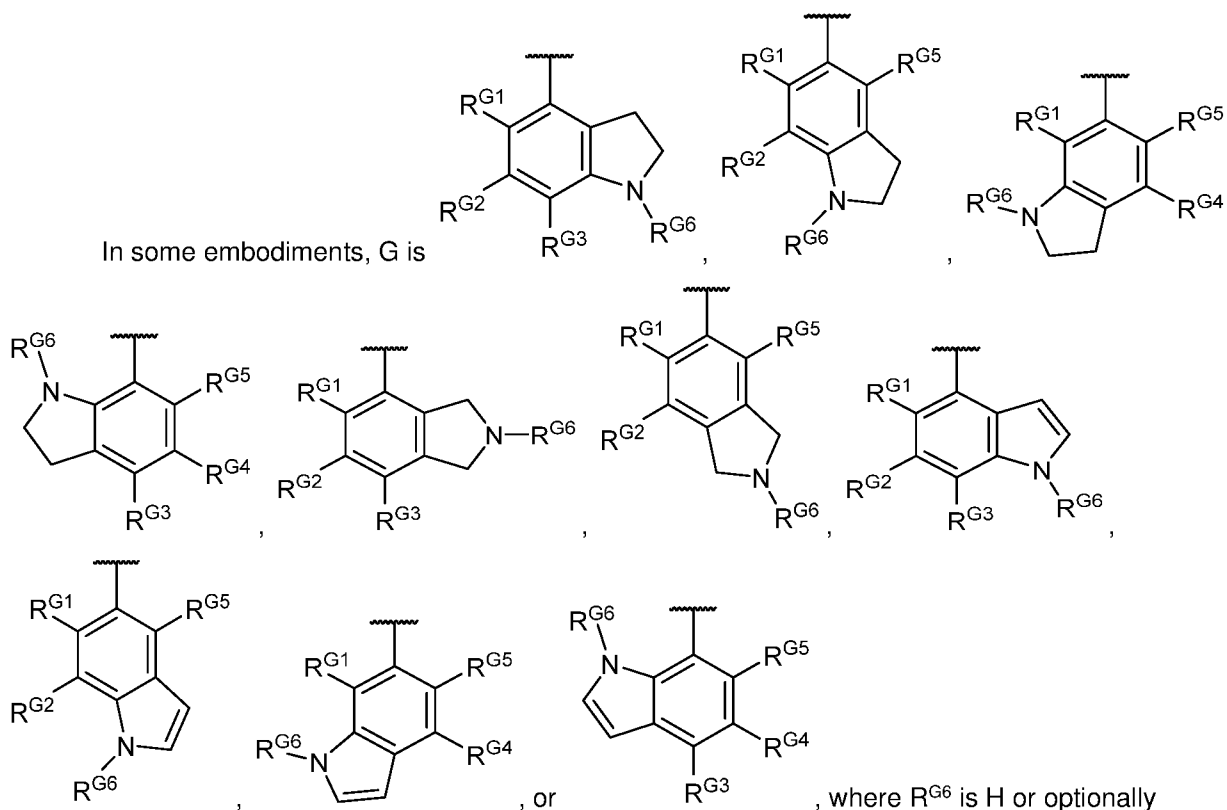
substituted C₁-C₆ alkyl. In some embodiments, G is



, where R^{G6} is H or optionally substituted C₁-C₆ alkyl.

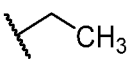
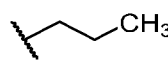
In some embodiments, R^{G1} and R^{G2}, R^{G2} and R^{G3}, R^{G3} and R^{G4}, and/or R^{G4} and R^{G5}, together with the carbon atoms to which each is attached, combine to form optionally substituted C₂-C₉ heterocyclyl or optionally substituted C₂-C₉ heteroaryl.

In some embodiments, G is



substituted C₁-C₆ alkyl.

10

In some embodiments, R^{G6} is H, , , or .

In some embodiments, R^{G6} is H or .

In some embodiments, R^{G6} is H.

In some embodiments, R^{G1} is H, F, , , , , , , , , , , , , , , , , , , or . In some embodiments, R^{G1} is H.

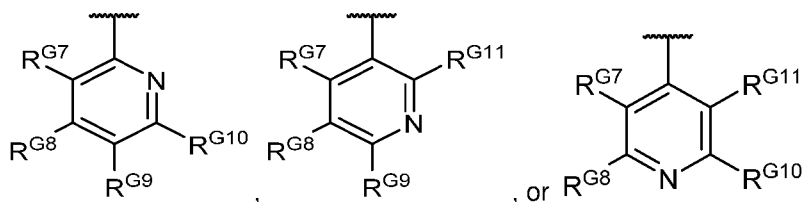
5 In some embodiments, R^{G2} is H, F, , , , , , , , , , , , , , , , , , , or . In some embodiments, R^{G2} is H.

In some embodiments, R^{G3} is H, F, , , , , , , , , , , , , , , , , , , or . In some embodiments, R^{G3} is H.

10 In some embodiments, R^{G4} is H, F, , , , , , , , , , , , , , , , , , , or . In some embodiments, R^{G4} is H.

15 In some embodiments, R^{G5} is H, F, , , , , , , , , , , , , , , , , , , or . In some embodiments, R^{G5} is H.

In some embodiments, one or more of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is H. In some embodiments, two or more of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is H. In some embodiments, three or more of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is H. In some embodiments, each of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is H.



In some embodiments, G is

where

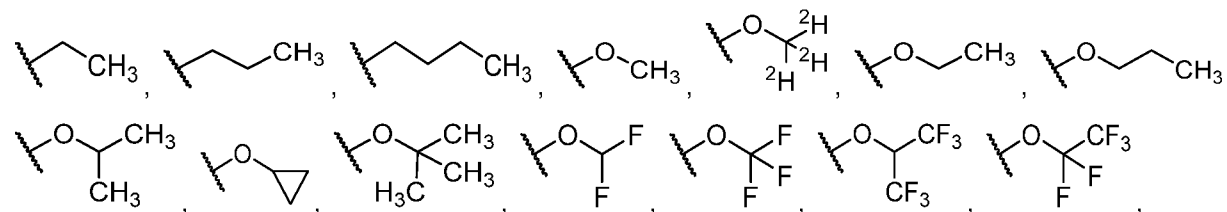
each of R^{G7} , R^{G8} , R^{G9} , R^{G10} , and R^{G11} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted $-O$ - C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_2 - C_5 heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or R^{G7} and R^{G8} , R^{G8} and R^{G9} , R^{G9} and R^{G10} , and/or R^{G10} and R^{G11} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or C_2 - C_9 heterocyclyl.

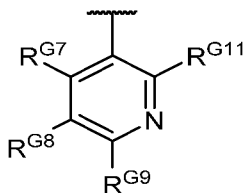
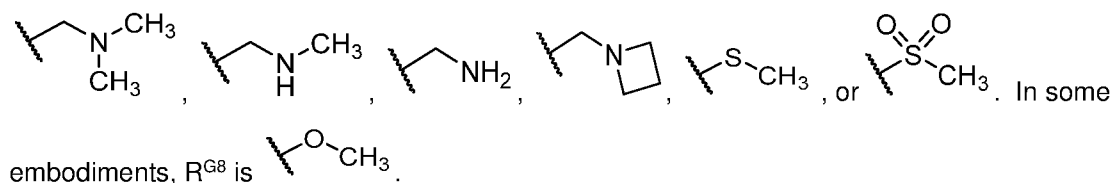
In some embodiments, each of R^{G7} , R^{G8} , R^{G9} , R^{G10} , and R^{G11} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, hydroxyl, thiol, or optionally substituted amino; or R^{G7} and R^{G8} , R^{G8} and R^{G9} , R^{G9} and R^{G10} , and/or R^{G10} and R^{G11} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or C_2 - C_9 heterocyclyl.

In some embodiments, each of R^{G7} , R^{G8} , R^{G9} , R^{G10} , and R^{G11} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted $-O$ - C_3 - C_6 carbocyclyl, or optionally substituted $-C_1$ - C_3 alkyl- C_2 - C_5 heterocyclyl; or R^{G7} and R^{G8} , R^{G8} and R^{G9} , R^{G9} and R^{G10} , and/or R^{G10} and R^{G11} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or C_2 - C_9 heterocyclyl.

In some embodiments, each of R^{G7} , R^{G8} , R^{G9} , R^{G10} , and R^{G11} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted $-O$ - C_3 - C_6 carbocyclyl, or optionally substituted $-C_1$ - C_3 alkyl- C_2 - C_5 heterocyclyl.

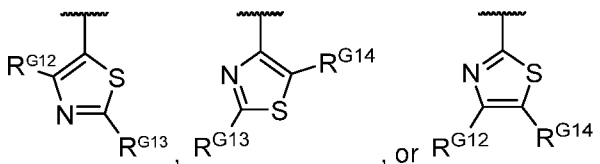
In some embodiments, each of R^{G7} , R^{G8} , R^{G9} , R^{G10} , and R^{G11} is, independently, H, F, Cl, ,





In some embodiments, G is

In some embodiments, R^{G7} is H; R^{G8} is ; R^{G9} is H; and R^{G11} is H.

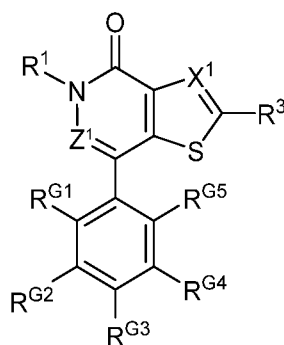


5 In some embodiments, G is
where

each of R^{G12} , R^{G13} , and R^{G14} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted $-O$ - C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_2 - C_5 heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or R^{G12} and R^{G14} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or optionally substituted C_2 - C_9 heterocyclyl.

15 In some embodiments, each of R^{G12} , R^{G13} , and R^{G14} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, hydroxyl, thiol, or optionally substituted amino; or R^{G12} and R^{G14} , together with the carbon atoms to which each is
20 attached, combine to form optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or optionally substituted C_2 - C_9 heterocyclyl.

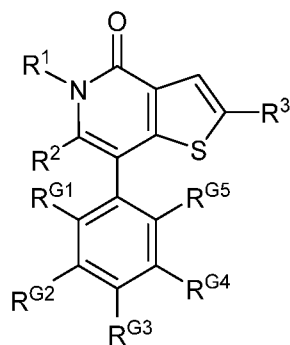
In some embodiments, the compound of **Formula IA** has the structure of **Formula IAa**:



Formula IAa,

25 or a pharmaceutically acceptable salt thereof.

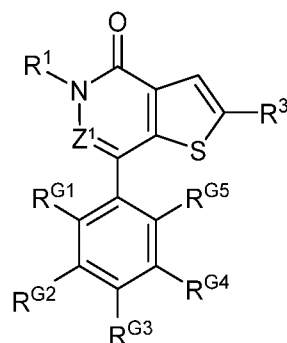
In some embodiments, the compound of **Formula IA** has the structure of **Formula IAb**:



Formula IAb,

or a pharmaceutically acceptable salt thereof.

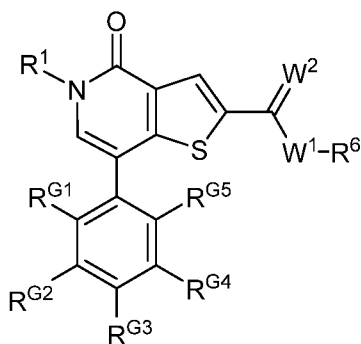
5 In some embodiments, the compound of **Formula IA** has the structure of **Formula IAc**:



Formula IAc,

or a pharmaceutically acceptable salt thereof.

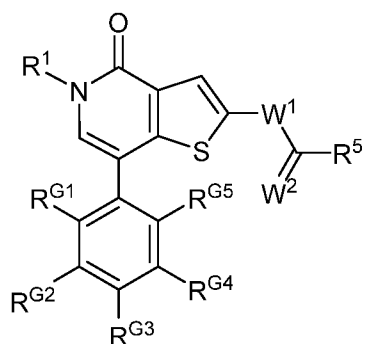
In some embodiments, the compound of **Formula IA** has the structure of **Formula IAd**:



Formula IAd,

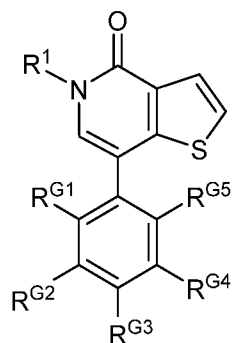
or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound of **Formula IA** has the structure of **Formula IAe**:

**Formula IAe,**

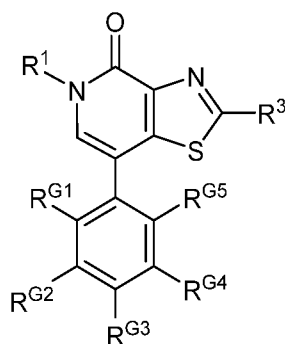
or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound of **Formula IA** has the structure of **Formula IAf**:

**Formula IAf,**

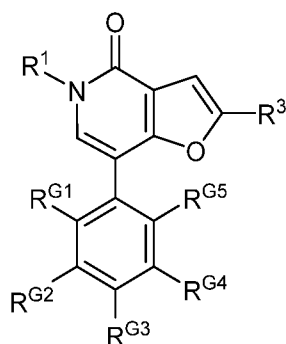
or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound of **Formula IA** has the structure of **Formula IAg**:

**Formula IAg,**

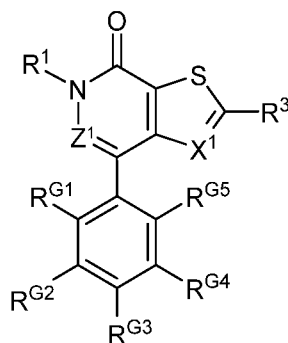
or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound of **Formula IA** has the structure of **Formula IAh**:

**Formula IAh,**

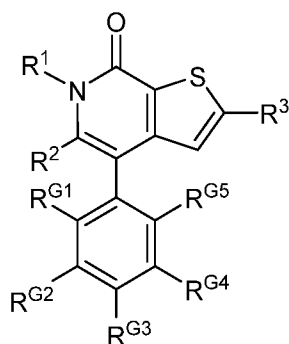
or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound of **Formula IB** has the structure of **Formula IBa**:

**Formula IBa,**

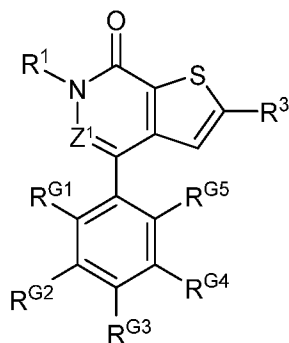
or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound of **Formula IB** has the structure of **Formula IBb**:

**Formula IBb,**

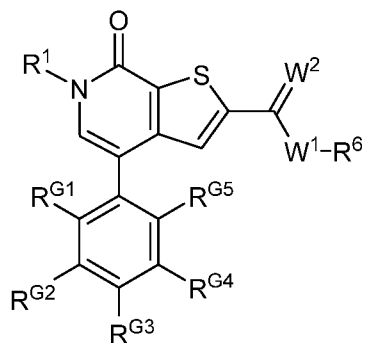
or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound of **Formula IB** has the structure of **Formula IBc**:

**Formula IBc,**

or a pharmaceutically acceptable salt thereof.

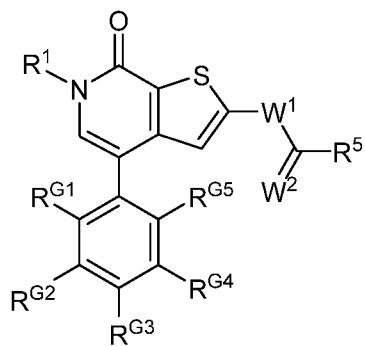
In some embodiments, the compound of **Formula IB** has the structure of **Formula IBd**:



Formula IBd,

5 or a pharmaceutically acceptable salt thereof.

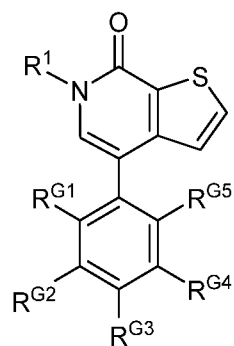
In some embodiments, the compound of **Formula IB** has the structure of **Formula IBe**:



Formula IBe,

or a pharmaceutically acceptable salt thereof.

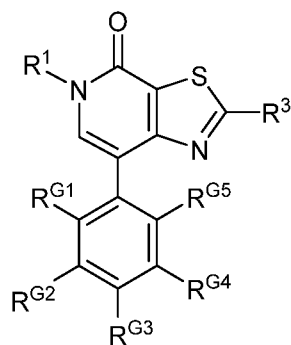
10 In some embodiments, the compound of **Formula IB** has the structure of **Formula IBf**:



Formula IBf,

or a pharmaceutically acceptable salt thereof.

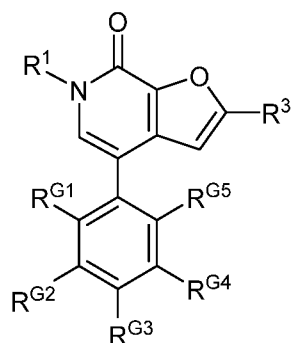
In some embodiments, the compound of **Formula IB** has the structure of **Formula IBg**:



Formula IBg,

or a pharmaceutically acceptable salt thereof.

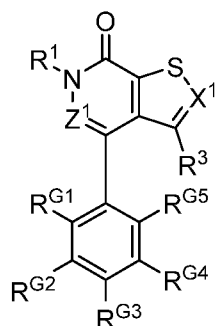
5 In some embodiments, the compound of **Formula IB** has the structure of **Formula IBh**:



Formula IBh,

or a pharmaceutically acceptable salt thereof.

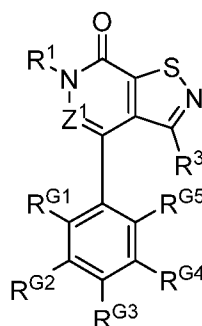
In some embodiments, the compound of **Formula IC** has the structure of **Formula ICa**:



Formula ICa,

or a pharmaceutically acceptable salt thereof.

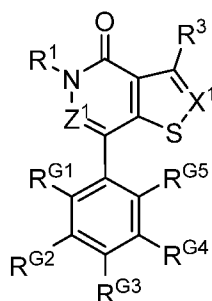
In some embodiments, the compound of **Formula IC** has the structure of **Formula ICb**:



Formula ICb,

or a pharmaceutically acceptable salt thereof.

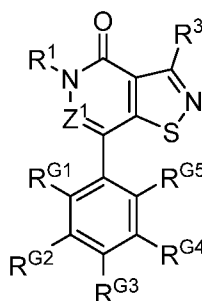
5 In some embodiments, the compound of **Formula ID** has the structure of **Formula IDa**:



Formula IDa,

or a pharmaceutically acceptable salt thereof.

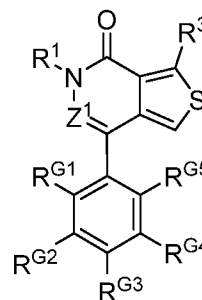
In some embodiments, the compound of **Formula ID** has the structure of **Formula IDb**:



Formula IDb,

or a pharmaceutically acceptable salt thereof.

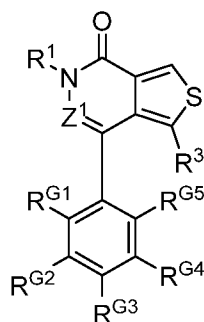
In some embodiments, the compound of **Formula IE** has the structure of **Formula IEa**:



Formula IEa,

or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound of **Formula IF** has the structure of **Formula IF**:



Formula IFa,

or a pharmaceutically acceptable salt thereof.

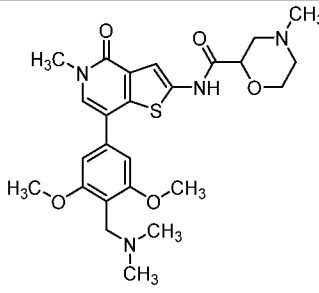
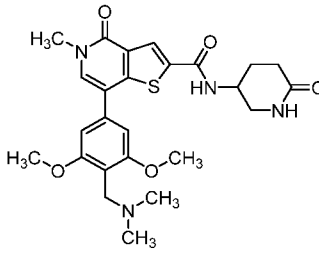
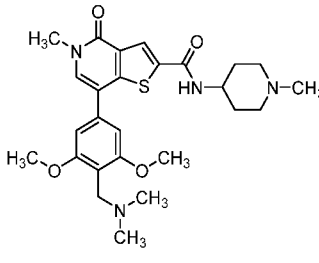
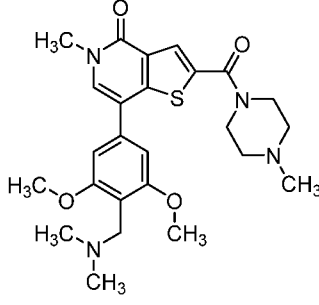
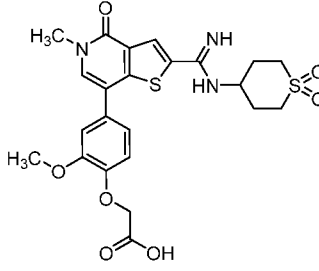
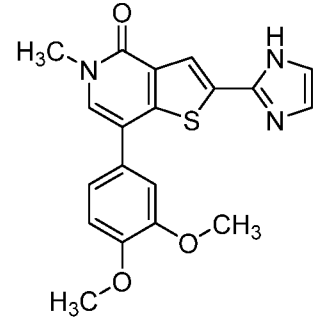
5 In some embodiments, the compound has the structure of any one of compounds B1-B11 in Table 1, or a pharmaceutically acceptable salt thereof. In some embodiments, the compound has the structure of any one of compounds B1-B10 in Table 1, or a pharmaceutically acceptable salt thereof.

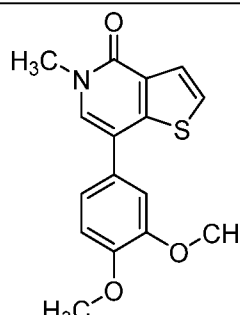
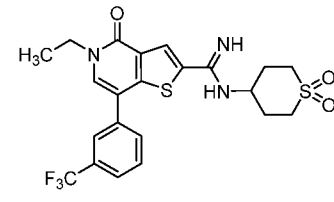
In an aspect, the disclosure features a compound having the structure of any one of compounds B1-B11 in Table 1, or a pharmaceutically acceptable salt thereof.

10 In another aspect, the disclosure features a compound having the structure of any one of compounds B1-B10 in Table 1, or a pharmaceutically acceptable salt thereof.

Table 1. Compounds B1-B11 of the Disclosure

Compound No.	Structure
B1	Structure of B1: A thienopyridine core with a carbonyl group at position 2, a methyl group at position 3, and a trifluoromethyl group at position 4. The thiophene ring is substituted with a sulfonamide group at position 5.
B2	Structure of B2: A thienopyridine core with a carbonyl group at position 2, a methyl group at position 3, and a pyridine ring at position 4. The thiophene ring is substituted with a dimethylamino group at position 5. The pyridine ring is substituted with a dimethylamino group at position 6.
B3	Structure of B3: A thienopyridine core with a carbonyl group at position 2, a methyl group at position 3, and a dimethylamino group at position 4. The thiophene ring is substituted with a dimethylamino group at position 5. The pyridine ring is substituted with a dimethylamino group at position 6.

Compound No.	Structure
B4	
B5	
B6	
B7	
B8	
B9	

Compound No.	Structure
B10	
B11	

In an aspect, the disclosure features a compound having the structure of **Formula II**:

A-L-B

Formula II,

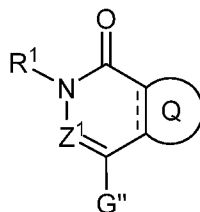
5

where

L is a linker;

B is a degradation moiety; and

A has the structure of **Formula III**:



10

Formula III,

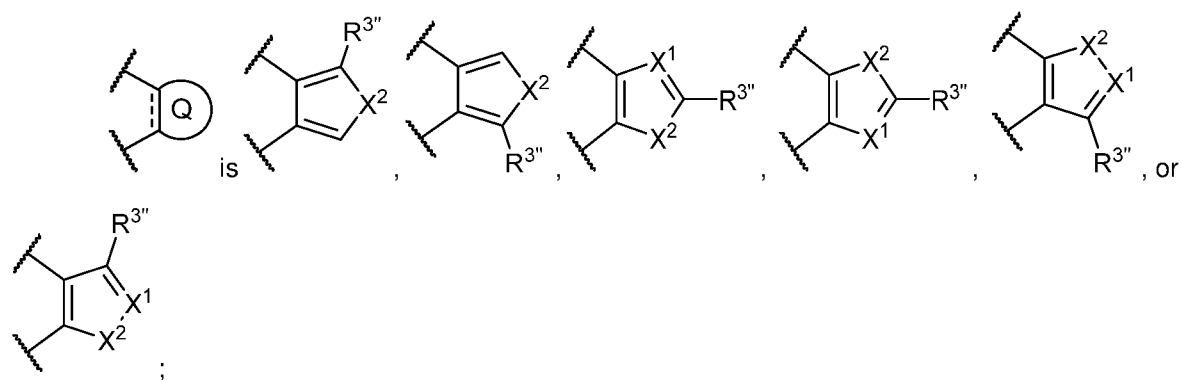
where

R¹ is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₁₀ carbocyclyl;

Z¹ is CR² or N;

15

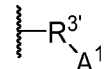
R² is H, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, or optionally substituted C₂-C₉ heteroaryl;



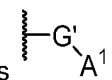
X¹ is CR^{X1} or N;

X² is O or S;

5 R^{X1} is H or optionally substituted C₁-C₆ alkyl;

R^{3''} is H, , cyano, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₁-C₆ alkoxy, optionally substituted amino, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₃-C₁₀ heterocyclyl, or optionally substituted C₂-C₉ heteroaryl;

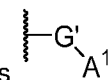
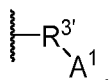
10 R^{3'} is absent, optionally substituted C₁-C₆ alkylene, optionally substituted C₂-C₉ heteroarylene, or optionally substituted C₁-C₆ heteroalkylene;

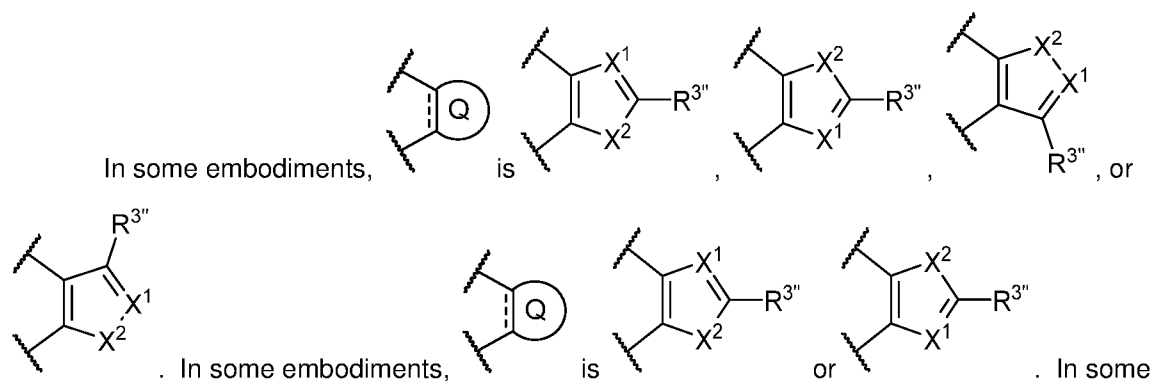
G'' is , optionally substituted C₃-C₁₀ carbocyclyl, C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, or optionally substituted C₂-C₉ heteroaryl;

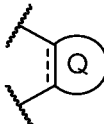
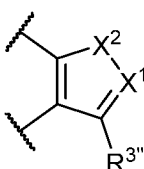
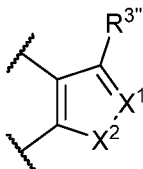
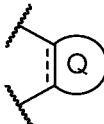
G' is optionally substituted C₃-C₁₀ carbocyclylene, C₂-C₉ heterocyclylene, optionally substituted C₆-C₁₀ arylene, or optionally substituted C₂-C₉ heteroarylene; and

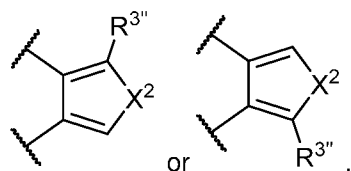
15 A¹ is a bond between A and the linker,

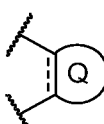
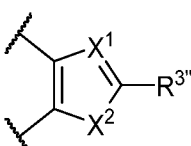
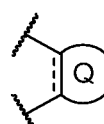
A¹ is a bond between A and the linker,

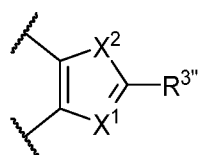
where G'' is  or R^{3''} is , or a pharmaceutically acceptable salt thereof.



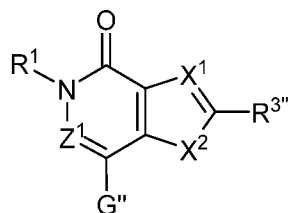
embodiments,  is  or . In some embodiments,  is



In some embodiments,  is . In some embodiments,  is



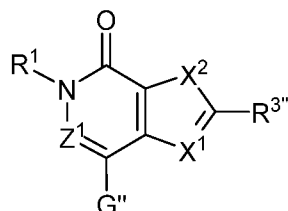
5 In some embodiments, the compound of **Formula III** has the structure of **Formula IIIA**:



Formula IIIA,

or a pharmaceutically acceptable salt thereof.

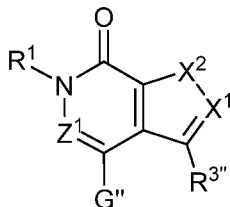
In some embodiments, the compound of **Formula III** has the structure of **Formula IIIB**:



Formula IIIB,

or a pharmaceutically acceptable salt thereof.

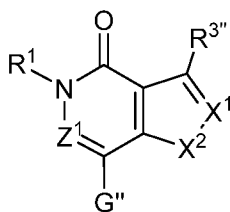
In some embodiments, the compound of **Formula III** has the structure of **Formula IIIC**:



Formula IIIC,

or a pharmaceutically acceptable salt thereof.

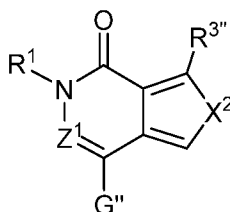
In some embodiments, the compound of **Formula III** has the structure of **Formula IIID**:



Formula IIID,

or a pharmaceutically acceptable salt thereof.

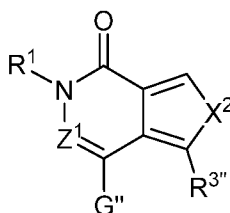
In some embodiments, the compound of **Formula III** has the structure of **Formula IIIE**:



Formula IIIE,

or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound of **Formula III** has the structure of **Formula IIIF**:



Formula IIIF,

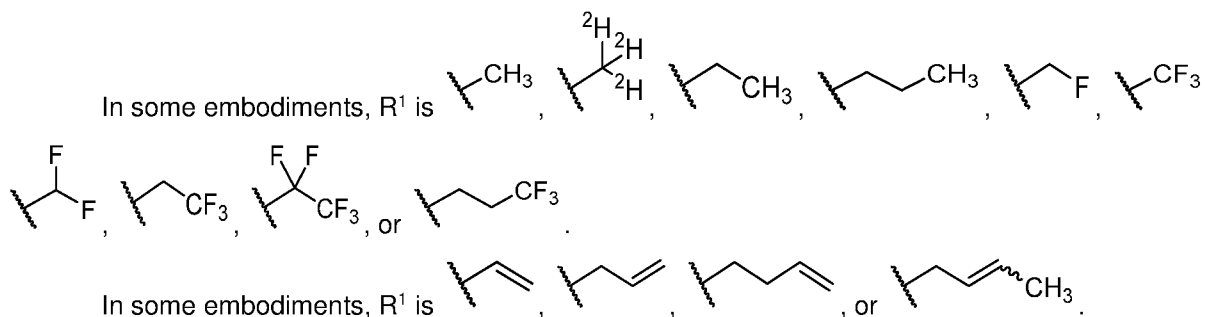
or a pharmaceutically acceptable salt thereof.

In some embodiments, R¹ is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₁₀ carbocyclyl. In some embodiments, R¹ is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₂-C₆ alkenyl, or optionally substituted C₃-C₁₀ carbocyclyl.

In some embodiments, R¹ is H, optionally substituted C₁-C₆ alkyl, or optionally substituted C₃-C₁₀ carbocyclyl.

In some embodiments, R¹ is H. In some embodiments, R¹ is optionally substituted C₁-C₆ alkyl. In some embodiments, R¹ is optionally substituted C₂-C₆ alkenyl. In some embodiments, R¹ is optionally substituted C₃-C₁₀ carbocyclyl.

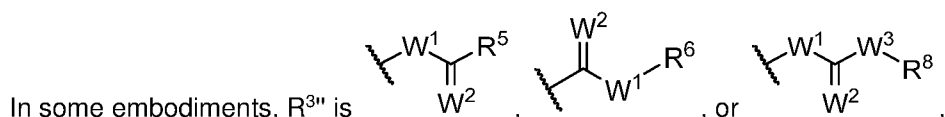
In some embodiments, optionally substituted C₁-C₆ alkyl is C₁-C₆ perfluoroalkyl.



In some embodiments, $R^{3''}$ is H, cyano, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_1 - C_6 alkoxy, optionally substituted amino, optionally substituted C_3 - C_{10} heterocyclyl, or optionally substituted C_2 - C_9 heteroaryl. In some embodiments, $R^{3''}$ is optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, or optionally substituted C_3 - C_{10} heterocyclyl. In some embodiments, $R^{3''}$ is cyano, optionally substituted C_1 - C_6 alkoxy, or optionally substituted amino.

In some embodiments, $R^{3''}$ is H, optionally substituted C_1 - C_6 alkyl, or optionally substituted C_1 - C_6 heteroalkyl. In some embodiments, $R^{3''}$ is H or optionally substituted C_1 - C_6 alkyl. In some embodiments, $R^{3''}$ is H. In some embodiments, $R^{3''}$ is optionally substituted C_1 - C_6 alkyl.

In some embodiments, $R^{3''}$ is optionally substituted C_2 - C_9 heteroaryl or optionally substituted C_1 - C_6 heteroalkyl. In some embodiments, $R^{3''}$ is optionally substituted C_1 - C_6 heteroalkyl.



where

W^1 is NR^4 or O;

W^2 is NH, O, or S;

W^3 is NR^7 or O;

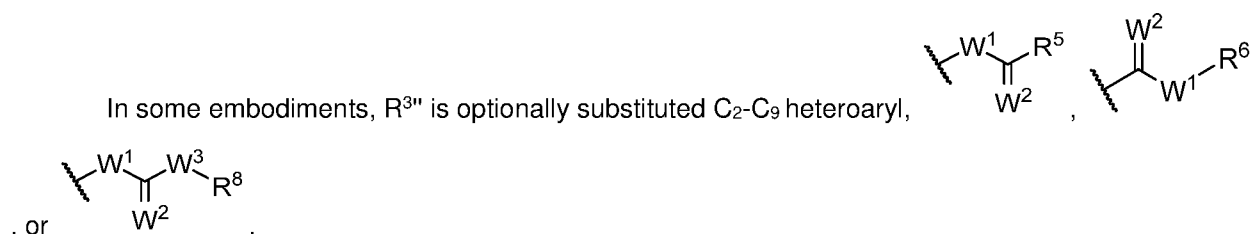
R^4 is H or optionally substituted C_1 - C_6 alkyl;

R^5 is optionally substituted C_1 - C_6 alkyl, optionally substituted C_3 - C_{10} carbocyclyl, or optionally substituted C_2 - C_9 heterocyclyl;

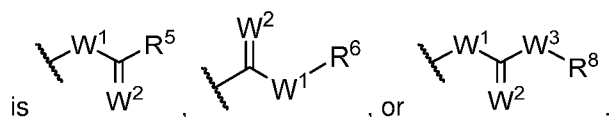
R^6 is H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_3 - C_{10} carbocyclyl, or optionally substituted C_2 - C_9 heterocyclyl;

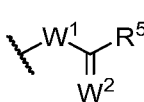
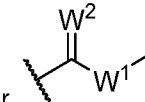
R^7 is H or optionally substituted C_1 - C_6 alkyl; and

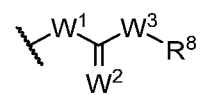
R^8 is H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_3 - C_{10} carbocyclyl, or optionally substituted C_2 - C_9 heterocyclyl.



In some embodiments, $R^{3''}$ is optionally substituted C_2 - C_9 heteroaryl. In some embodiments, $R^{3''}$



In some embodiments, $R^{3''}$ is  or . In some embodiments, $R^{3''}$ is



In some embodiments, W^1 is NR^4 . In some embodiments, W^1 is O.

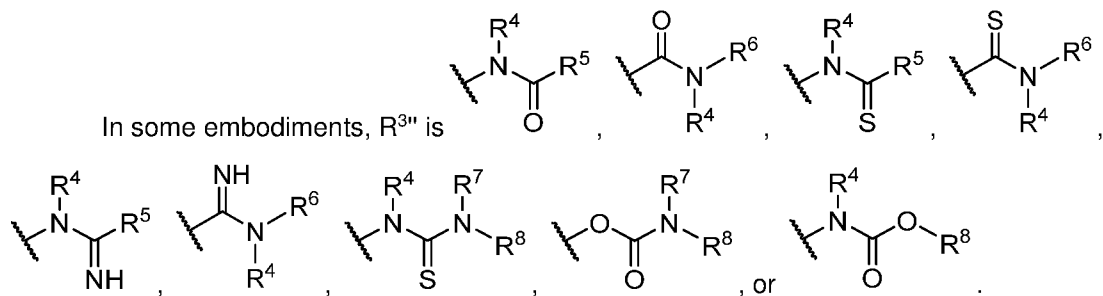
In some embodiments, W^2 is NH. In some embodiments, W^2 is O. In some embodiments, W^2 is

S.

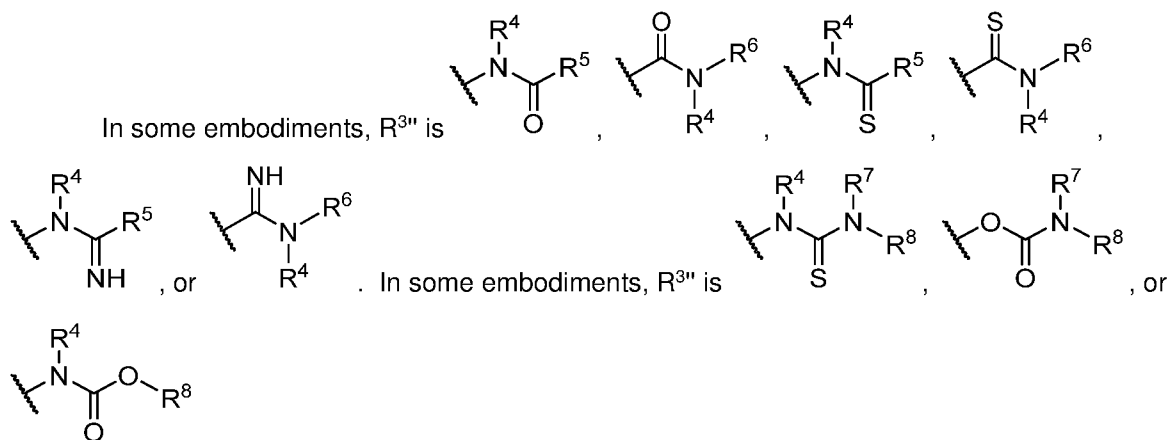
In some embodiments, W^3 is NR^7 . In some embodiments, W^3 is O.

5

In some embodiments, $R^{3''}$ is

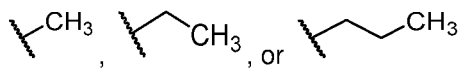


In some embodiments, $R^{3''}$ is

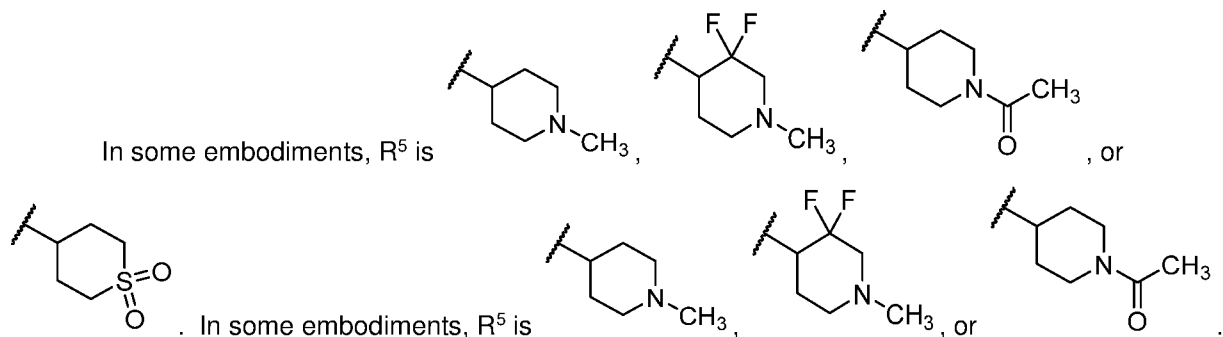


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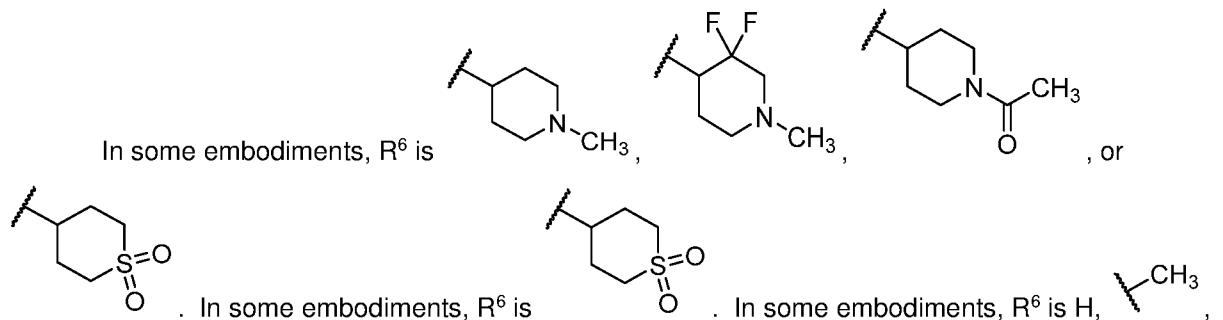
In some embodiments, R^4 is H,



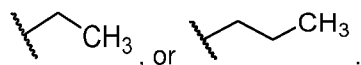
In some embodiments, R^5 is

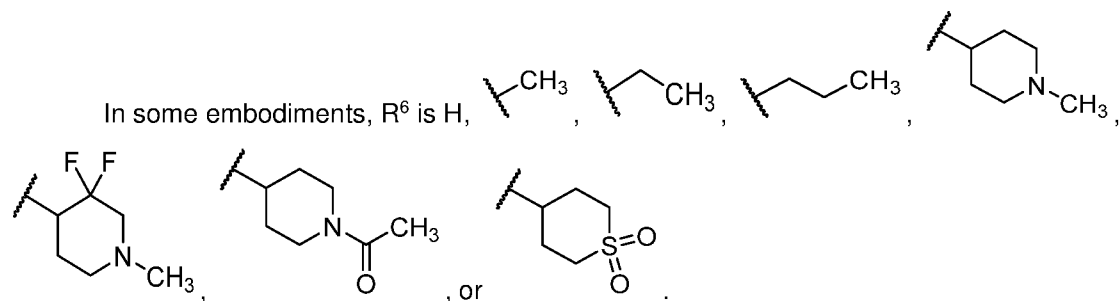


In some embodiments, R^6 is



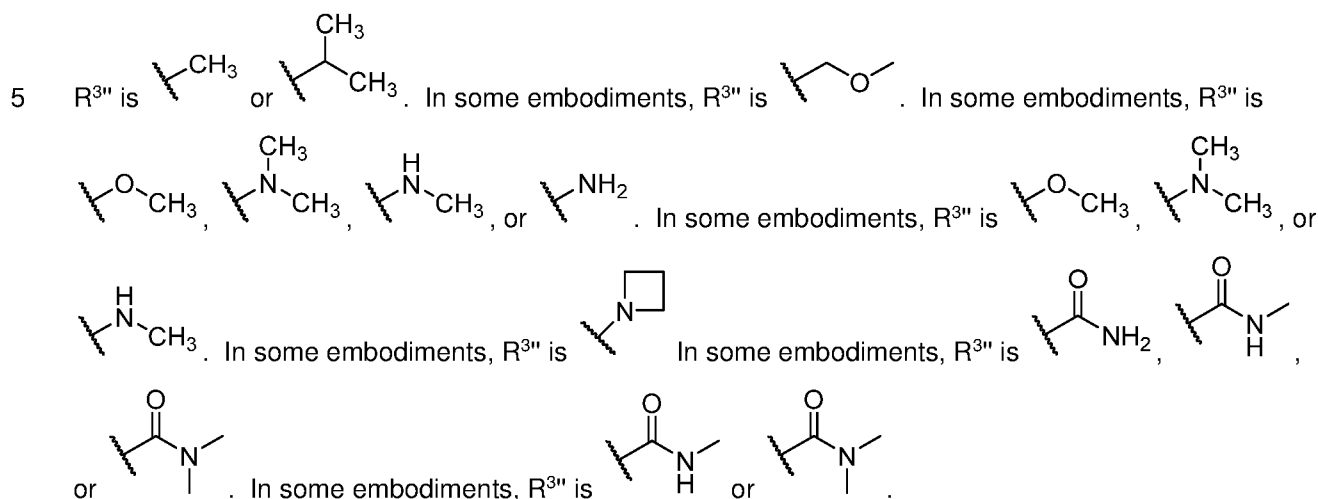
15





In some embodiments, R^7 is H, , , or .

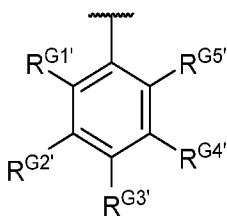
In some embodiments, $R^{3''}$ is H. In some embodiments, $R^{3''}$ is cyano. In some embodiments,



In some embodiments, G'' is .

10 In some embodiments, G' is optionally substituted C_3 - C_{10} carbocyclylene or optionally substituted C_2 - C_9 heterocyclylene. In some embodiments, G' is optionally substituted C_6 - C_{10} arylene or optionally substituted C_2 - C_9 heteroarylene.

In some embodiments, G' is optionally substituted C_3 - C_{10} carbocyclylene. In some embodiments, G' is optionally substituted C_6 - C_{10} arylene. In some embodiments, G' is optionally substituted C_2 - C_9 heterocyclylene. In some embodiments, G' is optionally substituted C_2 - C_9 heteroarylene.



In some embodiments, G' is

where

each of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$, and $R^{G5'}$ is, independently, H, A^1 , halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted $-O$ - C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_2 - C_5 heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or $R^{G1'}$ and

$R^{G2'}$, $R^{G2'}$ and $R^{G3'}$, $R^{G3'}$ and $R^{G4'}$, and/or $R^{G4'}$ and $R^{G5'}$, together with the carbon atoms to which each is

attached, combine to form $\textcircled{\text{M}}$; and $\textcircled{\text{M}}$ is optionally substituted $\text{C}_6\text{-C}_{10}$ aryl, optionally substituted $\text{C}_3\text{-C}_{10}$ carbocyclyl, optionally substituted $\text{C}_2\text{-C}_9$ heteroaryl, or optionally substituted $\text{C}_2\text{-C}_9$ heterocyclyl,

any of which is optionally substituted with A^1 , where one of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$, and $R^{G5'}$ is A^1 , or $\textcircled{\text{M}}$ is substituted with A^1 .

In some embodiments, each of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$, and $R^{G5'}$ is, independently, H, A^1 , halogen, optionally substituted $\text{C}_1\text{-C}_6$ alkyl, optionally substituted $\text{C}_1\text{-C}_6$ heteroalkyl, optionally substituted $\text{C}_3\text{-C}_{10}$ carbocyclyl, optionally substituted $\text{C}_2\text{-C}_9$ heterocyclyl, optionally substituted $\text{C}_6\text{-C}_{10}$ aryl, optionally substituted $\text{C}_2\text{-C}_9$ heteroaryl, optionally substituted $\text{C}_2\text{-C}_6$ alkenyl, optionally substituted $\text{C}_2\text{-C}_6$ heteroalkenyl, optionally substituted $-\text{O}-\text{C}_3\text{-C}_6$ carbocyclyl, optionally substituted $-\text{C}_1\text{-C}_3$ alkyl- $\text{C}_3\text{-C}_6$ carbocyclyl, optionally substituted $-\text{C}_1\text{-C}_3$ alkyl- $\text{C}_2\text{-C}_5$ heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or $R^{G1'}$ and $R^{G2'}$, $R^{G2'}$ and $R^{G3'}$, $R^{G3'}$ and $R^{G4'}$, and/or $R^{G4'}$ and $R^{G5'}$, together with the carbon atoms

to which each is attached, combine to form $\textcircled{\text{M}}$; and $\textcircled{\text{M}}$ is optionally substituted $\text{C}_6\text{-C}_{10}$ aryl, optionally substituted $\text{C}_3\text{-C}_{10}$ carbocyclyl, optionally substituted $\text{C}_2\text{-C}_9$ heteroaryl, or optionally substituted $\text{C}_2\text{-C}_9$ heterocyclyl, any of which is optionally substituted with A^1 , where one of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$, and

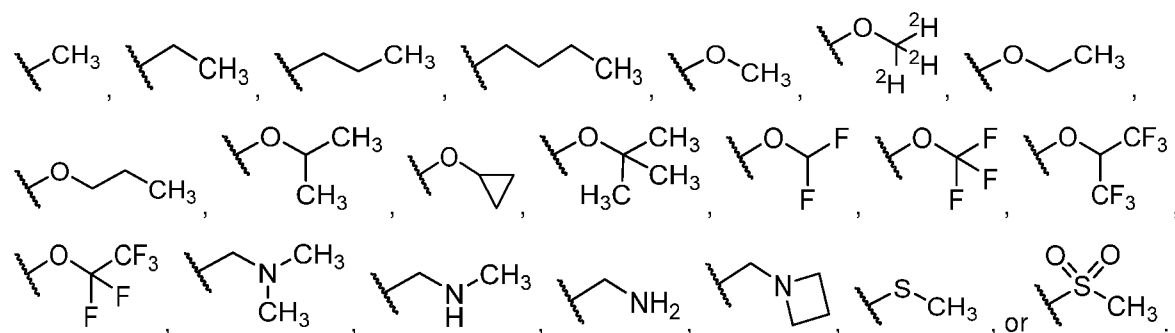
$R^{G5'}$ is A^1 , or $\textcircled{\text{M}}$ is substituted with A^1 .

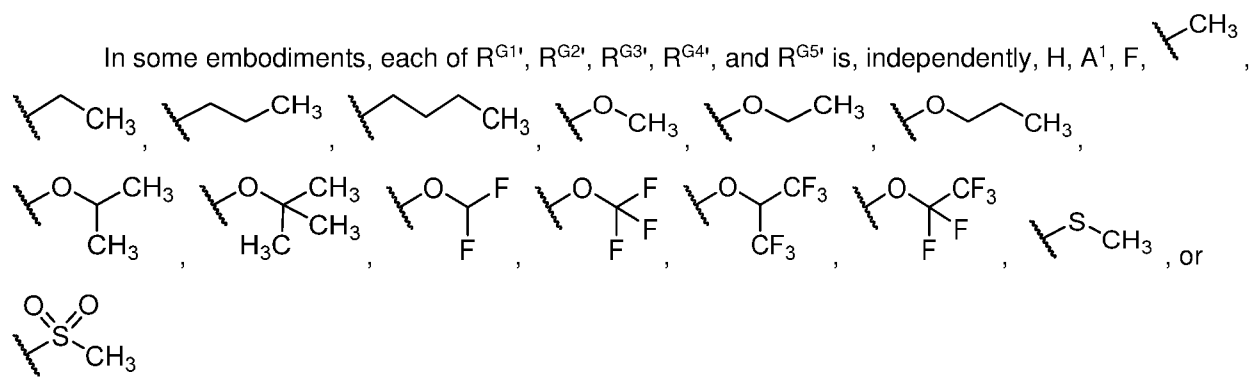
In some embodiments, each of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$, and $R^{G5'}$ is, independently, H, A^1 , halogen, optionally substituted $\text{C}_1\text{-C}_6$ alkyl, optionally substituted $\text{C}_1\text{-C}_6$ heteroalkyl, optionally substituted $-\text{O}-\text{C}_3\text{-C}_6$ carbocyclyl, or optionally substituted $-\text{C}_1\text{-C}_3$ alkyl- $\text{C}_2\text{-C}_5$ heterocyclyl; or $R^{G1'}$ and $R^{G2'}$, $R^{G2'}$ and $R^{G3'}$, $R^{G3'}$ and $R^{G4'}$, and/or $R^{G4'}$ and $R^{G5'}$, together with the carbon atoms to which each is attached, combine to form

$\textcircled{\text{M}}$; and $\textcircled{\text{M}}$ is optionally substituted $\text{C}_2\text{-C}_9$ heteroaryl or optionally substituted $\text{C}_2\text{-C}_9$ heterocyclyl, any of which is optionally substituted with A^1 , where one of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$, and $R^{G5'}$ is A^1 , or $\textcircled{\text{M}}$ is substituted with A^1 .

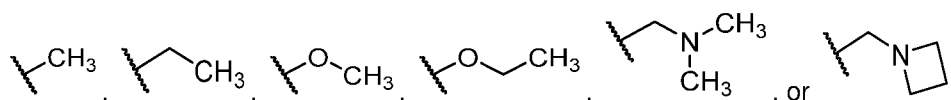
In some embodiments, each of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$, and $R^{G5'}$ is, independently, H, A^1 , halogen, optionally substituted $\text{C}_1\text{-C}_6$ alkyl, optionally substituted $\text{C}_1\text{-C}_6$ heteroalkyl, optionally substituted $-\text{O}-\text{C}_3\text{-C}_6$ carbocyclyl, or optionally substituted $-\text{C}_1\text{-C}_3$ alkyl- $\text{C}_2\text{-C}_5$ heterocyclyl.

In some embodiments, each of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$, and $R^{G5'}$ is, independently, H, A^1 , F, Cl,

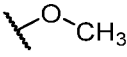
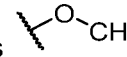


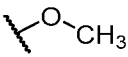
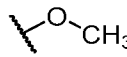


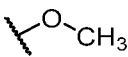
5 In some embodiments, each of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$, and $R^{G5'}$ is, independently, H, A^1 , F, Cl,

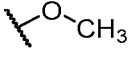


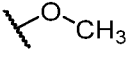
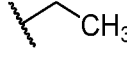
In some embodiments, $R^{G3'}$ is A^1 .

In some embodiments, $R^{G1'}$ is H; $R^{G2'}$ is ; $R^{G3'}$ is A^1 ; $R^{G4'}$ is ; and $R^{G5'}$ is H.

In some embodiments, $R^{G1'}$ is H; $R^{G2'}$ is ; $R^{G3'}$ is A^1 ; $R^{G4'}$ is H; and $R^{G5'}$ is . In some

10 embodiments, $R^{G1'}$ is H; $R^{G2'}$ is ; $R^{G3'}$ is A^1 ; $R^{G4'}$ is Cl or F; and $R^{G5'}$ is H. In some

embodiments, $R^{G1'}$ is H; $R^{G2'}$ is ; $R^{G3'}$ is A^1 ; $R^{G4'}$ is H; and $R^{G5'}$ is H. In some embodiments,

$R^{G1'}$ is H; $R^{G2'}$ is ; $R^{G3'}$ is A^1 ; $R^{G4'}$ is ; and $R^{G5'}$ is H.

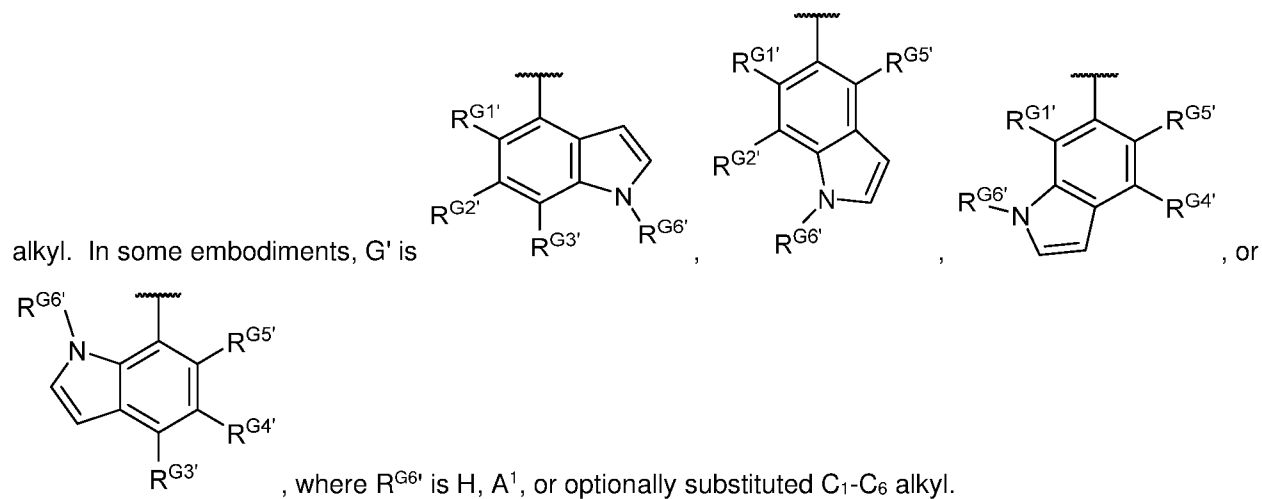
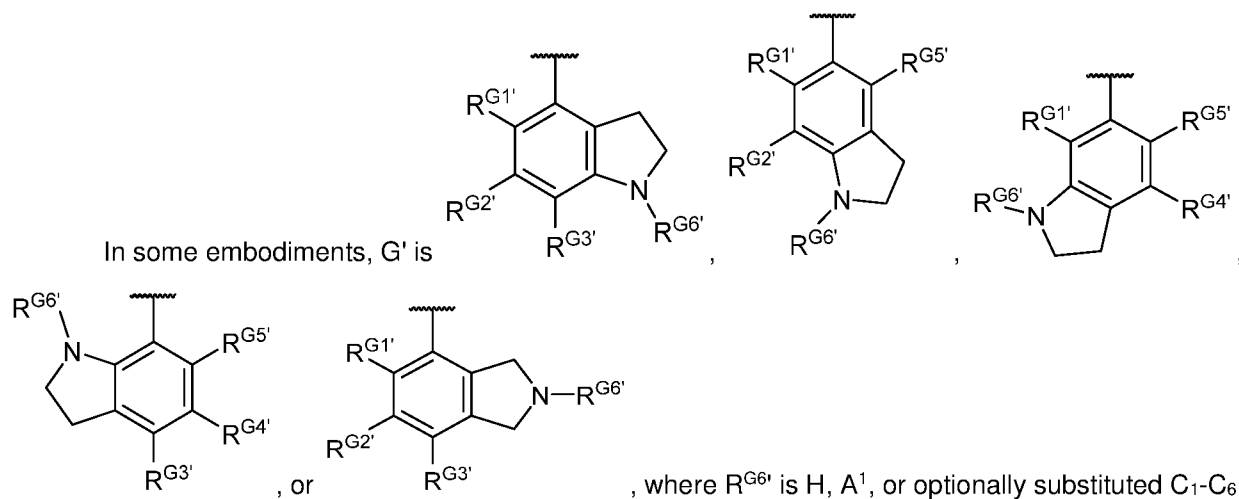
In some embodiments, $R^{G1'}$ and $R^{G2'}$, $R^{G2'}$ and $R^{G3'}$, $R^{G3'}$ and $R^{G4'}$, and/or $R^{G4'}$ and $R^{G5'}$, together

15 with the carbon atoms to which each is attached, combine to form ; and  is optionally substituted C_2 - C_9 heterocyclyl, which is optionally substituted with A^1 , where one of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$,

and $R^{G5'}$ is A^1 , or  is substituted with A^1 . In some embodiments, $R^{G1'}$ and $R^{G2'}$, $R^{G2'}$ and $R^{G3'}$, $R^{G3'}$ and $R^{G4'}$, and/or $R^{G4'}$ and $R^{G5'}$, together with the carbon atoms to which each is attached, combine to form

; and  is optionally substituted C_2 - C_9 heteroaryl, which is optionally substituted with A^1 , where

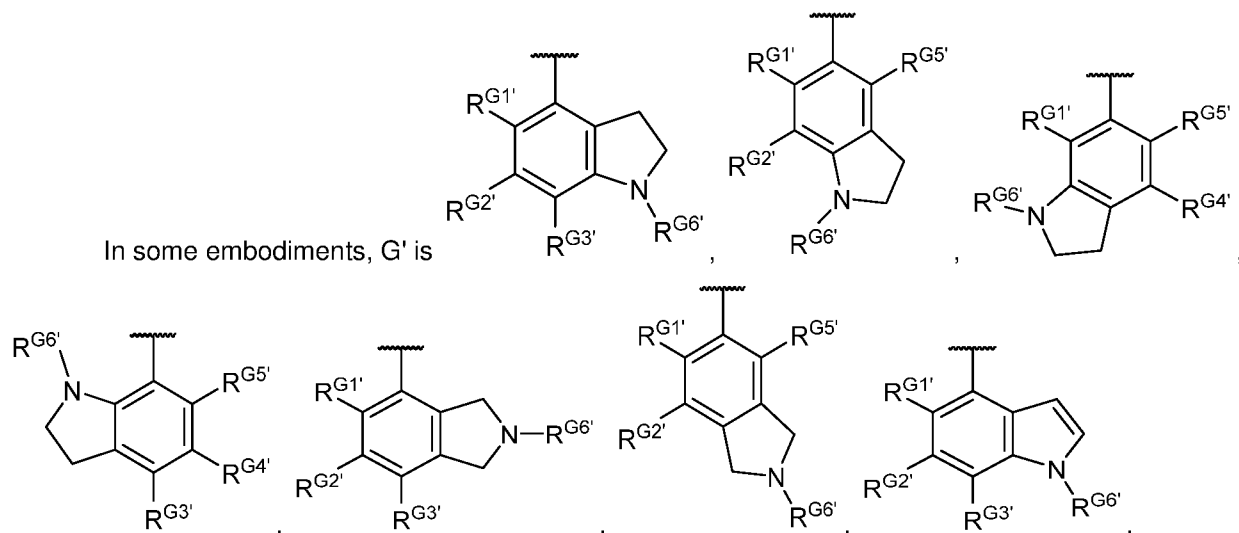
one of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$, and $R^{G5'}$ is A^1 , or  is substituted with A^1 .



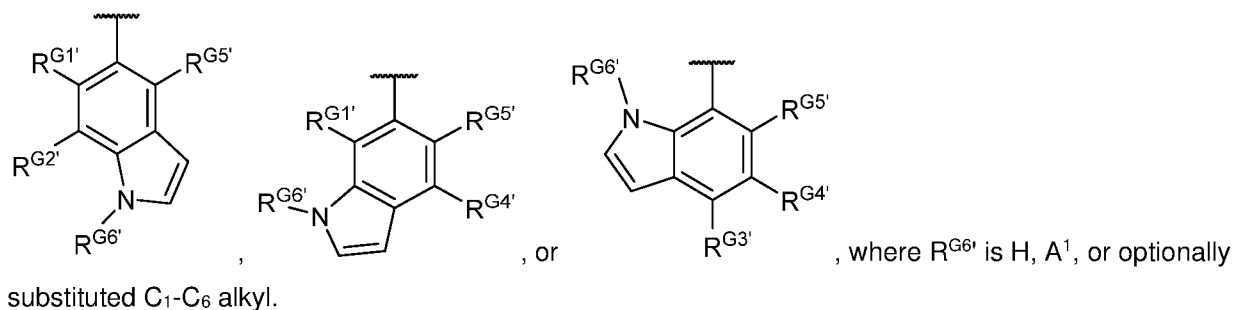
5 In some embodiments, R^{G1'} and R^{G2'}, R^{G2'} and R^{G3'}, R^{G3'} and R^{G4'}, and/or R^{G4'} and R^{G5'}, together

with the carbon atoms to which each is attached, combine to form $\textcircled{\text{M}}$; and $\textcircled{\text{M}}$ is optionally substituted C₂-C₉ heterocyclyl or optionally substituted C₂-C₉ heteroaryl, any of which is optionally

substituted with A¹, where one of R^{G1'}, R^{G2'}, R^{G3'}, R^{G4'}, and R^{G5'} is A¹, or $\textcircled{\text{M}}$ is substituted with A¹.



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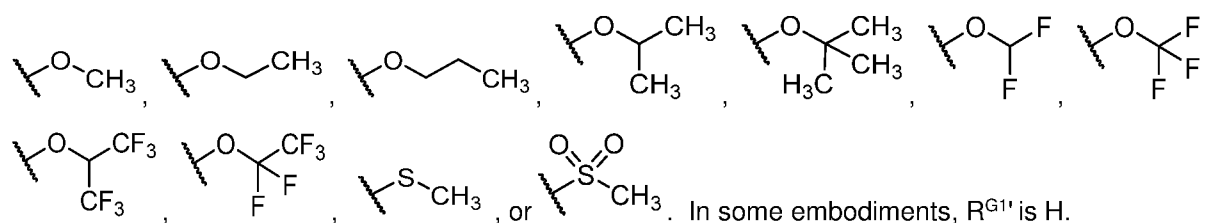
In some embodiments, $R^{G6'}$ is H, A^1 , , , or .

In some embodiments, $R^{G6'}$ is H, A^1 , or .

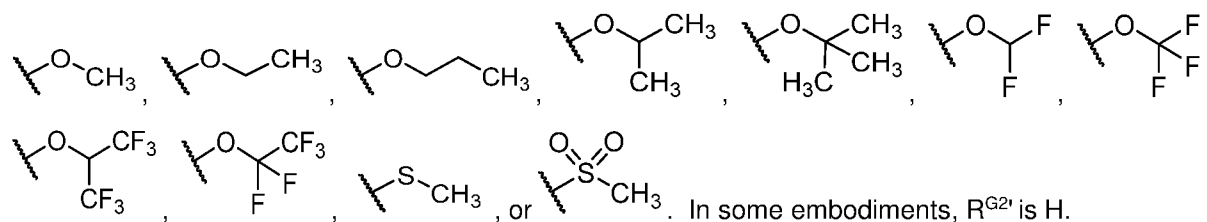
5 In some embodiments, $R^{G6'}$ is H or A^1 .

In some embodiments, $R^{G6'}$ is H. In some embodiments, $R^{G6'}$ is A^1 .

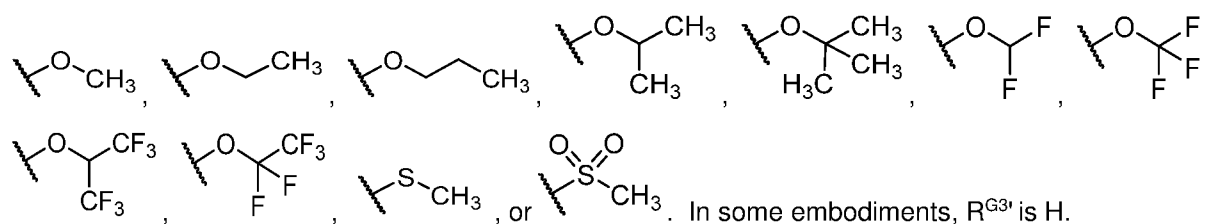
In some embodiments, $R^{G1'}$ is H, A^1 , F, , , , ,



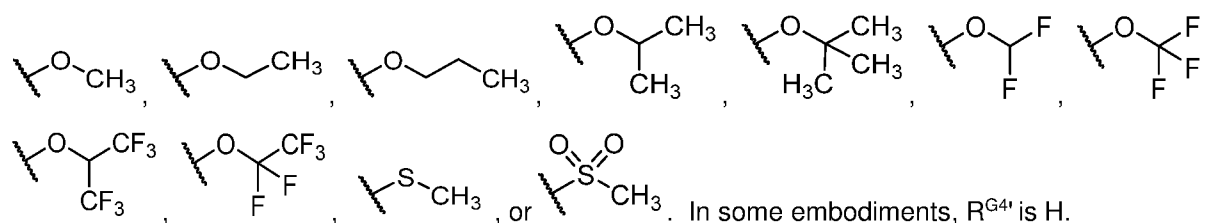
10 In some embodiments, $R^{G2'}$ is H, A^1 , F, , , , ,

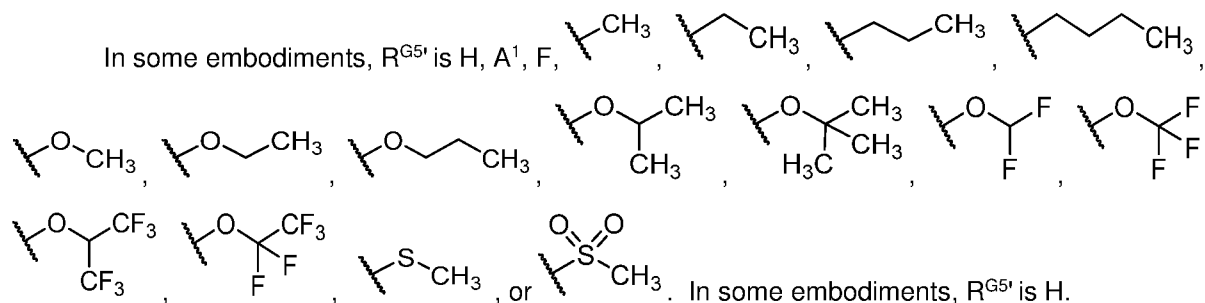


In some embodiments, $R^{G3'}$ is H, A^1 , F, , , , ,



15 In some embodiments, $R^{G4'}$ is H, A^1 , F, , , , ,



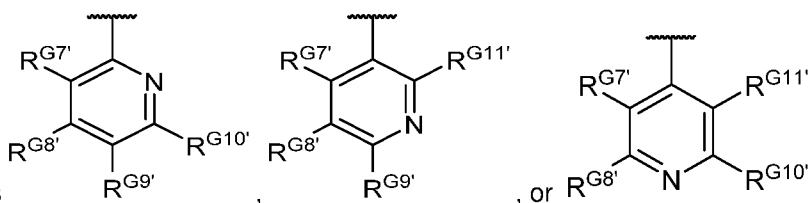


In some embodiments, one or more of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$, and $R^{G5'}$ is H. In some
 5 embodiments, two or more of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$, and $R^{G5'}$ is H. In some embodiments, three or more of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$, and $R^{G5'}$ is H.

In some embodiments, $R^{G1'}$ is A^1 . In some embodiments, $R^{G2'}$ is A^1 . In some embodiments, $R^{G3'}$

is A^1 . In some embodiments, $R^{G4'}$ is A^1 . In some embodiments, $R^{G5'}$ is A^1 . In some embodiments,
 is substituted with A^1 .

(M)



10 In some embodiments, G^1 is
 where

each of $R^{G7'}$, $R^{G8'}$, $R^{G9'}$, $R^{G10'}$, and $R^{G11'}$ is, independently, H, A^1 , halogen, optionally substituted
 C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally
 substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl,
 15 optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally
 substituted -O- C_3 - C_6 carbocyclyl, optionally substituted - C_1 - C_3 alkyl- C_3 - C_6 carbocyclyl, optionally
 substituted - C_1 - C_3 alkyl- C_2 - C_5 heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or $R^{G7'}$ and
 $R^{G8'}$, $R^{G8'}$ and $R^{G9'}$, $R^{G9'}$ and $R^{G10'}$, and/or $R^{G10'}$ and $R^{G11'}$, together with the carbon atoms to which each is

attached, combine to form (M); and (M) is optionally substituted C_6 - C_{10} aryl, optionally substituted
 20 C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or C_2 - C_9 heterocyclyl, any of which is

optionally substituted with A^1 , where one of $R^{G7'}$, $R^{G8'}$, $R^{G9'}$, $R^{G10'}$, and $R^{G11'}$ is A^1 ; or (M) is substituted
 with A^1 .

In some embodiments, each of $R^{G7'}$, $R^{G8'}$, $R^{G9'}$, $R^{G10'}$, and $R^{G11'}$ is, independently, H, A^1 , halogen,
 optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10}
 25 carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally
 substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6
 heteroalkenyl, optionally substituted -O- C_3 - C_6 carbocyclyl, optionally substituted - C_1 - C_3 alkyl- C_3 - C_6
 carbocyclyl, optionally substituted - C_1 - C_3 alkyl- C_2 - C_5 heterocyclyl, hydroxyl, thiol, or optionally substituted
 amino; or $R^{G7'}$ and $R^{G8'}$, $R^{G8'}$ and $R^{G9'}$, $R^{G9'}$ and $R^{G10'}$, and/or $R^{G10'}$ and $R^{G11'}$, together with the carbon

atoms to which each is attached, combine to form $\textcircled{\text{M}}$; and $\textcircled{\text{M}}$ is optionally substituted C₆-C₁₀ aryl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heteroaryl, or C₂-C₉ heterocyclyl,

any of which is optionally substituted with A¹, where one of R^{G7'}, R^{G8'}, R^{G9'}, R^{G10'}, and R^{G11'} is A¹; or $\textcircled{\text{M}}$ is substituted with A¹.

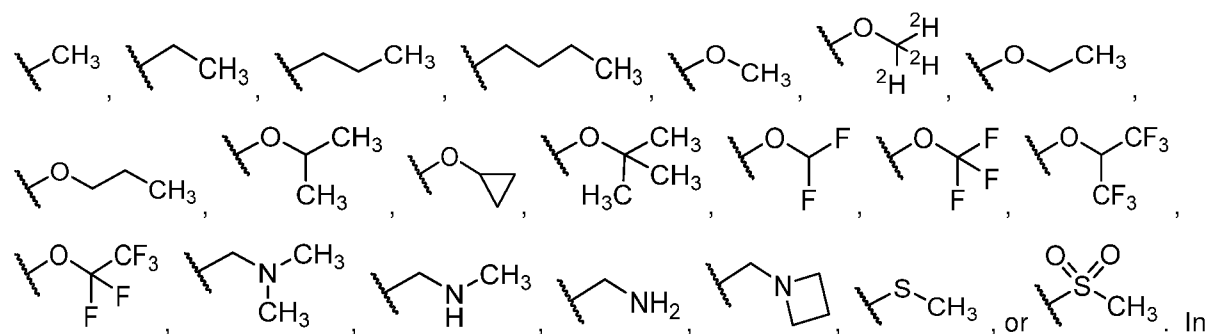
5 In some embodiments, each of R^{G7'}, R^{G8'}, R^{G9'}, R^{G10'}, and R^{G11'} is, independently, H, A¹, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted -O-C₃-C₆ carbocyclyl, or optionally substituted -C₁-C₃ alkyl-C₂-C₅ heterocyclyl; or R^{G7'} and R^{G8'}, R^{G8'} and R^{G9'}, R^{G9'} and R^{G10'}, and/or R^{G10'} and R^{G11'}, together with the carbon atoms to which each is attached, combine to

form $\textcircled{\text{M}}$; and $\textcircled{\text{M}}$ is optionally substituted C₆-C₁₀ aryl, optionally substituted C₃-C₁₀ carbocyclyl, 10 optionally substituted C₂-C₉ heteroaryl, or C₂-C₉ heterocyclyl, any of which is optionally substituted with

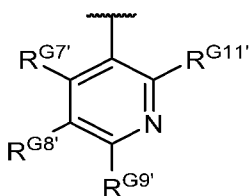
A¹, where one of R^{G7'}, R^{G8'}, R^{G9'}, R^{G10'}, and R^{G11'} is A¹; or $\textcircled{\text{M}}$ is substituted with A¹.

In some embodiments, each of R^{G7'}, R^{G8'}, R^{G9'}, R^{G10'}, and R^{G11'} is, independently, H, A¹, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted -O-C₃-C₆ carbocyclyl, or optionally substituted -C₁-C₃ alkyl-C₂-C₅ heterocyclyl.

15 In some embodiments, each of R^{G7'}, R^{G8'}, R^{G9'}, R^{G10'}, and R^{G11'} is, independently, H, A¹, F, Cl,

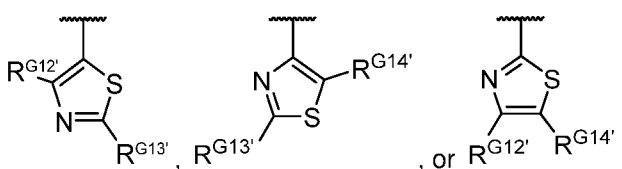


some embodiments, R^{G8'} is $\text{H}-\text{O}-\text{CH}_3$.



20 In some embodiments, G' is

In some embodiments, R^{G7'} is H; R^{G8'} is $\text{H}-\text{O}-\text{CH}_3$; R^{G9'} is A¹; and R^{G11'} is H.



In some embodiments, G' is
where

each of $R^{G12'}$, $R^{G13'}$, and $R^{G14'}$ is, independently, H, A^1 , halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted -O- C_3 - C_6 carbocyclyl, optionally substituted - C_1 - C_3 alkyl- C_3 - C_6 carbocyclyl, optionally substituted - C_1 - C_3 alkyl- C_2 - C_5 heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or $R^{G12'}$ and $R^{G14'}$, together with the carbon

atoms to which each is attached, combine to form $\textcircled{M}$; and $\textcircled{M}$ is optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or optionally substituted C_2 - C_9 heterocyclyl, any of which is optionally substituted with A^1 , where one of $R^{G12'}$, $R^{G13'}$, and $R^{G14'}$ is

10 A^1 ; or $\textcircled{M}$ is substituted with A^1 .

In some embodiments, each of $R^{G12'}$, $R^{G13'}$, and $R^{G14'}$ is, independently, H, A^1 , halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted -O- C_3 - C_6 carbocyclyl, optionally substituted - C_1 - C_3 alkyl- C_3 - C_6 carbocyclyl, optionally substituted - C_1 - C_3 alkyl- C_2 - C_5 heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or $R^{G12'}$ and

$R^{G14'}$, together with the carbon atoms to which each is attached, combine to form $\textcircled{M}$; and $\textcircled{M}$ is optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or optionally substituted C_2 - C_9 heterocyclyl, any of which is optionally substituted with A^1 ,

20 where one of $R^{G12'}$, $R^{G13'}$, and $R^{G14'}$ is A^1 ; or $\textcircled{M}$ is substituted with A^1 .

In some embodiments, $R^{3''}$ is $\begin{array}{c} | \\ \text{---}R^{3'} \\ | \\ A^1 \end{array}$.

In some embodiments, $R^{3'}$ is absent.

In some embodiments, $R^{3''}$ is $\begin{array}{c} | \\ \text{---}R^{3'} \\ | \\ A^1 \end{array}$, and $R^{3'}$ is absent.

In some embodiments, $R^{3'}$ is optionally substituted C_1 - C_6 alkylene, optionally substituted C_2 - C_9 heteroarylene, or optionally substituted C_1 - C_6 heteroalkylene. In some embodiments, optionally substituted C_2 - C_9 heteroarylene or optionally substituted C_1 - C_6 heteroalkylene.

In some embodiments, $R^{3'}$ is $\begin{array}{c} \diagup W^1 \diagdown \\ | \\ W^2 \end{array} R^{5'}$, $\begin{array}{c} W^2 \\ | \\ \text{---}W^1 \text{---}R^{6'} \end{array}$, or $\begin{array}{c} \diagup W^1 \diagdown \\ | \\ W^2 \end{array} W^3 R^{8'}$,

where

30 W^1 is $NR^{4'}$ or O;

W^2 is NH, O, or S;

W^3 is $NR^{7'}$ or O;

$R^{4'}$ is H or optionally substituted C_1 - C_6 alkyl;

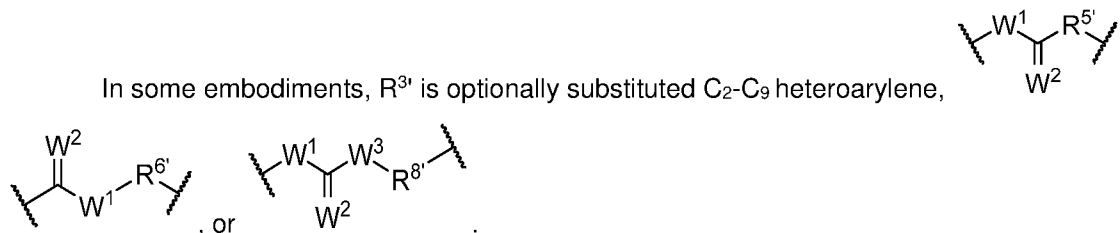
$R^{5'}$ is absent, optionally substituted C_1 - C_6 alkylene, optionally substituted C_3 - C_{10} carbocyclylene, or optionally substituted C_2 - C_9 heterocyclylene;

$R^{6'}$ is absent, optionally substituted C_1 - C_6 alkylene, optionally substituted C_3 - C_{10} carbocyclylene, or optionally substituted C_2 - C_9 heterocyclylene,

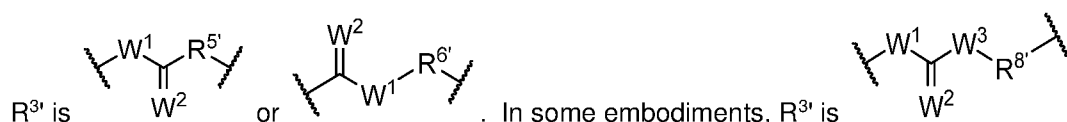
5 $R^{7'}$ is H or optionally substituted C_1 - C_6 alkyl; and

$R^{8'}$ is absent, optionally substituted C_1 - C_6 alkyl, optionally substituted C_3 - C_{10} carbocyclyl, or optionally substituted C_2 - C_9 heterocyclyl.

In some embodiments, $R^{3'}$ is optionally substituted C_2 - C_9 heteroarylene,



10 In some embodiments, $R^{3'}$ is optionally substituted C_2 - C_9 heteroarylene. In some embodiments,

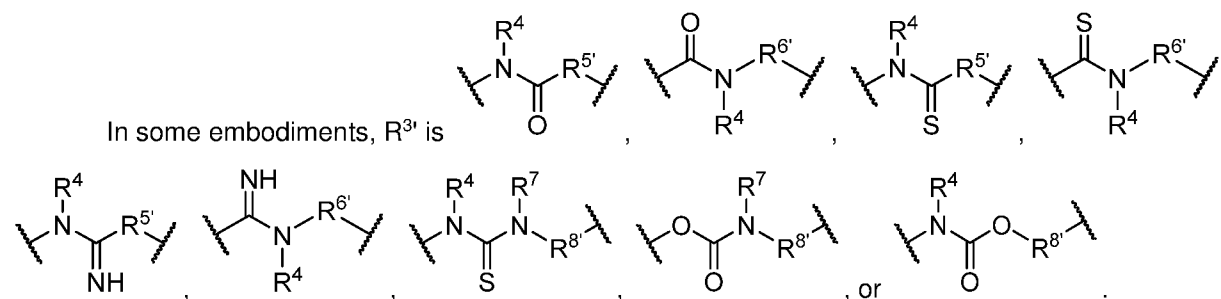


In some embodiments, W^1 is $NR^{4'}$. In some embodiments, W^1 is O.

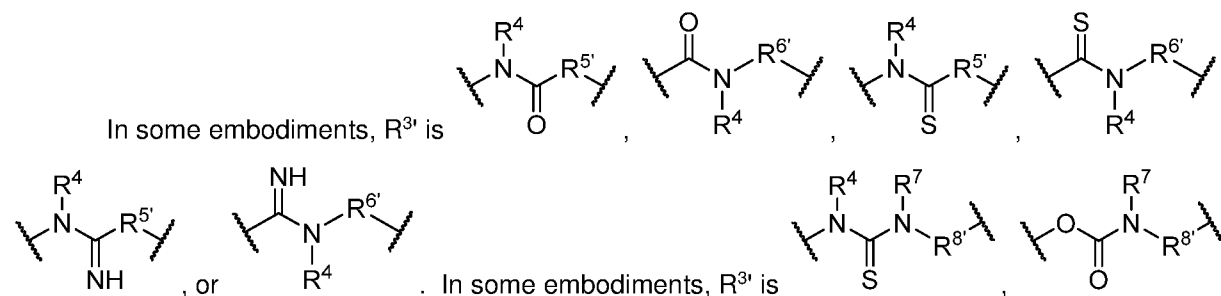
In some embodiments, W^2 is NH. In some embodiments, W^2 is O. In some embodiments, W^2 is

S.

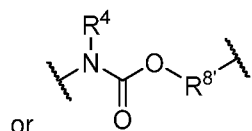
15 In some embodiments, W^3 is $NR^{7'}$. In some embodiments, W^3 is O.



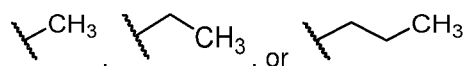
In some embodiments, $R^{3'}$ is



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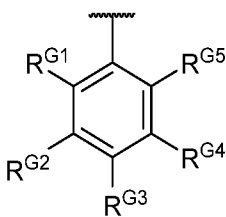
In some embodiments, $R^{4'}$ is H,



In some embodiments, R^7 is H, , , or .

In some embodiments, G'' is optionally substituted C_3 - C_{10} carbocyclyl or optionally substituted C_2 - C_9 heterocyclyl. In some embodiments, G'' is optionally substituted C_6 - C_{10} aryl or optionally substituted C_2 - C_9 heteroaryl.

5 In some embodiments, G'' is optionally substituted C_3 - C_{10} carbocyclyl. In some embodiments, G is optionally substituted C_6 - C_{10} aryl. In some embodiments, G is optionally substituted C_2 - C_9 heterocyclyl. In some embodiments, G'' is optionally substituted C_2 - C_9 heteroaryl.



In some embodiments, G'' is
where

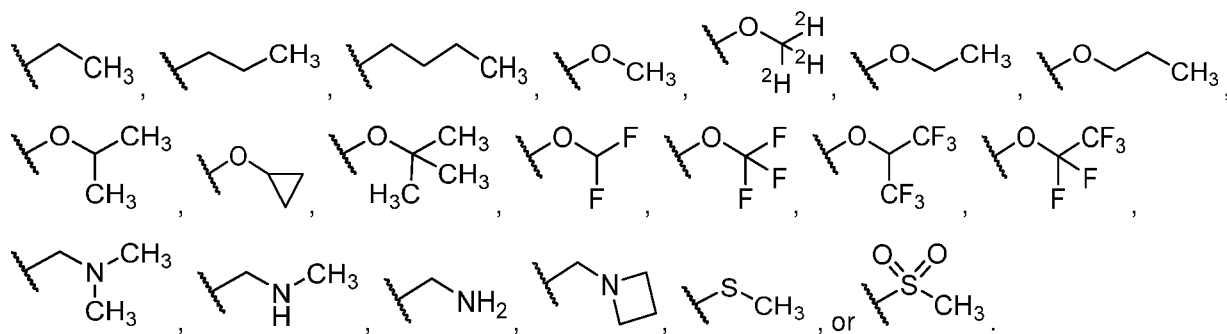
10 each of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted - O - C_3 - C_6 carbocyclyl, optionally substituted - C_1 - C_3 alkyl- C_3 - C_6 carbocyclyl, optionally substituted - C_1 - C_3 alkyl- C_2 - C_5 heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or R^{G1} and R^{G2} , R^{G2} and R^{G3} , R^{G3} and R^{G4} , and/or R^{G4} and R^{G5} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or optionally substituted C_2 - C_9 heterocyclyl.

In some embodiments, each of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted - O - C_3 - C_6 carbocyclyl, optionally substituted - C_1 - C_3 alkyl- C_3 - C_6 carbocyclyl, optionally substituted - C_1 - C_3 alkyl- C_2 - C_5 heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or R^{G1} and R^{G2} , R^{G2} and R^{G3} , R^{G3} and R^{G4} , and/or R^{G4} and R^{G5} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or optionally substituted C_2 - C_9 heterocyclyl.

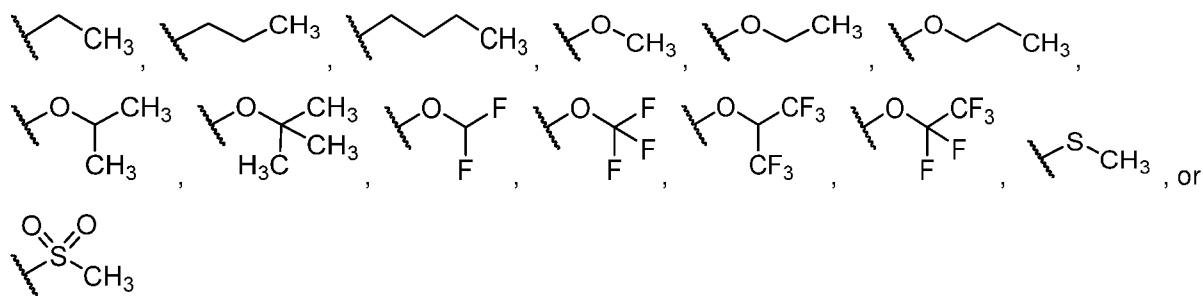
In some embodiments, each of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted - O - C_3 - C_6 carbocyclyl, or optionally substituted - C_1 - C_3 alkyl- C_2 - C_5 heterocyclyl; or R^{G1} and R^{G2} , R^{G2} and R^{G3} , R^{G3} and R^{G4} , and/or R^{G4} and R^{G5} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_2 - C_9 heteroaryl or optionally substituted C_2 - C_9 heterocyclyl.

In some embodiments, each of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted - O - C_3 - C_6 carbocyclyl, or optionally substituted - C_1 - C_3 alkyl- C_2 - C_5 heterocyclyl.

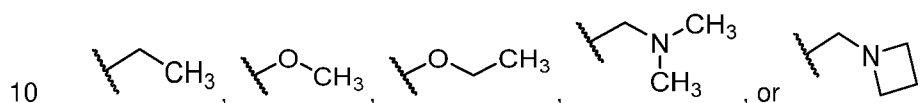
In some embodiments, each of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is, independently, H, F, Cl, ,

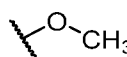
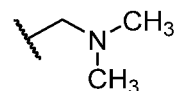
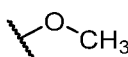


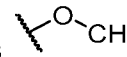
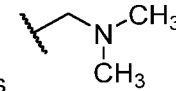
5 In some embodiments, each of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is, independently, H, F, ,

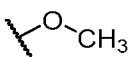
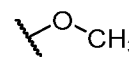
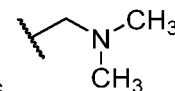


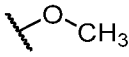
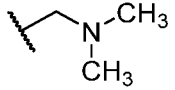
In some embodiments, each of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is, independently, H, F, Cl, ,

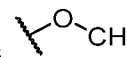
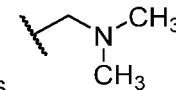
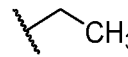


In some embodiments, R^{G1} is H; R^{G2} is ; R^{G3} is ; R^{G4} is ; and

R^{G5} is H. In some embodiments, R^{G1} is H; R^{G2} is ; R^{G3} is ; R^{G4} is H; and R^{G5} is

. In some embodiments, R^{G1} is H; R^{G2} is ; R^{G3} is ; R^{G4} is Cl or F;

and R^{G5} is H. In some embodiments, R^{G1} is H; R^{G2} is ; R^{G3} is ; R^{G4} is H; and

15 R^{G5} is H. In some embodiments, R^{G1} is H; R^{G2} is ; R^{G3} is ; R^{G4} is ; and R^{G5} is H.

In some embodiments, R^{G1} and R^{G2} , R^{G2} and R^{G3} , R^{G3} and R^{G4} , and/or R^{G4} and R^{G5} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_2 - C_9 heteroaryl or optionally substituted C_2 - C_9 heterocyclyl.

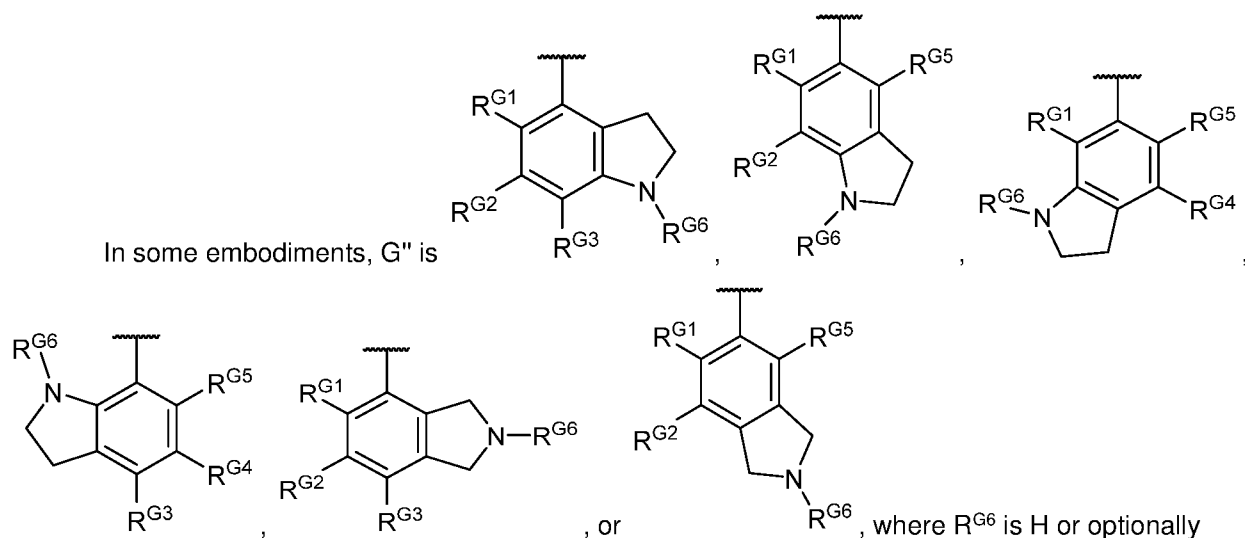
20 In some embodiments, R^{G1} and R^{G2} , R^{G2} and R^{G3} , R^{G3} and R^{G4} , and/or R^{G4} and R^{G5} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_2 - C_9 heterocyclyl. In

some embodiments, R^{G1} and R^{G2} , R^{G2} and R^{G3} , R^{G3} and R^{G4} , and/or R^{G4} and R^{G5} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_2 - C_9 heteroaryl.

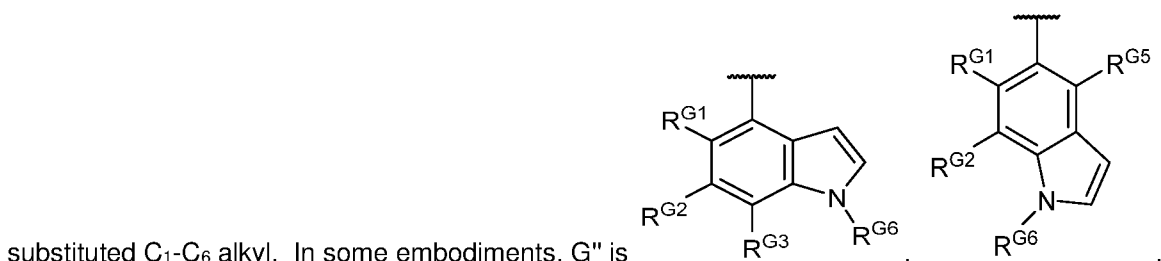
In some embodiments, R^{G1} and R^{G2} , R^{G2} and R^{G3} , R^{G3} and R^{G4} , and/or R^{G4} and R^{G5} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_2 - C_9 heterocyclyl. In

5 some embodiments, R^{G1} and R^{G2} , R^{G2} and R^{G3} , R^{G3} and R^{G4} , and/or R^{G4} and R^{G5} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_2 - C_9 heteroaryl.

In some embodiments, G'' is

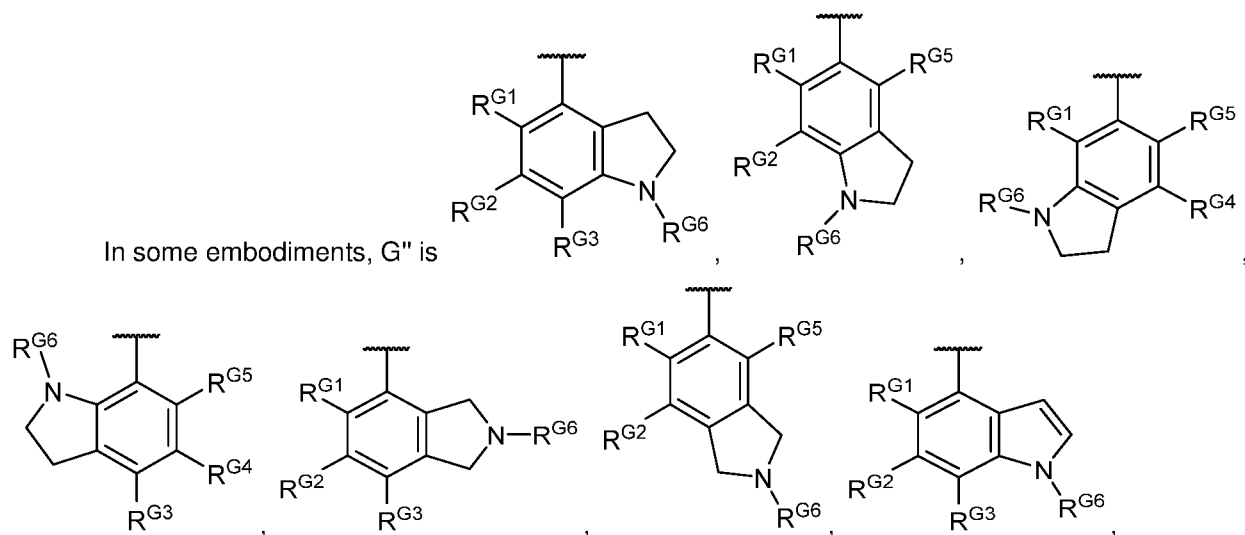


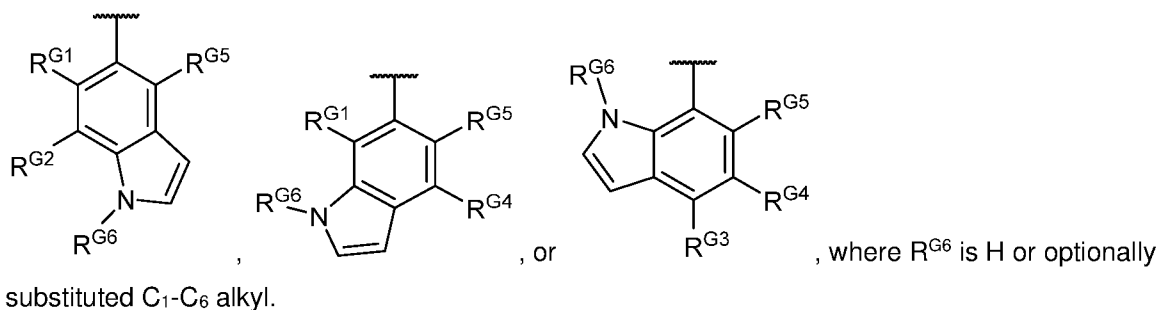
substituted C_1 - C_6 alkyl. In some embodiments, G'' is



10 , or , where R^{G6} is H or optionally substituted C_1 - C_6 alkyl.

In some embodiments, G'' is



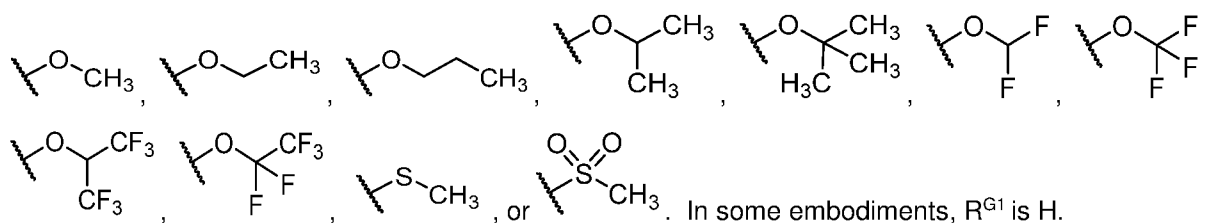


In some embodiments, R^{G6} is H, , , or .

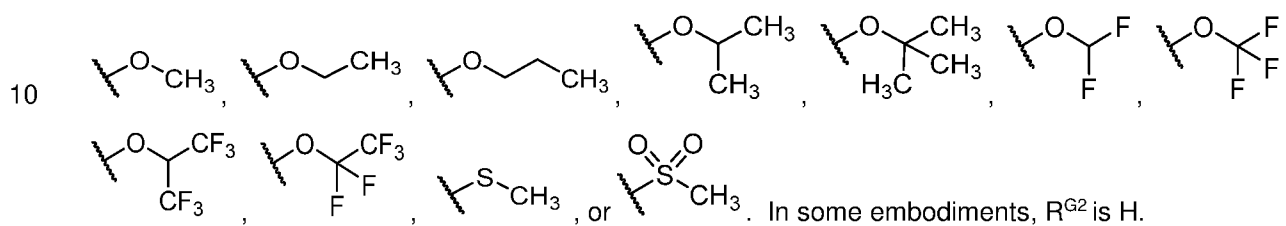
In some embodiments, R^{G6} is H or .

5 In some embodiments, R^{G6} is H.

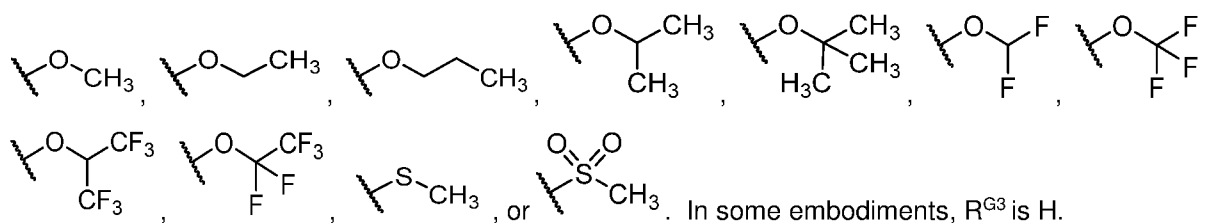
In some embodiments, R^{G1} is H, F, , , , ,



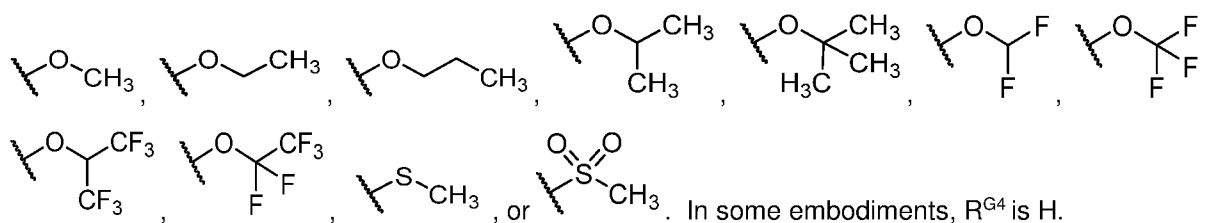
In some embodiments, R^{G2} is H, F, , , , ,

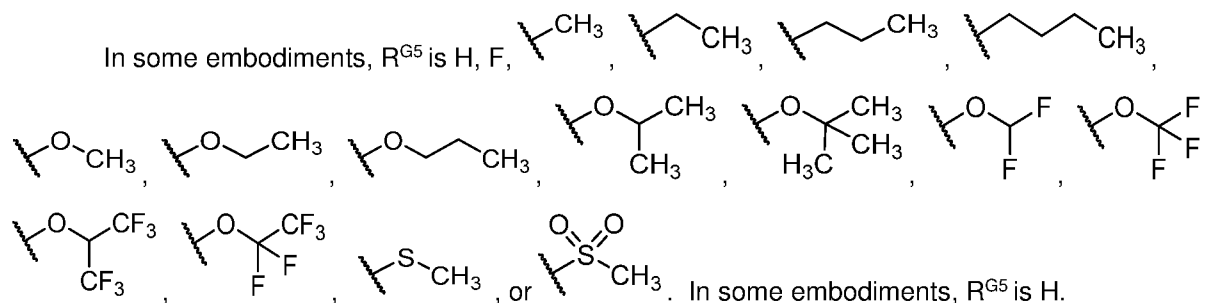


In some embodiments, R^{G3} is H, F, , , , ,

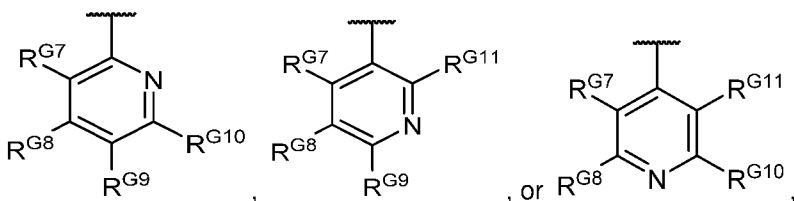


15 In some embodiments, R^{G4} is H, F, , , , ,





In some embodiments, one or more of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is H. In some embodiments, two or more of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is H. In some embodiments, three or more of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is H. In some embodiments, each of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is H.



In some embodiments, G" is

where

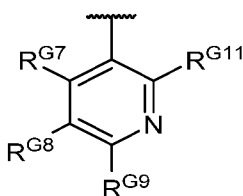
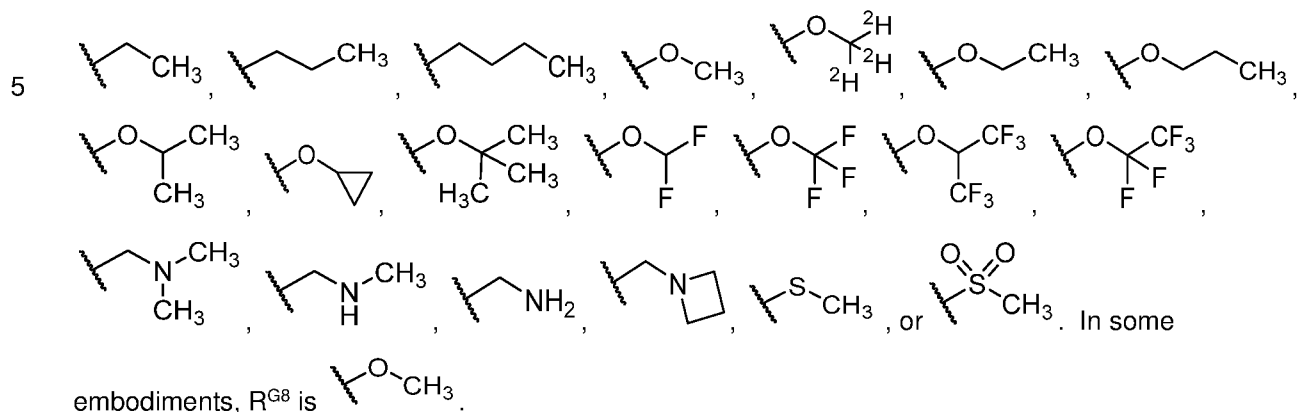
each of R^{G7} , R^{G8} , R^{G9} , R^{G10} , and R^{G11} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted $-O$ - C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_2 - C_5 heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or R^{G7} and R^{G8} , R^{G8} and R^{G9} , R^{G9} and R^{G10} , and/or R^{G10} and R^{G11} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or C_2 - C_9 heterocyclyl.

In some embodiments, each of R^{G7} , R^{G8} , R^{G9} , R^{G10} , and R^{G11} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, hydroxyl, thiol, or optionally substituted amino; or R^{G7} and R^{G8} , R^{G8} and R^{G9} , R^{G9} and R^{G10} , and/or R^{G10} and R^{G11} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or C_2 - C_9 heterocyclyl.

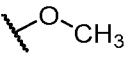
In some embodiments, each of R^{G7} , R^{G8} , R^{G9} , R^{G10} , and R^{G11} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted $-O$ - C_3 - C_6 carbocyclyl, or optionally substituted $-C_1$ - C_3 alkyl- C_2 - C_5 heterocyclyl; or R^{G7} and R^{G8} , R^{G8} and R^{G9} , R^{G9} and R^{G10} , and/or R^{G10} and R^{G11} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or C_2 - C_9 heterocyclyl.

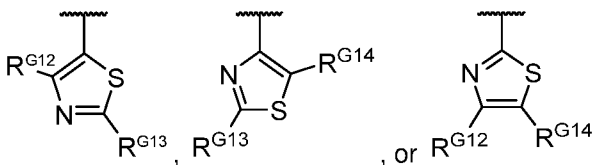
In some embodiments, each of R^{G7} , R^{G8} , R^{G9} , R^{G10} , and R^{G11} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted $-O$ - C_3 - C_6 carbocyclyl, or optionally substituted $-C_1$ - C_3 alkyl- C_2 - C_5 heterocyclyl.

In some embodiments, each of R^{G7} , R^{G8} , R^{G9} , R^{G10} , and R^{G11} is, independently, H, F, Cl, ,



In some embodiments, G'' is

10 In some embodiments, R^{G7} is H; R^{G8} is ; R^{G9} is H; and R^{G11} is H.



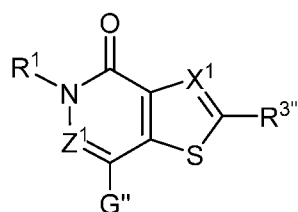
In some embodiments, G'' is

where

each of R^{G12} , R^{G13} , and R^{G14} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted $-O$ - C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_2 - C_5 heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or R^{G12} and R^{G14} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or optionally substituted C_2 - C_9 heterocyclyl.

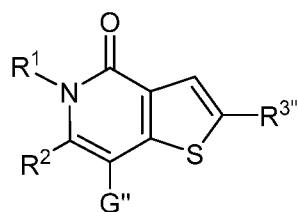
In some embodiments, each of R^{G12} , R^{G13} , and R^{G14} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, hydroxyl, thiol, or optionally substituted amino; or R^{G12} and R^{G14} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or optionally substituted C_2 - C_9 heterocyclyl.

In some embodiments, A has the structure of **Formula IIIAa**:

**Formula IIIAa,**

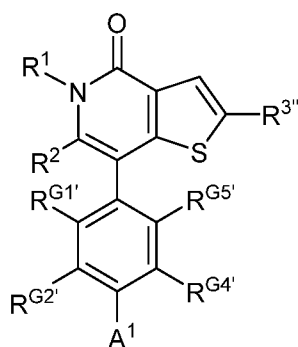
or a pharmaceutically acceptable salt thereof.

In some embodiments, A has the structure of **Formula IIIAb**:

**Formula IIIAb,**

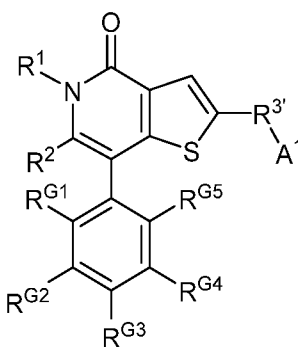
or a pharmaceutically acceptable salt thereof.

In some embodiments, A has the structure of **Formula IIIAc**:

**Formula IIIAc,**

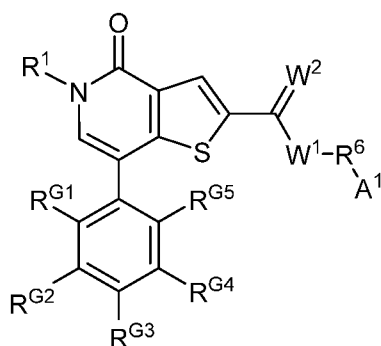
or a pharmaceutically acceptable salt thereof.

In some embodiments, A has the structure of **Formula IIIAd**:

**Formula IIIAd,**

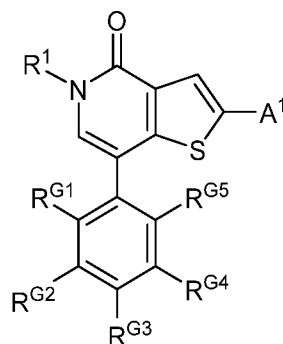
or a pharmaceutically acceptable salt thereof.

In some embodiments, A has the structure of **Formula IIIAe**:

**Formula IIIAe,**

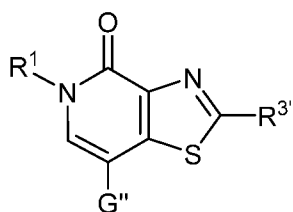
or a pharmaceutically acceptable salt thereof.

In some embodiments, A has the structure of **Formula IIIAf**:

**Formula IIIAf,**

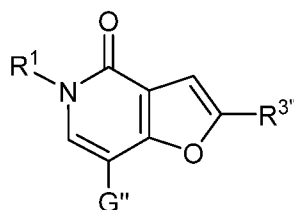
or a pharmaceutically acceptable salt thereof.

In some embodiments, A has the structure of **Formula IIIAg**:

**Formula IIIAg,**

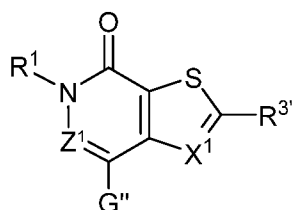
or a pharmaceutically acceptable salt thereof.

In some embodiments, A has the structure of **Formula IIIAh**:

**Formula IIIAh,**

or a pharmaceutically acceptable salt thereof.

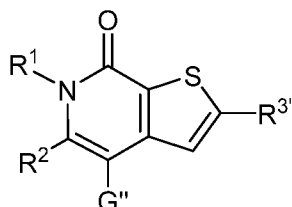
In some embodiments, A has the structure of **Formula IIIBa**:



Formula IIIBa,

or a pharmaceutically acceptable salt thereof.

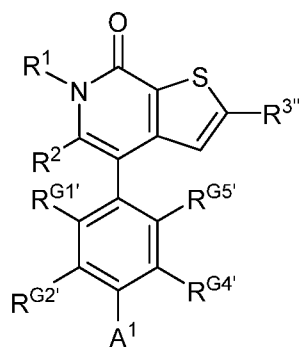
5 In some embodiments, A has the structure of **Formula IIIBb**:



Formula IIIBb,

or a pharmaceutically acceptable salt thereof.

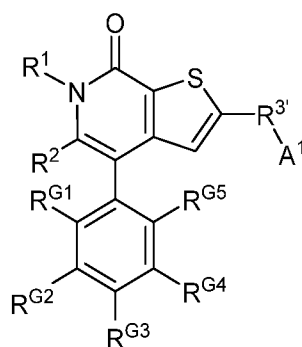
In some embodiments, A has the structure of **Formula IIIBc**:



Formula IIIBc,

or a pharmaceutically acceptable salt thereof.

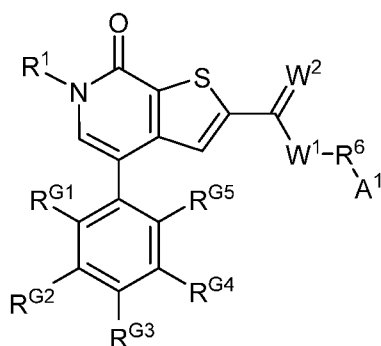
In some embodiments, A has the structure of **Formula IIIBd**:



Formula IIIBd,

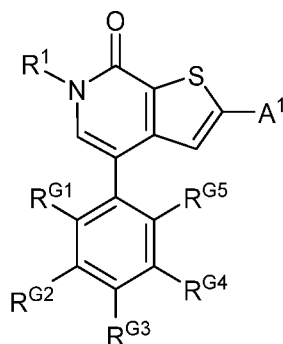
or a pharmaceutically acceptable salt thereof.

In some embodiments, A has the structure of **Formula IIIBe**:

**Formula IIIBe,**

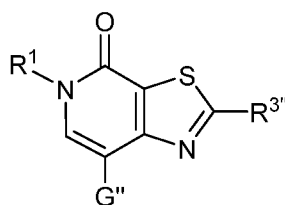
or a pharmaceutically acceptable salt thereof.

In some embodiments, A has the structure of **Formula IIIBf**:

**Formula IIIBf,**

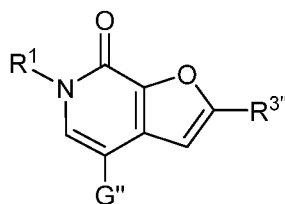
or a pharmaceutically acceptable salt thereof.

In some embodiments, A has the structure of **Formula IIIBg**:

**Formula IIIBg,**

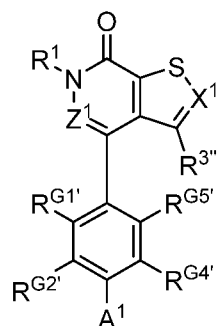
or a pharmaceutically acceptable salt thereof.

In some embodiments, A has the structure of **Formula IIIBh**:

**Formula IIIBh,**

or a pharmaceutically acceptable salt thereof.

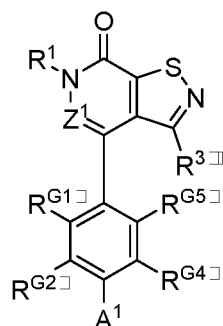
In some embodiments, the compound of **Formula IIIC** has the structure of **Formula IIICa**:



Formula IIICa,

or a pharmaceutically acceptable salt thereof.

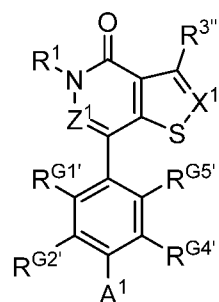
5 In some embodiments, the compound of **Formula IIIC** has the structure of **Formula IIICb**:



Formula IIICb,

or a pharmaceutically acceptable salt thereof.

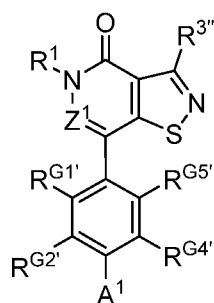
In some embodiments, the compound of **Formula IIID** has the structure of **Formula IIIDa**:



Formula IIIDa,

or a pharmaceutically acceptable salt thereof.

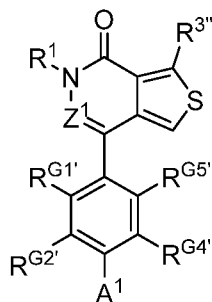
In some embodiments, the compound of **Formula IIID** has the structure of **Formula IIIDb**:



Formula IIIDb,

or a pharmaceutically acceptable salt thereof.

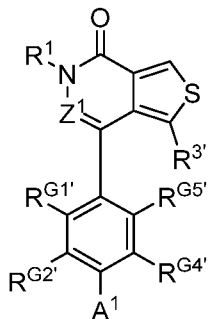
In some embodiments, the compound of **Formula III E** has the structure of **Formula III Ea**:



Formula III Ea,

or a pharmaceutically acceptable salt thereof.

5 In some embodiments, the compound of **Formula III F** has the structure of **Formula III F**:



Formula III Fa,

or a pharmaceutically acceptable salt thereof.

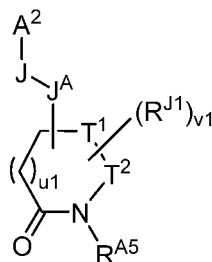
In some embodiments, the degradation moiety is a ubiquitin ligase binding moiety.

10 In some embodiments, the ubiquitin ligase binding moiety comprises Cereblon ligands, IAP (Inhibitors of Apoptosis) ligands, mouse double minute 2 homolog (MDM2), or von Hippel-Lindau (VHL) ligands, or derivatives or analogs thereof.

In some embodiments, the degradation moiety is a ubiquitin ligase binding moiety.

15 In some embodiments, the ubiquitin ligase binding moiety comprises Cereblon ligands, IAP (Inhibitors of Apoptosis) ligands, mouse double minute 2 homolog (MDM2), or von Hippel-Lindau (VHL) ligands, or derivatives or analogs thereof.

In some embodiments, the degradation moiety includes the structure of **Formula Y**:



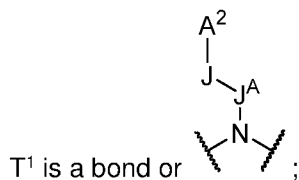
Formula Y,

20 where

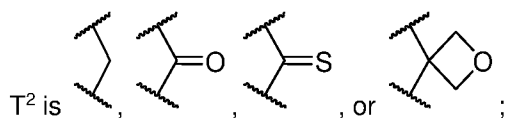
A² is a bond between the degradation moiety and the linker;

v₁ is 0, 1, 2, 3, 4, or 5;

u₁ is 1, 2, or 3;



T^1 is a bond or   ;



T^2 is , , or ;

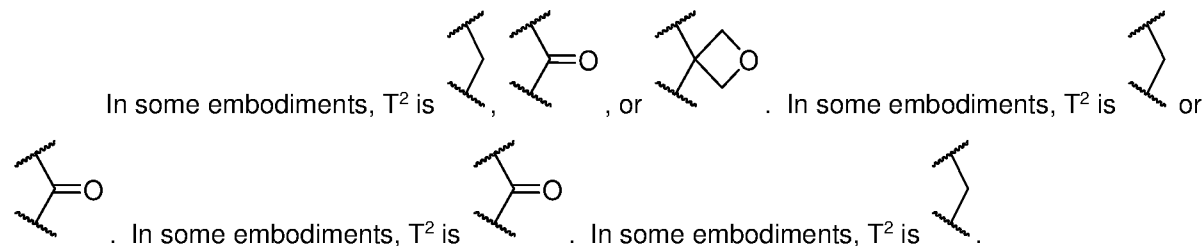
R^{5A} is H, optionally substituted C₁-C₆ alkyl, or optionally substituted C₁-C₆ heteroalkyl;

each R^{J1} is, independently, halogen, optionally substituted C₁-C₆ alkyl, or optionally substituted

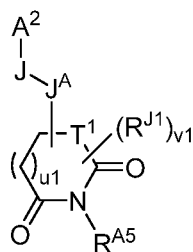
5 C₁-C₆ heteroalkyl;

J^A is absent, O, optionally substituted amino, optionally substituted C₁-C₆ alkyl, or optionally substituted C₁-C₆ heteroalkyl; and

J is absent, optionally substituted C₃-C₁₀ carbocyclylene, optionally substituted C₆-C₁₀ arylene, optionally substituted C₂-C₉ heterocyclylene, or optionally substituted C₂-C₉ heteroarylene, or a pharmaceutically acceptable salt thereof.

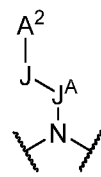


In some embodiments, the structure of **Formula Y** has the structure of **Formula Y1**:



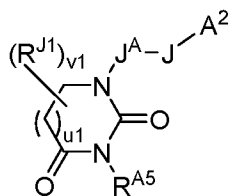
Formula Y1,

or a pharmaceutically acceptable salt thereof.



In some embodiments, T^1 is a bond. In some embodiments, T^1 is

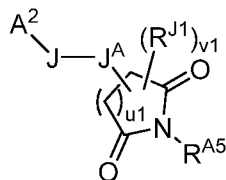
In some embodiments, the structure of **Formula Y** has the structure of **Formula Y2**:



Formula Y2,

or a pharmaceutically acceptable salt thereof.

In some embodiments, the structure of **Formula Y** has the structure of **Formula Z**:

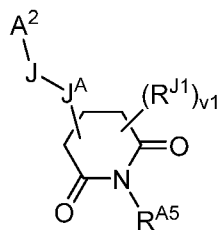


Formula Z,

5 or a pharmaceutically acceptable salt thereof.

In some embodiments, u_1 is 1. In some embodiments, u_1 is 2. In some embodiments u_1 is 3.

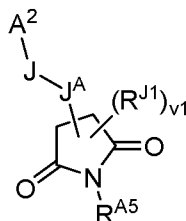
In some embodiments, the structure of **Formula Z** has the structure of **Formula AA0**:



Formula AA0,

10 or a pharmaceutically acceptable salt thereof.

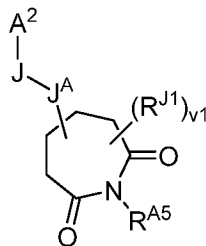
In some embodiments, the structure of **Formula Z** has the structure of **Formula AB**:



Formula AB,

or a pharmaceutically acceptable salt thereof.

15 In some embodiments, the structure of **Formula Z** has the structure of **Formula AC**:



Formula AC,

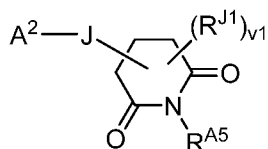
or a pharmaceutically acceptable salt thereof.

In some embodiments, J^A is absent. In some embodiments, J^A is optionally substituted C_1 - C_6 alkyl. In some embodiments, J^A is optionally substituted C_1 - C_6 heteroalkyl. In some embodiments, J^A is O or optionally substituted amino.



In some embodiments, J^A is .

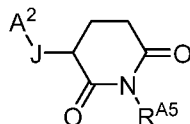
In some embodiments, the structure of **Formula AA0** has the structure of **Formula AA0**:

**Formula AA,**

or a pharmaceutically acceptable salt thereof.

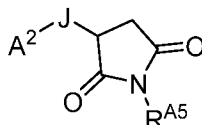
In some embodiments, v_1 is 0, 1, 2, or 3. In some embodiments, v_1 is 0. In some embodiments, v_1 is 1. In some embodiments, v_1 is 2. In some embodiments, v_1 is 3.

In some embodiments, the structure of **Formula AA** has the structure of **Formula AA1**:

**Formula AA1,**

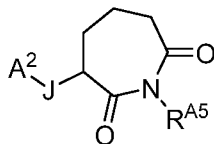
or a pharmaceutically acceptable salt thereof.

In some embodiments, the structure of **Formula AB** has the structure of **Formula AB1**:

**Formula AB1,**

or a pharmaceutically acceptable salt thereof.

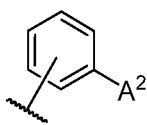
In some embodiments, the structure of **Formula AC** has the structure of **Formula AC1**:

**Formula AC1,**

or a pharmaceutically acceptable salt thereof.

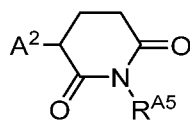
In some embodiments, J is absent. In some embodiments, J is optionally substituted C₃-C₁₀ carbocyclylene or optionally substituted C₆-C₁₀ arylene. In some embodiments, J is optionally substituted C₂-C₉ heterocyclylene or optionally substituted C₂-C₉ heteroarylene.

In some embodiments, J is optionally substituted heterocyclylene. In some embodiments, J is optionally substituted C₆-C₁₀ arylene.



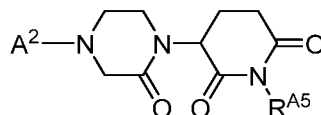
In some embodiments, J is

In some embodiments, the structure of **Formula AA** has the structure of **Formula AA2**:

**Formula AA2,**

or a pharmaceutically acceptable salt thereof.

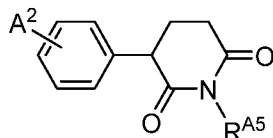
In some embodiments, the structure of **Formula AA** has the structure of **Formula AA3**:



Formula AA3,

or a pharmaceutically acceptable salt thereof.

In some embodiments, the structure of **Formula AA** has the structure of **Formula AA4**:



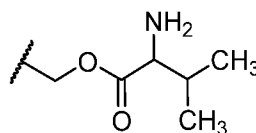
Formula AA4,

or a pharmaceutically acceptable salt thereof.

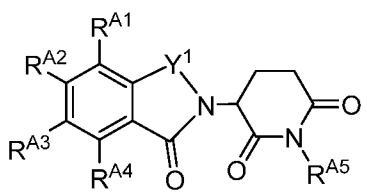
In some embodiments, R^{A5} is H or optionally substituted C₁-C₆ alkyl. In some embodiments, R^{A5} is optionally substituted C₁-C₆ heteroalkyl.

In some embodiments, R^{A5} is H or methyl. In some embodiments, R^{A5} is H. In some

embodiments, R^{A5} is methyl. In some embodiments, R^{A5} is

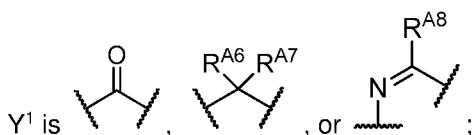


5 In some embodiments, the structure of **Formula AA** has the structure of **Formula A**:



Formula A

where



10 R^{A5} is H, optionally substituted C₁-C₆ alkyl, or optionally substituted C₁-C₆ heteroalkyl;

R^{A6} is H or optionally substituted C₁-C₆ alkyl; and R^{A7} is H or optionally substituted C₁-C₆ alkyl; or R^{A6} and R^{A7}, together with the carbon atom to which each is bound, combine to form optionally substituted C₃-C₆ carbocyclyl or optionally substituted C₂-C₅ heterocyclyl; or R^{A6} and R^{A7}, together with the carbon atom to which each is bound, combine to form optionally substituted C₃-C₆ carbocyclyl or optionally substituted C₂-C₅ heterocyclyl;

R^{A8} is H, optionally substituted C₁-C₆ alkyl, or optionally substituted C₁-C₆ heteroalkyl;

each of R^{A1}, R^{A2}, R^{A3}, and R^{A4} is, independently, H, A², halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₂-C₉ heteroaryl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, optionally substituted -O-C₃-C₆

carbocyclyl, hydroxyl, thiol, or optionally substituted amino; or R^{A1} and R^{A2} , R^{A2} and R^{A3} , and/or R^{A3} and

R^{A4} , together with the carbon atoms to which each is attached, combine to form ; and  is optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or C_2 - C_9 heterocyclyl, any of which is optionally substituted with A^2 , where one of R^{A1} , R^{A2} ,

5 R^{A3} , and R^{A4} is A^2 , or  is substituted with A^2 , or a pharmaceutically acceptable salt thereof.

In some embodiments, each of R^{A1} , R^{A2} , R^{A3} , and R^{A4} is, independently, H, A^2 , halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, hydroxyl, thiol,
10 or optionally substituted amino; or R^{A1} and R^{A2} , R^{A2} and R^{A3} , and/or R^{A3} and R^{A4} , together with the carbon

atoms to which each is attached, combine to form ; and  is optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or C_2 - C_9 heterocyclyl,

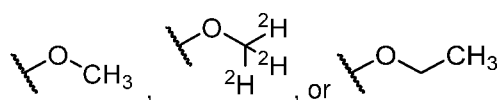
any of which is optionally substituted with A^2 , where one of R^{A1} , R^{A2} , R^{A3} , and R^{A4} is A^2 , or  is substituted with A^2 , or a pharmaceutically acceptable salt thereof.

15 In some embodiments, each of R^{A1} , R^{A2} , R^{A3} , and R^{A4} is, H, A^2 , halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted $-O$ - C_3 - C_6 carbocyclyl, hydroxyl, optionally substituted amino; or R^{A1} and R^{A2} , R^{A2} and R^{A3} , or R^{A3} and R^{A4} , together with the carbon atoms

to which each is attached, combine to form ; and  is optionally substituted C_2 - C_9 heterocyclyl,

which is optionally substituted with A^2 , where one of R^{A1} , R^{A2} , R^{A3} , and R^{A4} is A^2 , or  is substituted
20 with A^2 .

In some embodiments, each of R^{A1} , R^{A2} , R^{A3} , and R^{A4} is, independently, H, A^2 , F, ,



; or R^{A1} and R^{A2} , R^{A2} and R^{A3} , or R^{A3} and R^{A4} , together with the

carbon atoms to which each is attached, combine to form ; and  is optionally substituted C_2 - C_9 heterocyclyl, which is optionally substituted with A^2 , where one of R^{A1} , R^{A2} , R^{A3} , and R^{A4} is A^2 , or

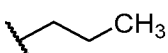
25  is substituted with A^2 .

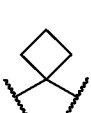
In some embodiments, R^{A1} is A^2 . In some embodiments, R^{A2} is A^2 . In some embodiments, R^{A3} is A^2 . In some embodiments, R^{A4} is A^2 . In some embodiments, R^{A5} is A^2 .

In some embodiments, R^{A5} is H or optionally substituted C_1 - C_6 alkyl.

In some embodiments, R^{A5} is H or . In some embodiments, R^{A5} is H. In some embodiments, R^{A5} is .

In some embodiments, Y^1 is  or . In some embodiments, Y^1 is . In some embodiments, Y^1 is .

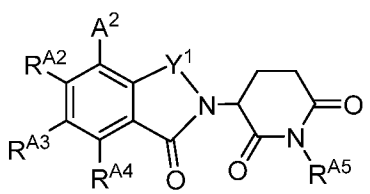
5 In some embodiments, each of R^{A6} and R^{A7} is, independently, H, F, , , or ; or R^{A6} and R^{A7} , together with the carbon atom to which each is bound, combine to form

, , , or . In some embodiments, R^{A6} is H and R^{A7} is H.

In some embodiments, Y^1 is , , , , , , or . In some embodiments, Y^1 is , , , , , or . In

10 some embodiments, Y^1 is .

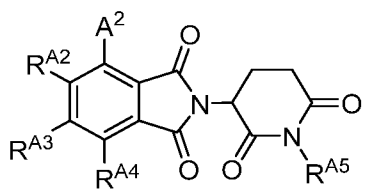
In some embodiments, the structure of **Formula A** has the structure of **Formula A1**:



Formula A1

or a pharmaceutically acceptable salt thereof.

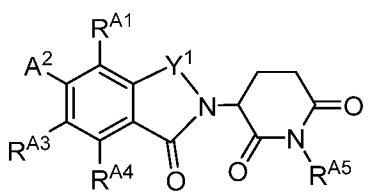
15 In some embodiments, the structure of **Formula A** has the structure of **Formula A2**:



Formula A2

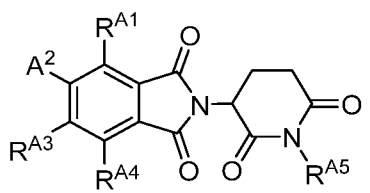
or a pharmaceutically acceptable salt thereof.

In some embodiments, the structure of **Formula A** has the structure of **Formula A3**:

**Formula A3**

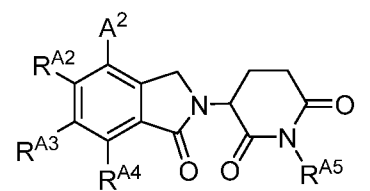
or a pharmaceutically acceptable salt thereof.

In some embodiments, the structure of **Formula A** has the structure of **Formula A4**:

**Formula A4**

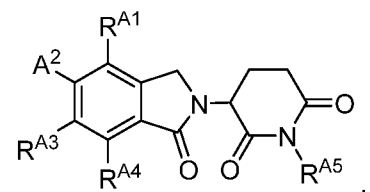
or a pharmaceutically acceptable salt thereof.

In some embodiments, the structure of **Formula A** has the structure of **Formula A5**:

**Formula A5**

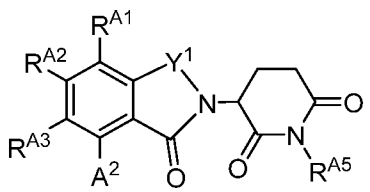
or a pharmaceutically acceptable salt thereof.

In some embodiments, the structure of **Formula A** has the structure of **Formula A6**:

**Formula A6**

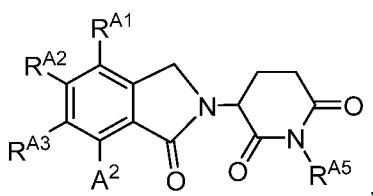
or a pharmaceutically acceptable salt thereof.

In some embodiments, the structure of **Formula A** has the structure of **Formula A7**:

**Formula A7**

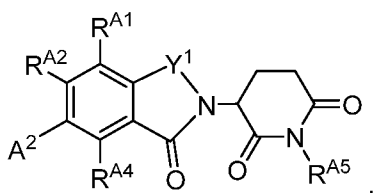
or a pharmaceutically acceptable salt thereof.

In some embodiments, the structure of **Formula A** has the structure of **Formula A8**:

**Formula A8**

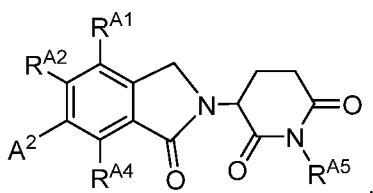
or a pharmaceutically acceptable salt thereof.

In some embodiments, the structure of **Formula A** has the structure of **Formula A9**:

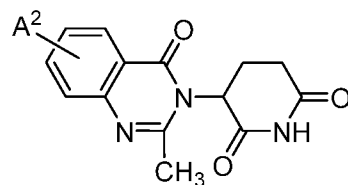
**Formula A9**

or a pharmaceutically acceptable salt thereof.

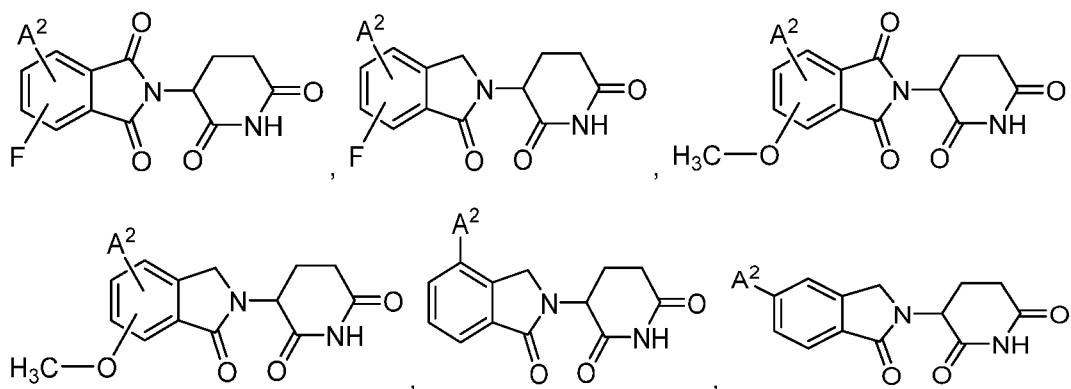
In some embodiments, the structure of **Formula A** has the structure of **Formula A10**:

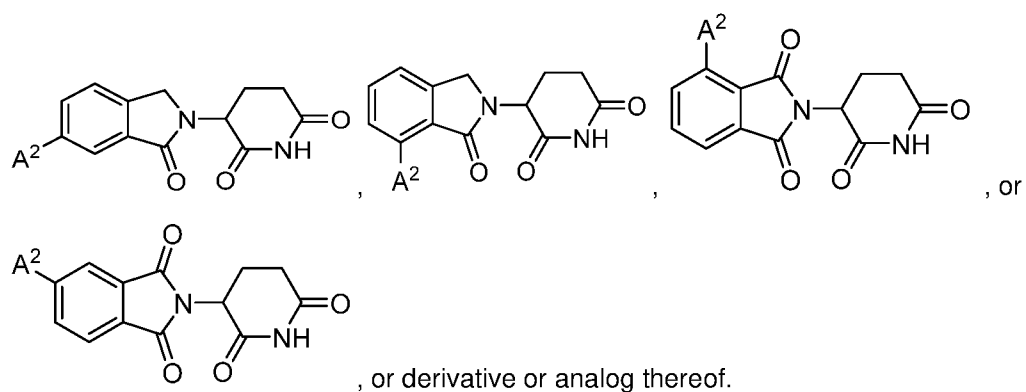
**Formula A10**

or a pharmaceutically acceptable salt thereof.

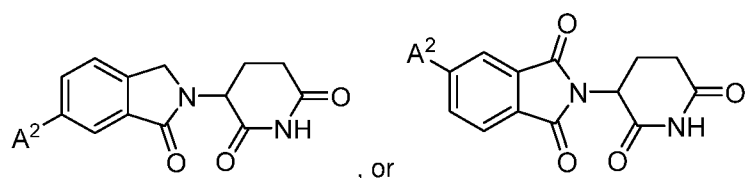


In some embodiments, wherein the structure of **Formula A** is



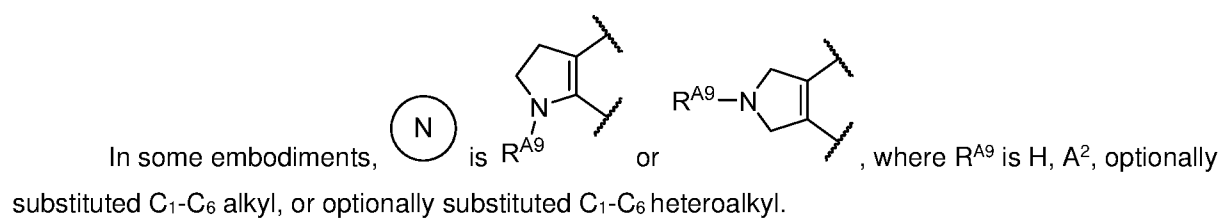
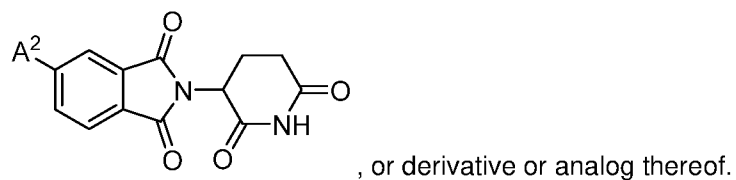


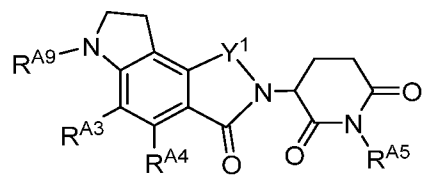
In some embodiments, the structure of **Formula A** is



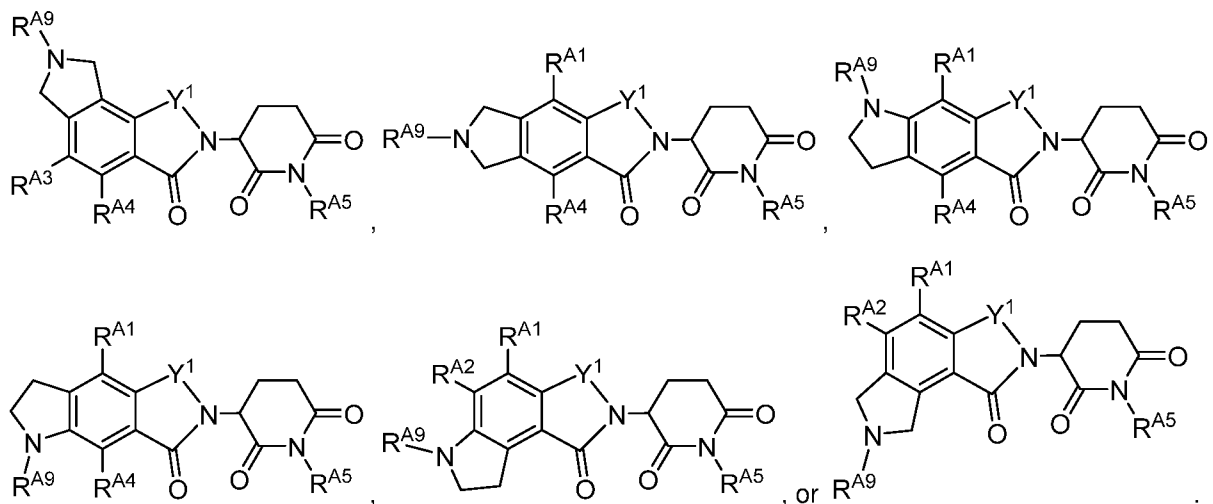
5

In some embodiments, the structure of **Formula A** is

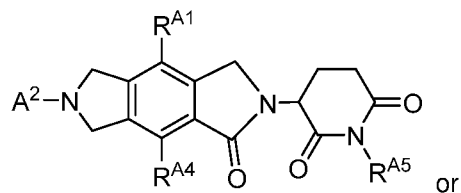




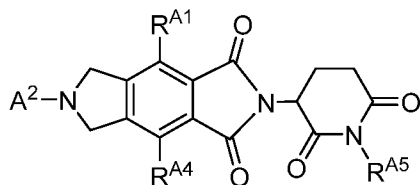
In some embodiments, the structure of **Formula A** is



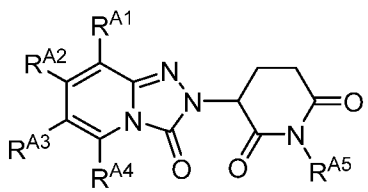
In some embodiments, R^{A9} is H, A², or optionally substituted C₁-C₆ alkyl. In some embodiments, R^{A9} is H, A², or methyl. In some embodiments, R^{9A} is H. In some embodiments, R^{9A} is methyl. In some embodiments, R^{A9} is A².



In some embodiments, the structure of **Formula A** is



In some embodiments, the structure of **Formula AA** has the structure of **Formula B**:



Formula B

where

R^{A5} is H, optionally substituted C₁-C₆ alkyl, or optionally substituted C₁-C₆ heteroalkyl;

each of R^{A1}, R^{A2}, R^{A3}, and R^{A4} is, independently, H, A², halogen, optionally substituted C₁-C₆ alkyl,

optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₂-C₉ heteroaryl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, optionally substituted -O-C₃-C₆ carbocyclyl, hydroxyl, thiol, or optionally substituted amino; or R^{A1} and R^{A2}, R^{A2} and R^{A3}, and/or R^{A3} and

R^{A4} , together with the carbon atoms to which each is attached, combine to form ; and  is optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or C_2 - C_9 heterocyclyl, any of which is optionally substituted with A^2 , where one of R^{A1} , R^{A2} ,

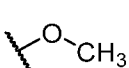
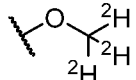
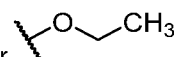
R^{A3} , and R^{A4} is A^2 , or  is substituted with A^2 , or a pharmaceutically acceptable salt thereof.

5 In some embodiments, each of R^{A1} , R^{A2} , R^{A3} , and R^{A4} is, H, A^2 , halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted -O- C_3 - C_6 carbocyclyl, hydroxyl, optionally substituted amino; or R^{A1} and R^{A2} , R^{A2} and R^{A3} , or R^{A3} and R^{A4} , together with the carbon atoms

to which each is attached, combine to form ; and  is optionally substituted C_2 - C_9 heterocyclyl,

10 which is optionally substituted with A^2 , where one of R^{A1} , R^{A2} , R^{A3} , and R^{A4} is A^2 , or  is substituted with A^2 .

In some embodiments, each of R^{A1} , R^{A2} , R^{A3} , and R^{A4} is, independently, H, A^2 , F, ,

, , or ; or R^{A1} and R^{A2} , R^{A2} and R^{A3} , or R^{A3} and R^{A4} , together with the

carbon atoms to which each is attached, combine to form ; and  is optionally substituted C_2 - C_9 heterocyclyl, which is optionally substituted with A^2 , where one of R^{A1} , R^{A2} , R^{A3} , and R^{A4} is A^2 , or

15  is substituted with A^2 .

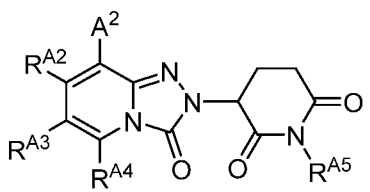
In some embodiments, R^{A1} is A^2 . In some embodiments, R^{A2} is A^2 . In some embodiments, R^{A3} is A^2 . In some embodiments, R^{A4} is A^2 . In some embodiments, R^{A5} is A^2 .

In some embodiments, R^{A5} is H or optionally substituted C_1 - C_6 alkyl.

In some embodiments, R^{A5} is H or . In some embodiments, R^{A5} is H. In some

20 embodiments, R^{A5} is .

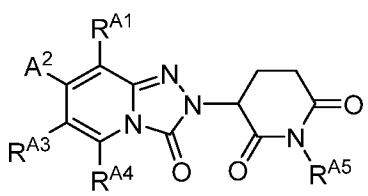
In some embodiments, the structure of **Formula B** has the structure of **Formula B1**:



Formula B1

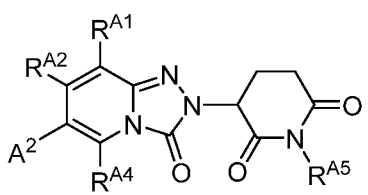
or a pharmaceutically acceptable salt thereof.

25 In some embodiments, the structure of **Formula B** has the structure of **Formula B2**:

**Formula B2**

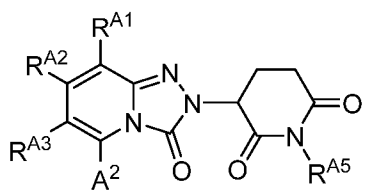
or a pharmaceutically acceptable salt thereof.

In some embodiments, the structure of **Formula B** has the structure of **Formula B3**:

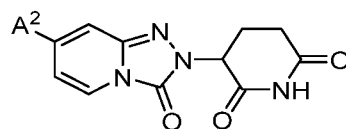
**Formula B3**

or a pharmaceutically acceptable salt thereof.

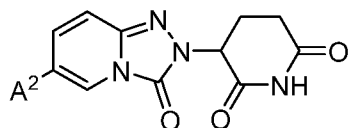
In some embodiments, the structure of **Formula B** has the structure of **Formula B4**:

**Formula B4**

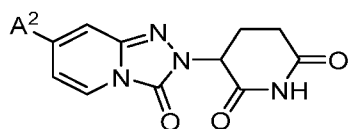
or a pharmaceutically acceptable salt thereof.



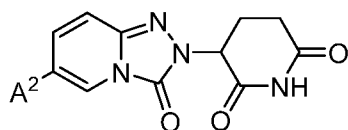
In some embodiments, the structure of **Formula B** is



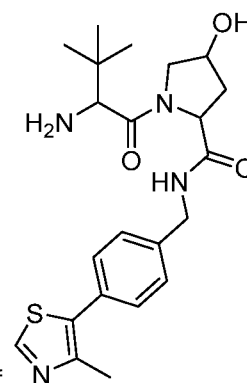
. In some embodiments, the structure of **Formula B** is



. In some embodiments, the structure of **Formula B** is

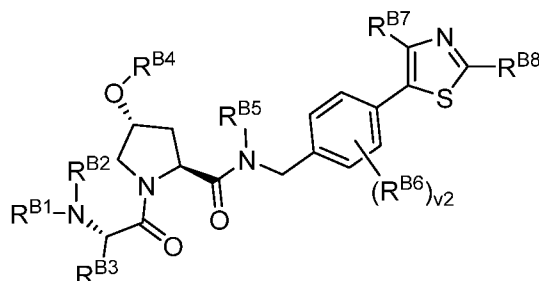


In some embodiments, the ubiquitin ligase binding moiety comprises a von Hippel-Lindau ligand.



In some embodiments, the von Hippel-Lindau ligand has the structure of or derivative or analog thereof.

In some embodiments, the degradation moiety includes the structure of **Formula C**:



Formula C,

where

R^{B1} is H, A², optionally substituted C₁-C₆ alkyl, or optionally substituted C₁-C₆ heteroalkyl;

R^{B2} is H, optionally substituted C₁-C₆ alkyl, or optionally substituted C₁-C₆ heteroalkyl;

R^{B3} is A², optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₁-C₆ alkyl C₃-C₁₀ carbocyclyl, or optionally substituted C₁-C₆ alkyl C₆-C₁₀ aryl;

R^{B4} is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₁-C₆ alkyl C₃-C₁₀ carbocyclyl, or optionally substituted C₁-C₆ alkyl C₆-C₁₀ aryl;

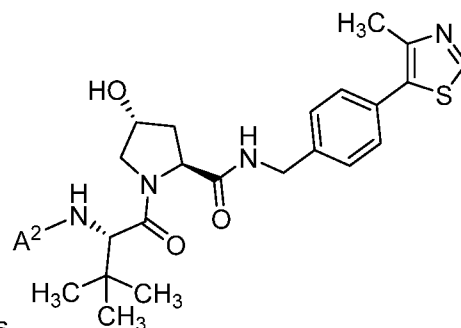
R^{B5} is H, optionally substituted C₁-C₆ alkyl, or optionally substituted C₁-C₆ heteroalkyl;

v₂ is 0, 1, 2, 3, or 4;

each R^{B6} is, independently, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₂-C₉ heteroaryl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, hydroxy, thiol, or optionally substituted amino; and

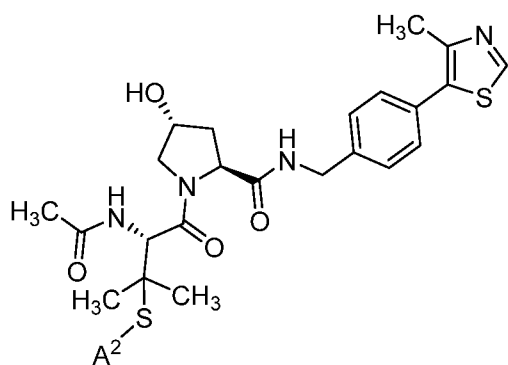
each of R^{B7} and R^{B8} is, independently, H, halogen, optionally substituted C₁-C₆ alkyl, or optionally substituted C₆-C₁₀ aryl,

where one of R^{B1} and R^{B3} is A², or a pharmaceutically acceptable salt thereof.

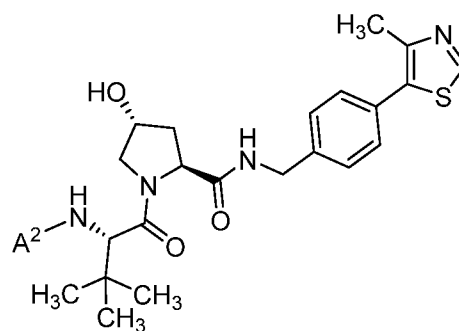


In some embodiments, the structure of **Formula C** is

or

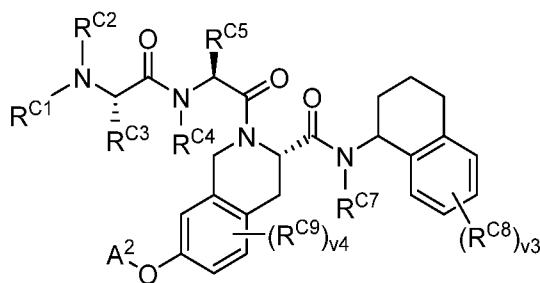


, or derivative or analog thereof.



In some embodiments, the structure of **Formula C** is

In some embodiments, the degrader moiety includes the structure of **Formula D**:



Formula D,

where

A² is a bond between B and the linker;

each of R^{C1}, R^{C2}, and R^{C7} is, independently, H, optionally substituted C₁-C₆ alkyl, or optionally substituted C₁-C₆ heteroalkyl;

R^{C3} is optionally substituted C₁-C₆ alkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₁-C₆ alkyl C₃-C₁₀ carbocyclyl, or optionally substituted C₁-C₆ alkyl C₆-C₁₀ aryl;

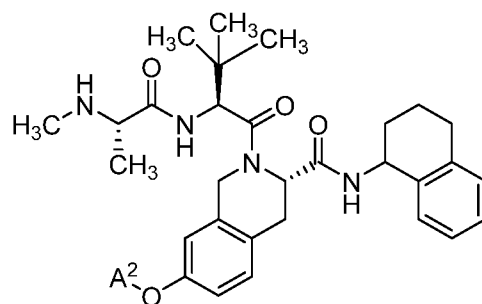
R^{C5} is optionally substituted C_1 - C_6 alkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_1 - C_6 alkyl C_3 - C_{10} carbocyclyl, or optionally substituted C_1 - C_6 alkyl C_6 - C_{10} aryl;

v_3 is 0, 1, 2, 3, or 4;

each R^{C8} is, independently, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, hydroxy, thiol, or optionally substituted amino;

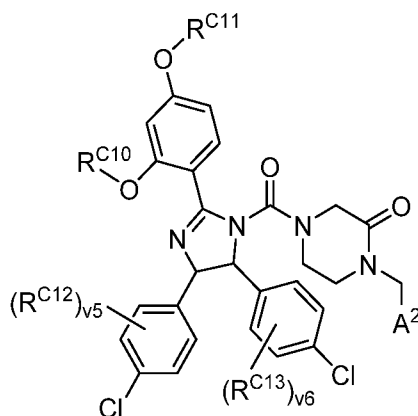
v_4 is 0, 1, 2, 3, or 4; and

each R^{C9} is, independently, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, hydroxy, thiol, or optionally substituted amino, or a pharmaceutically acceptable salt thereof.



In some embodiments, the structure of **Formula D** is derivative or analog thereof.

In some embodiments, the degrader moiety includes the structure of **Formula E**:



Formula E,

where

A^2 is a bond between B and the linker;

each of R^{C10} and R^{C11} is, independently, H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_1 - C_6 alkyl C_3 - C_{10} carbocyclyl, or optionally substituted C_1 - C_6 alkyl C_6 - C_{10} aryl;

v_5 is 0, 1, 2, 3, or 4;

each R^{C12} is, independently, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl,

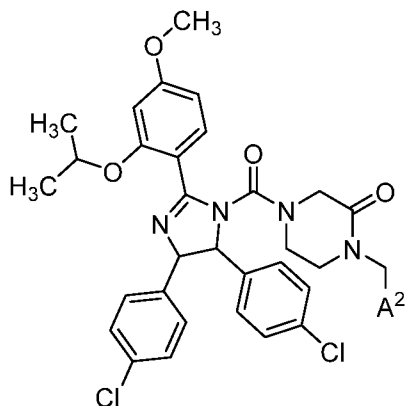
optionally substituted C₆-C₁₀ aryl, optionally substituted C₂-C₉ heteroaryl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, hydroxy, thiol, or optionally substituted amino;

v₆ is 0, 1, 2, 3, or 4; and

each R²¹ is, independently, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-

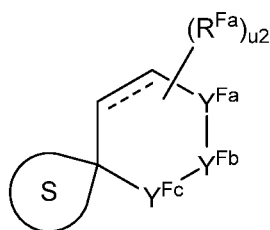
- 5 C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₂-C₉ heteroaryl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, hydroxy, thiol, or optionally substituted amino, or a pharmaceutically acceptable salt thereof.

In some embodiments, the structure of **Formula E** is



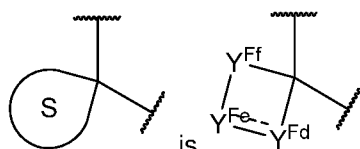
10 , or derivative or analog thereof.

In some embodiments, the degradation moiety includes the structure of **Formula FA**:



Formula FA,

where



- 15 is , or a bicyclic moiety which is substituted with A² and substituted with one or more groups independently selected from H, R^{FF1}, and oxo;

==== is a single bond or a double bond;

u₂ is 0, 1, 2, or 3;

A² is a bond between the degrader and the linker;

- 20 Y^{Fa} is CR^{Fb}R^{Fc}, C=O, C=S, C=CH₂, SO₂, S(O), P(O)Oalkyl, P(O)NHalkyl, P(O)N(alkyl)₂, P(O)alkyl, P(O)OH, P(O)NH₂;

Y^{Fb} is NH, NR^{FF1}, CH₂, CHR^{FF1}, C(R^{FF1})₂, O, or S;

Y^{Fc} is CR^{Fd}R^{Fe}, C=O, C=S, C=CH₂, SO₂, S(O), P(O)Oalkyl, P(O)NHalkyl, P(O)N(alkyl)₂, P(O)alkyl, P(O)OH, P(O)NH₂;

- 25 each of R^{Fb}, R^{Fc}, R^{Fd}, and R^{Fe} is, independently, H, alkyl, aliphatic, heteroaliphatic, aryl, heteroaryl, carbocyclyl, hydroxyl, alkoxy, amino, —NHalkyl, or —Nalkyl₂;

or R^{Fb} and R^{Fc} , together with the carbon atom to which each is attached, combine to form a 3-, 4-, 5-, or 6-membered spirocarbocyclene, or a 4-, 5-, or 6-membered spiroheterocyclene comprising 1 or 2 heteroatoms selected from N and O;

or R^{Fd} and R^{Fe} , together with the carbon atom to which each is attached, combine to form a 3-, 4-, 5-, or 6-membered spirocarbocyclene, or a 4-, 5-, or 6-membered spiroheterocyclene comprising 1 or 2 heteroatoms selected from N and O; and

or R^{Fd} and R^{Fb} , together with the carbon atoms to which each is attached, combine to form a 1, 2, 3, or 4 carbon bridged ring;

each of Y^{Fd} and Y^{Fi} is, independently, CH_2 , CHR^{FF2} , $C(R^{FF2})_2$, $C(O)$, N, NH, NR^{FF3} , O, S, or $S(O)$;

Y^{Fe} is a bond or a divalent moiety attached to Y^{Fd} and Y^{Fi} that contains 1 to 5 contiguous carbon atoms that form a 3 to 8-membered ring,

wherein 1, 2, or 3 carbon atoms can be replaced with a nitrogen, oxygen, or sulfur atom;

wherein one of the ring atoms is substituted with A^2 and the others are substituted with one or more groups independently selected from H and R^{FF1} ; and

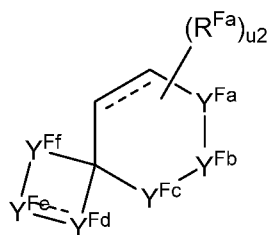
wherein the contiguous atoms of Y^{Fe} can be attached through a single or double bond; each R^{FF1} is, independently, H, alkyl, alkenyl, alkynyl, aliphatic, heteroaliphatic, carbocyclyl, halogen, hydroxyl, amino, cyano, alkoxy, aryl, heteroaryl, heterocyclyl, alkylamino, alkylhydroxyl, or haloalkyl;

each R^{FF2} is, independently, alkyl, alkene, alkyne, halogen, hydroxyl, alkoxy, azide, amino, $-C(O)H$, $-C(O)OH$, $-C(O)$ (aliphatic, including alkyl), $-C(O)O$ (aliphatic, including alkyl), $-NH$ (aliphatic, including alkyl), $-N$ (aliphatic including alkyl)(aliphatic including alkyl), $-NHSO_2$ alkyl, $-N$ (alkyl) SO_2 alkyl, $-NHSO_2$ aryl, $-N$ (alkyl) SO_2 aryl, $-NHSO_2$ alkenyl, $-N$ (alkyl) SO_2 alkenyl, $-NHSO_2$ alkynyl, $-N$ (alkyl) SO_2 alkynyl, aliphatic, heteroaliphatic, aryl, heteroaryl, heterocyclic, carbocyclic, cyano, nitro, nitroso, $-SH$, $-S$ alkyl, or haloalkyl; and

R^{FF3} is alkyl, alkenyl, alkynyl, $-C(O)H$, $-C(O)OH$, $-C(O)$ alkyl, or $-C(O)O$ alkyl,

wherein if Y^{Fd} or Y^{Fi} is substituted with A^2 , then Y^{Fe} is a bond, or a pharmaceutically acceptable salt thereof.

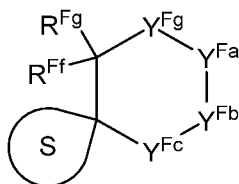
In some embodiments, the compound of **Formula FA** has the structure of **Formula FA1**:



Formula FA1,

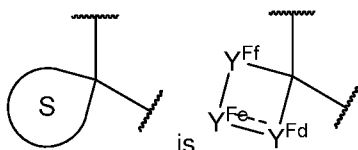
or a pharmaceutically acceptable salt thereof.

In some embodiments, the degradation moiety includes the structure of **Formula FB**:



Formula FB,

where



is , or a bicyclic moiety which is substituted with A^2 and substituted

5 with one or more groups independently selected from H, R^{FF1} , and oxo;

A^2 is a bond between the degrader and the linker;

Y^{Fa} is $CR^{Fb}R^{Fc}$, $C=O$, $C=S$, $C=CH_2$, SO_2 , $S(O)$, $P(O)Oalkyl$, $P(O)NHalkyl$, $P(O)N(alkyl)_2$, $P(O)alkyl$, $P(O)OH$, $P(O)NH_2$;

each of Y^{Fb} and Y^{Fg} is, independently, NH , NR^{FF1} , CH_2 , CHR^{FF1} , $C(R^{FF1})_2$, O , or S ;

10 Y^{Fc} is $CR^{Fd}R^{Fe}$, $C=O$, $C=S$, $C=CH_2$, SO_2 , $S(O)$, $P(O)Oalkyl$, $P(O)NHalkyl$, $P(O)N(alkyl)_2$, $P(O)alkyl$, $P(O)OH$, $P(O)NH_2$;

each of R^{Fb} , R^{Fc} , R^{Fd} , R^{Fe} , R^{Ff} , and R^{Fg} is, independently, H, alkyl, aliphatic, heteroaliphatic, aryl, heteroaryl, carbocyclyl, hydroxyl, alkoxy, amino, $-NHalkyl$, or $-Nalkyl_2$;

or R^{Fb} and R^{Fc} , together with the carbon atom to which each is attached, combine to form a 3-, 4-, 15 5-, or 6-membered spirocarbocyclylene, or a 4-, 5-, or 6-membered spiroheterocyclylene comprising 1 or 2 heteroatoms selected from N and O;

or R^{Fd} and R^{Fe} , together with the carbon atom to which each is attached, combine to form a 3-, 4-, 5-, or 6-membered spirocarbocyclylene, or a 4-, 5-, or 6-membered spiroheterocyclylene comprising 1 or 2 heteroatoms selected from N and O;

20 or R^{Ff} and R^{Fg} , together with the carbon atom to which each is attached, combine to form a 3-, 4-, 5-, or 6-membered spirocarbocyclylene, or a 4-, 5-, or 6-membered spiroheterocyclylene comprising 1 or 2 heteroatoms selected from N and O;

or R^{Fd} and R^{Fb} , together with the carbon atoms to which each is attached, combine to form a 1, 2, 3, or 4 carbon bridged ring;

25 or R^{Fd} and R^{Ff} , together with the carbon atoms to which each is attached, combine to form a 1, 2, 3, or 4 carbon bridged ring;

or R^{Fb} and R^{Fg} , together with the carbon atoms to which each is attached, combine to form a 1, 2, 3, or 4 carbon bridged ring;

each of Y^{Fd} and Y^{Ff} is, independently, CH_2 , CHR^{FF2} , $C(R^{FF2})_2$, $C(O)$, N, NH, NR^{FF3} , O, S, or $S(O)$;

30 Y^{Fe} is a bond or a divalent moiety attached to Y^{Fd} and Y^{Ff} that contains 1 to 5 contiguous carbon atoms that form a 3 to 8-membered ring,

wherein 1, 2, or 3 carbon atoms can be replaced with a nitrogen, oxygen, or sulfur atom;

wherein one of the ring atoms is substituted with A^2 and the others are substituted with one or more groups independently selected from H and R^{FF1} ; and

35 wherein the contiguous atoms of Y^{Fe} can be attached through a single or double bond;

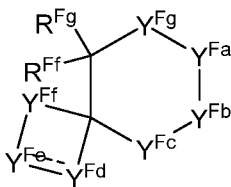
each R^{FF1} is, independently, H, alkyl, alkenyl, alkynyl, aliphatic, heteroaliphatic, carbocyclyl, halogen, hydroxyl, amino, cyano, alkoxy, aryl, heteroaryl, heterocyclyl, alkylamino, alkylhydroxyl, or haloalkyl;

each R^{FF2} is, independently, alkyl, alkene, alkyne, halogen, hydroxyl, alkoxy, azide, amino, —C(O)H, —C(O)OH, —C(O)(aliphatic, including alkyl), —C(O)O(aliphatic, including alkyl), —NH(aliphatic, including alkyl), —N(aliphatic including alkyl)(aliphatic including alkyl), —NHSO₂alkyl, —N(alkyl)SO₂alkyl, —NHSO₂aryl, —N(alkyl)SO₂aryl, —NHSO₂alkenyl, —N(alkyl)SO₂alkenyl, —NHSO₂alkynyl, —N(alkyl)SO₂alkynyl, aliphatic, heteroaliphatic, aryl, heteroaryl, heterocyclic, carbocyclic, cyano, nitro, nitroso, —SH, —Salkyl, or haloalkyl; and

R^{FF3} is alkyl, alkenyl, alkynyl, —C(O)H, —C(O)OH, —C(O)alkyl, or —C(O)Oalkyl,

wherein if Y^{Fd} or Y^{Ff} is substituted with A^2 , then Y^{Fe} is a bond, or a pharmaceutically acceptable salt thereof.

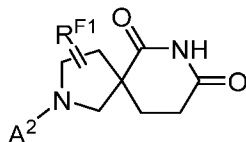
In some embodiments, the compound of **Formula FB** has the structure of **Formula FB1**:



Formula FB1,

or a pharmaceutically acceptable salt thereof.

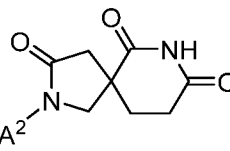
In some embodiments, the degradation moiety includes the structure of **Formula F1**:



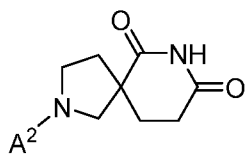
Formula F1,

where A^2 is a bond between the degrader and the linker; and R^{F1} is absent or O, or a pharmaceutically acceptable salt thereof.

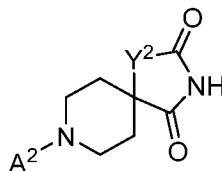
In some embodiments, R^{F1} is absent. In some embodiments, R^{F1} is O.



In some embodiments, the structure of **Formula F1** is A^2 or

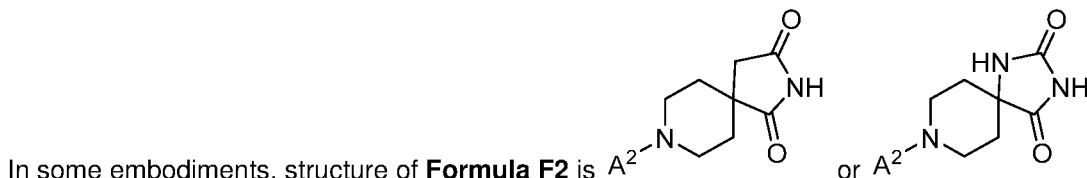


In some embodiments, the degradation moiety includes the structure **Formula F2**:

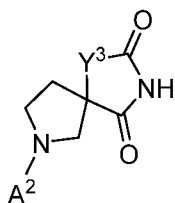
**Formula F2,**

where A^2 is a bond between the degrader and the linker; and Y^2 is CH_2 or NH , or a pharmaceutically acceptable salt thereof.

5 In some embodiments, Y^2 is NH . In some embodiments, Y^2 is CH_2 .

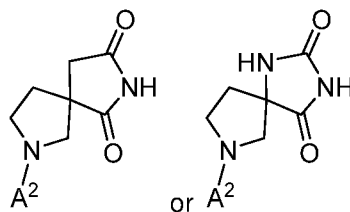


In some embodiments, the degradation moiety includes the structure **Formula G**:

**Formula G,**

10 where A^2 is a bond between the degrader and the linker; and Y^3 is CH_2 or NH , or a pharmaceutically acceptable salt thereof.

In some embodiments, Y^3 is NH . In some embodiments, Y^3 is CH_2 .

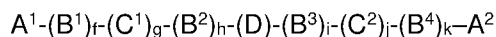


In some embodiments, structure of **Formula G** is A^2 or A^2 .

The degradation moiety may also include structures found in, e.g., WO2017/197036;

15 WO2019/204354, WO2019/236483, WO2020/010177; and WO2020/010227, the structures of which are herein incorporated by reference.

In some embodiments, the linker has the structure of **Formula IV**:

**Formula IV**

20 where

A^1 is a bond between the linker and A;

A^2 is a bond between B and the linker;

each of B^1 , B^2 , B^3 , and B^4 is, independently, optionally substituted C_{1-2} alkylene, optionally substituted C_{1-3} heteroalkylene, O, S, $S(O)_2$, or NR^N ;

25 each R^N is, independently, H, optionally substituted C_{1-4} alkyl, optionally substituted C_{2-4} alkenyl, optionally substituted C_{2-4} alkynyl, optionally substituted C_{2-6} heterocyclyl, optionally substituted C_{6-12} aryl, or optionally substituted C_{1-7} heteroalkyl;

each of C¹ and C² is, independently, carbonyl, thiocarbonyl, sulphonyl, or phosphoryl;

each of f, g, h, i, j , and k is, independently, 0 or 1; and

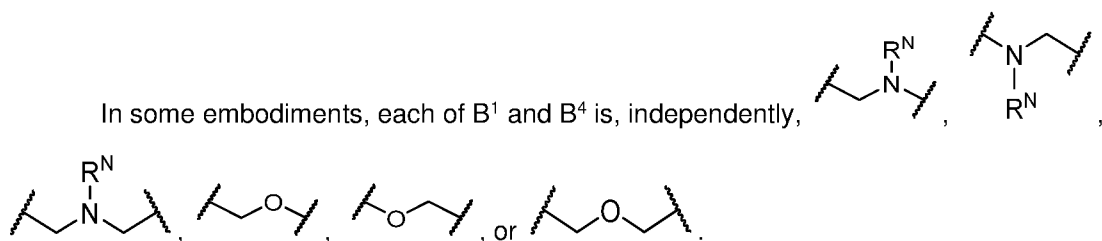
D is optionally substituted C₁₋₁₀ alkylene, optionally substituted C₂₋₁₀ alkenylene, optionally substituted C₂₋₁₀ alkynylene, optionally substituted C₂₋₆ heterocyclylene, optionally substituted C₆₋₁₂ arylene, optionally substituted C₂-C₁₀ polyethylene glycol, or optionally substituted C₁₋₁₀ heteroalkylene, or a chemical bond linking A¹-(B¹)_r-(C¹)_g-(B²)_h- to -(B³)_i-(C²)_j-(B⁴)_k-A².

In some embodiments, each of B¹, B², B³, and B⁴ is, independently, optionally substituted C₁-C₄ alkylene, optionally substituted C₁-C₄ heteroalkylene, or NR^N.

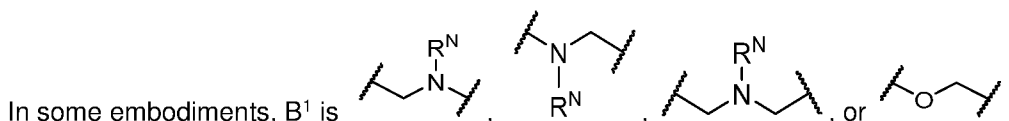
In some embodiments, each R^N is, independently, H or optionally substituted C₁-C₄ alkylene.

In some embodiments, each R^N is, independently, H or methyl.

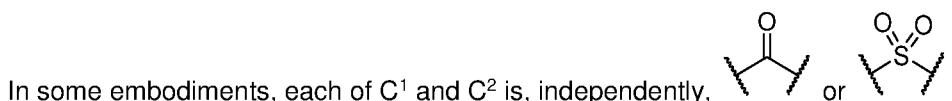
In some embodiments, each of B¹ and B⁴ is, independently,



In some embodiments, B¹ is



In some embodiments, each of C^1 and C^2 is, independently,



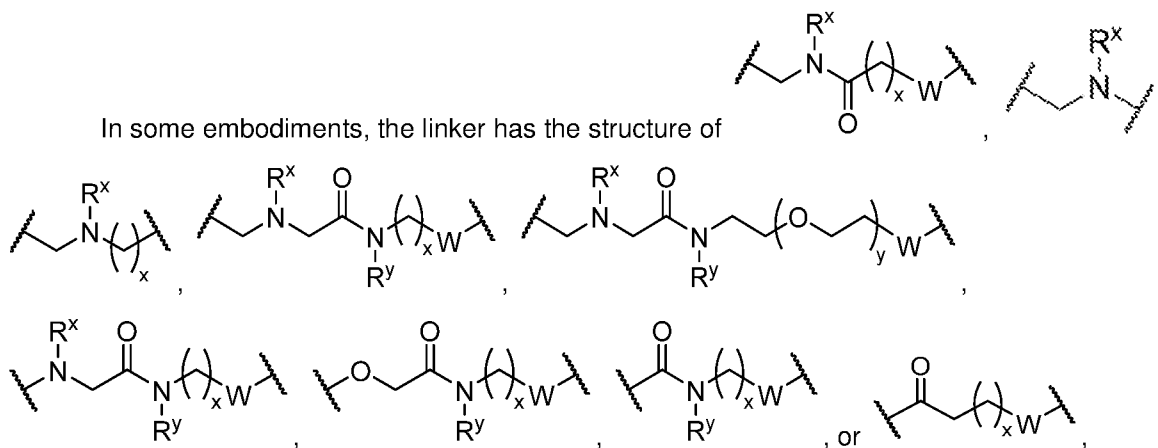
In some embodiments, C^1 is



In some embodiments, B² is NR^N. In some embodiments, B² is optionally substituted C₁-C₄ alkylene.

In some embodiments, f is 0. In some embodiments, f is 1. In some embodiments, g is 1. In some embodiments, h is 0. In some embodiments, h is 1. In some embodiments, i is 0. In some embodiments, j is 0. In some embodiments, k is 0.

In some embodiments, the linker has the structure of



wherein

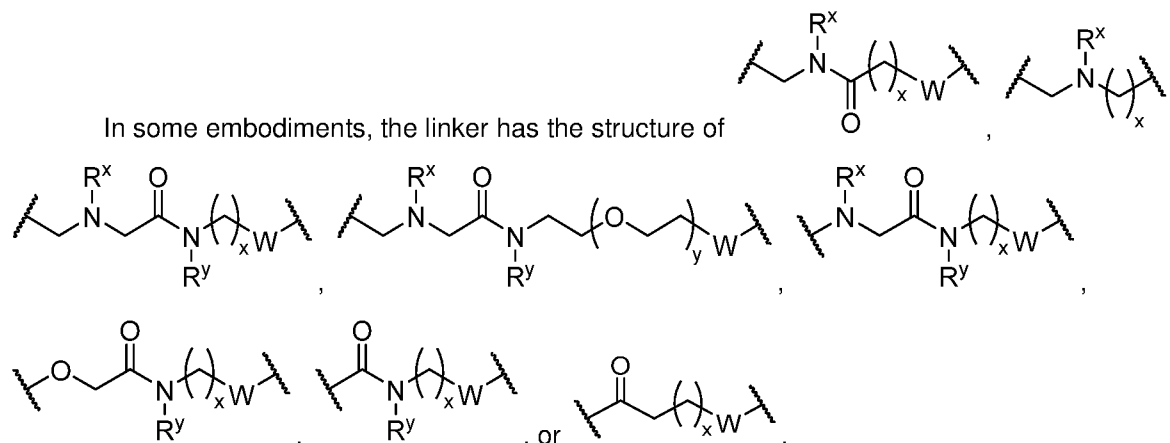
x is 1, 2, 3, 4, 5, 6, 7, or 8:

y is 1, 2, 3, or 4;

R^x is H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, or optionally substituted C_3 - C_6 carbocyclyl;

R^y is H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, or optionally substituted C_3 - C_6 carbocyclyl; and

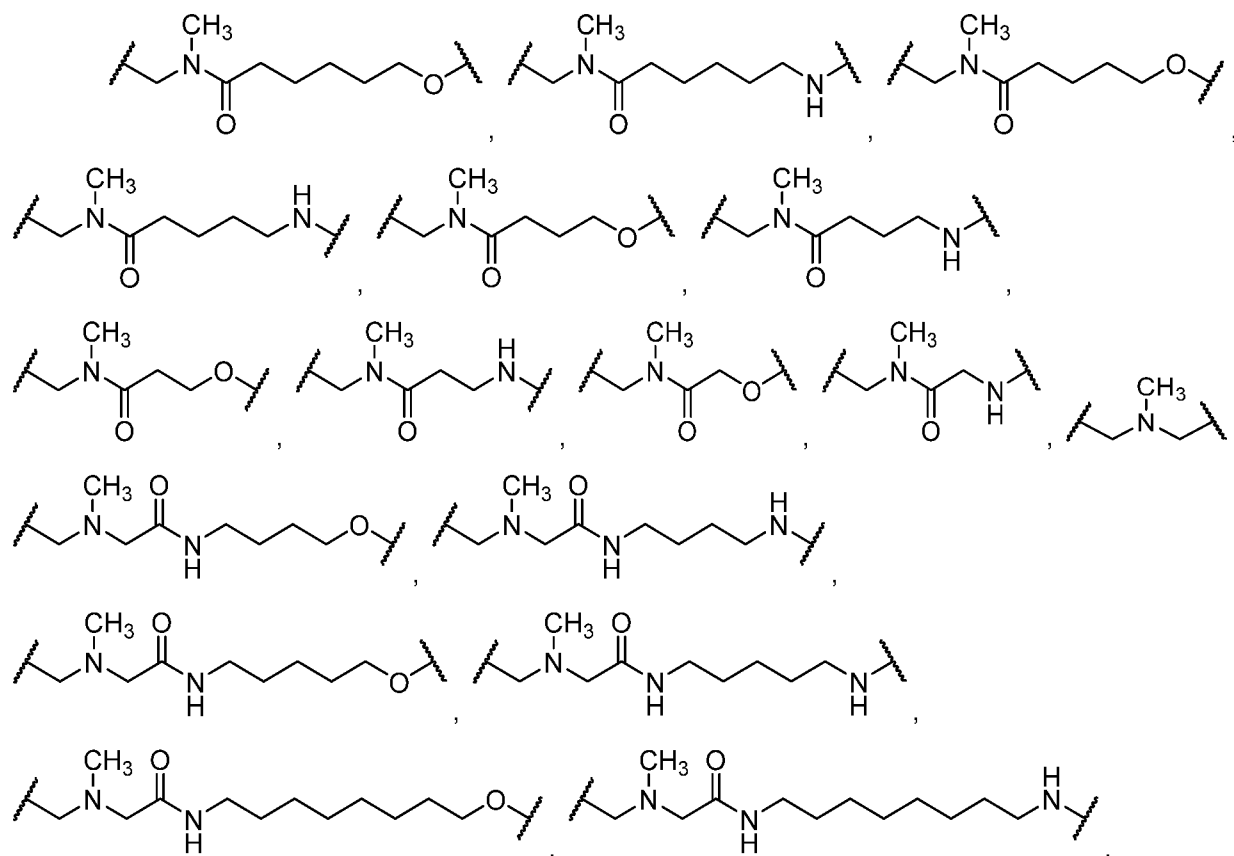
5 W is O or NR^w , wherein R^w is H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, or optionally substituted C_3 - C_6 carbocyclyl.



10 In some embodiments, R^x is H or me optionally substituted C_1 - C_6 alkyl. In some embodiments, R^y is H or optionally substituted C_1 - C_6 alkyl. In some embodiments, R^w is H or optionally substituted C_1 - C_6 alkyl.

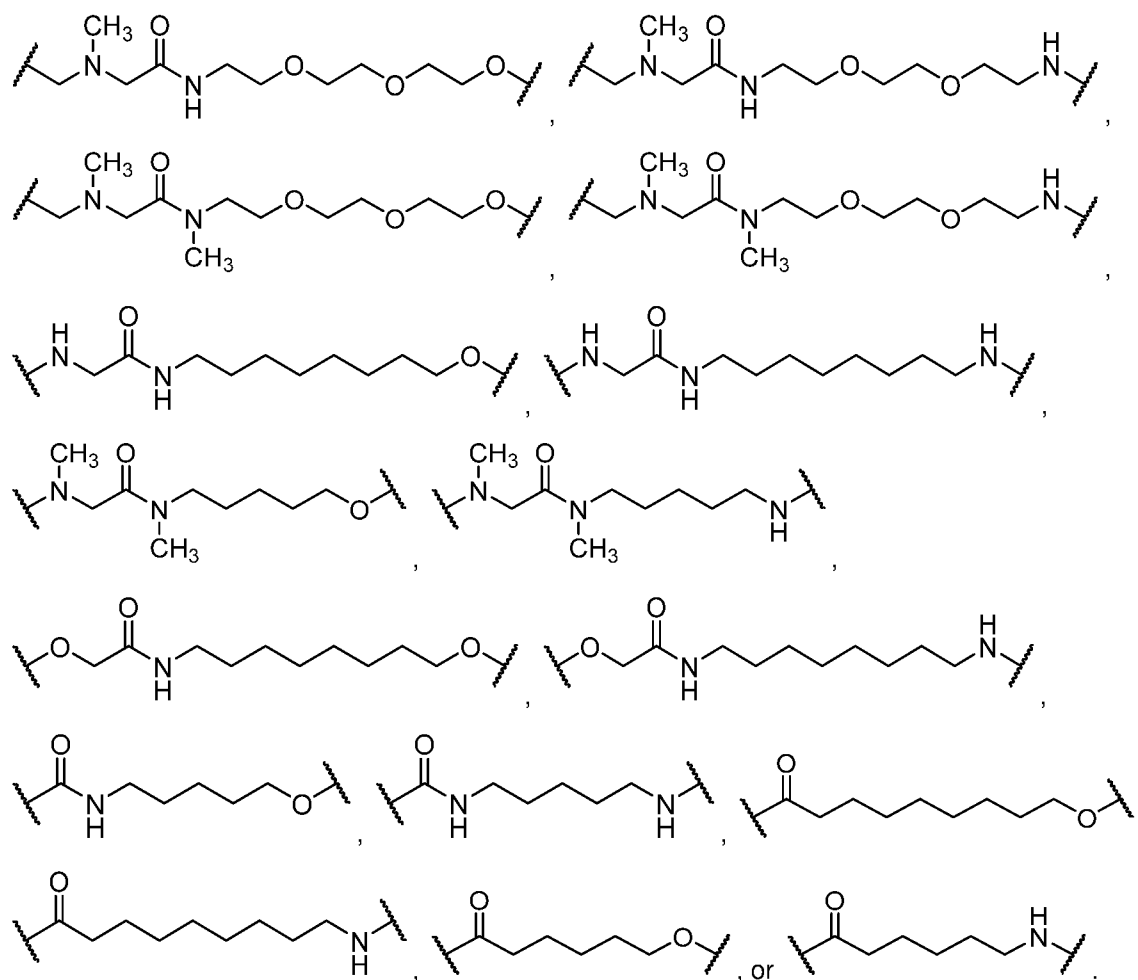
In some embodiments, R^x is H or methyl. In some embodiments, R^y is H or methyl. In some embodiments, R^w is H or methyl.

15 In some embodiments, the linker has the structure of

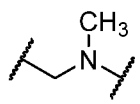


20

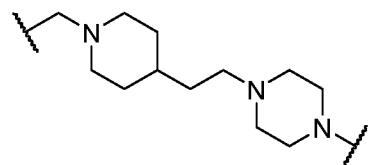
5



In some embodiments, the linker has the structure of

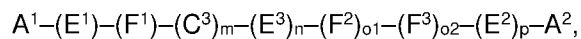


In some embodiments, the linker has the structure of



10

In some embodiments, the linker has the structure of **Formula V**:



Formula V

where

15

A¹ is a bond between the linker and A;

A² is a bond between B and the linker;

each of m, n, o₁, o₂, and p is, independently, 0 or 1;

each of E^1 and E^2 is, independently, O, S, NR^N , optionally substituted C_{1-10} alkylene, optionally substituted C_{2-10} alkenylene, optionally substituted C_{2-10} alkynylene, optionally substituted C_{2-10} polyethylene glycol, or optionally substituted C_{1-10} heteroalkylene;

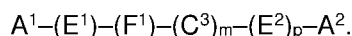
E^3 is optionally substituted C_1-C_6 alkylene, optionally substituted C_1-C_6 heteroalkylene, O, S, or NR^N ;

each R^N is, independently, H, optionally substituted C_{1-4} alkyl, optionally substituted C_{2-4} alkenyl, optionally substituted C_{2-4} alkynyl, optionally substituted C_{2-6} heterocyclyl, optionally substituted C_{6-12} aryl, or optionally substituted C_{1-7} heteroalkyl;

C^3 is carbonyl, thiocarbonyl, sulphonyl, or phosphoryl; and

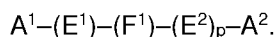
each of F^1 , F^2 , and F^3 is, independently, optionally substituted C_3-C_{10} carbocyclylene, optionally substituted C_{2-10} heterocyclylene, optionally substituted C_6-C_{10} arylene, or optionally substituted C_2-C_9 heteroarylene.

In some embodiments, the linker has the structure of **Formula Va**:



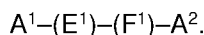
Formula Va

In some embodiments, the linker has the structure of **Formula Vb**:



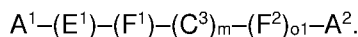
Formula Vb

In some embodiments, the linker has the structure of **Formula Vc**:



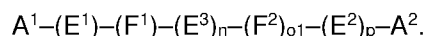
Formula Vc

In some embodiments, the linker has the structure of **Formula Vd**:



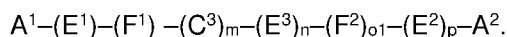
Formula Vd

In some embodiments, the linker has the structure of **Formula Ve**:



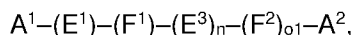
Formula Ve

In some embodiments, the linker has the structure of **Formula Vf**:



Formula Vf

In some embodiments, the linker has the structure of **Formula Vg**:



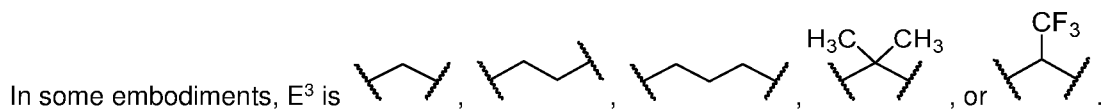
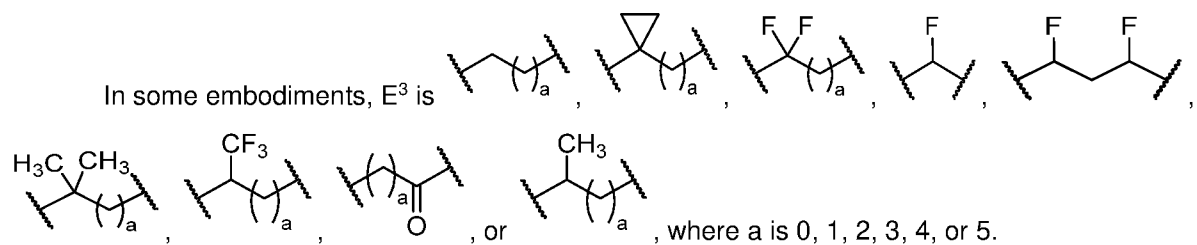
Formula Vg

In some embodiments, each of E^1 and E^2 is, independently, NR^N , optionally substituted C_{1-10} alkylene, optionally substituted C_{2-10} polyethylene glycolene, or optionally substituted C_{1-10} heteroalkylene.

In some embodiments, E^3 is optionally substituted C_1-C_6 alkylene, O, S, or NR^N ;

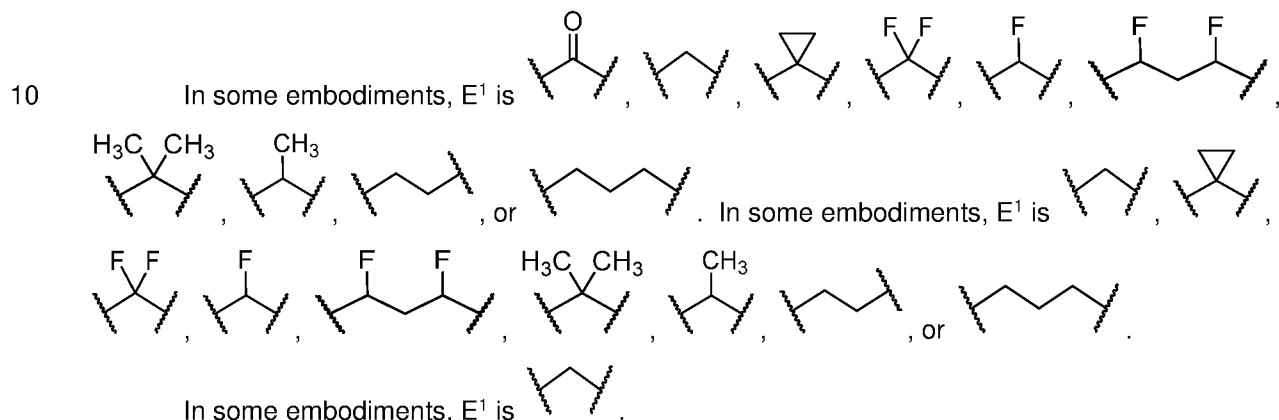
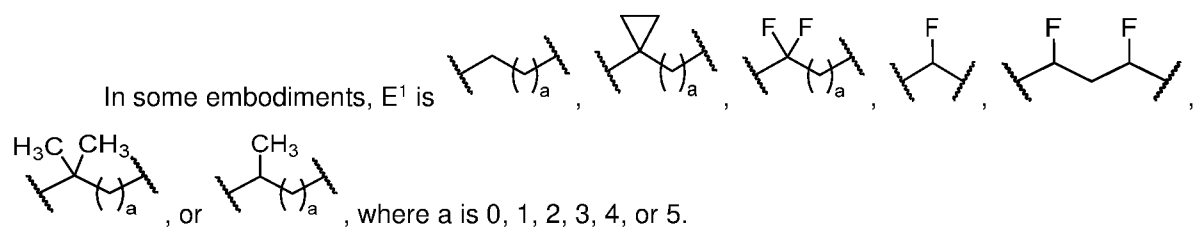
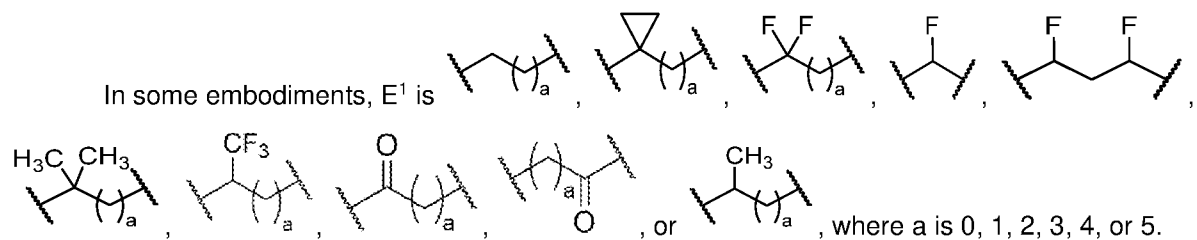
In some embodiments, E^3 is optionally substituted C_1-C_6 alkylene. In some embodiments, E^3 is optionally substituted C_1-C_3 alkylene. In some embodiments, E^3 is O, S, or NR^N .

In some embodiments, E^3 is C_1-C_6 alkylene. In some embodiments, E^3 is C_1-C_3 alkylene. In some embodiments, E^3 is O.

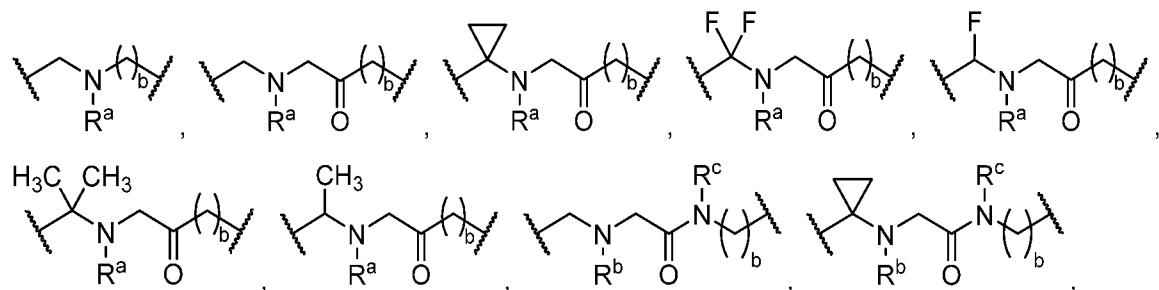
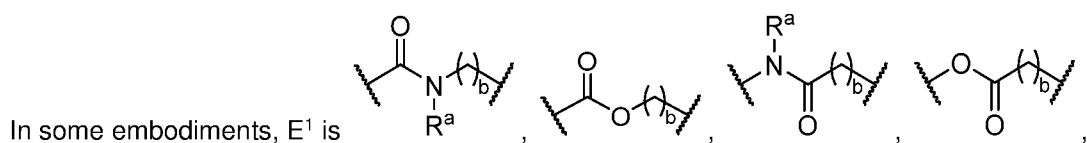


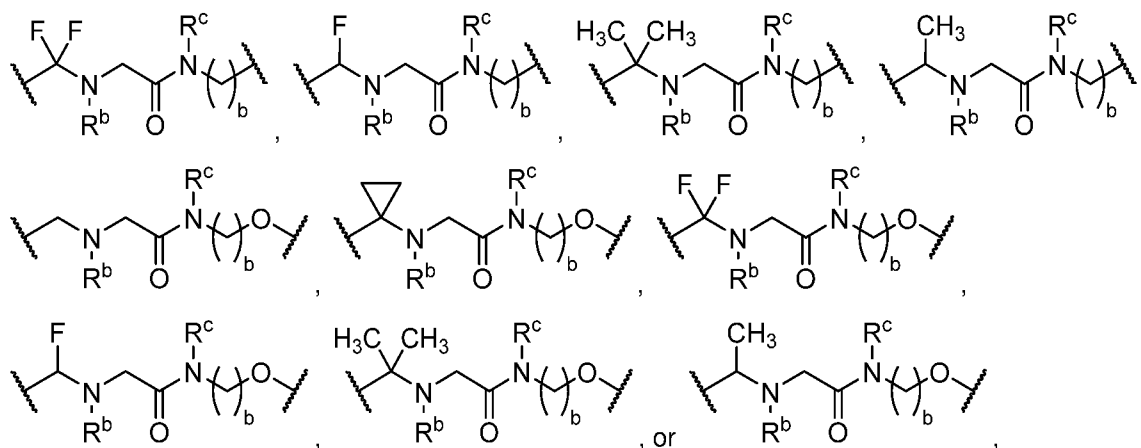
In some embodiments, each R^N is, independently, H or optionally substituted C₁₋₄ alkyl.

5 In some embodiments, each R^N is, independently, H or methyl.



In some embodiments, E¹ is .





where

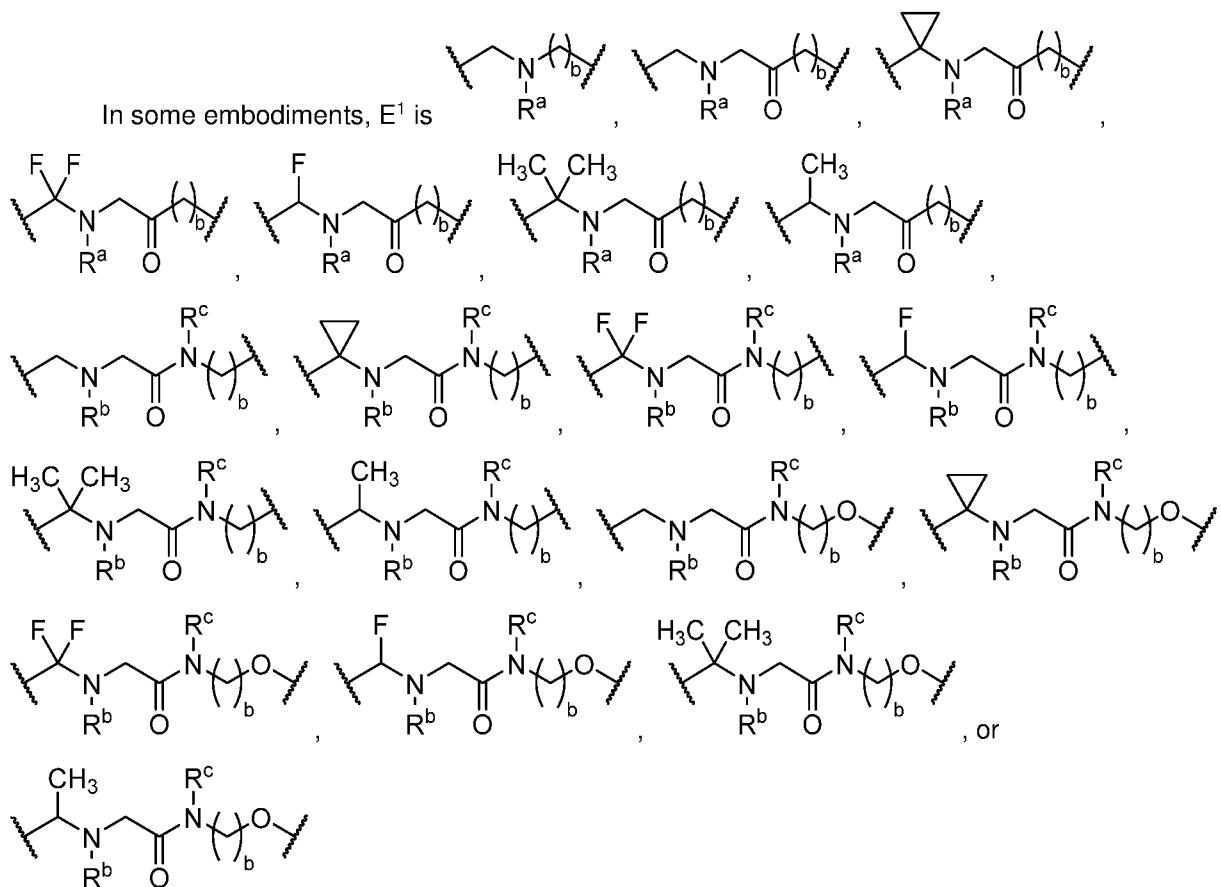
5 b is 0, 1, 2, 3, 4, 5, or 6;

R^a is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl;

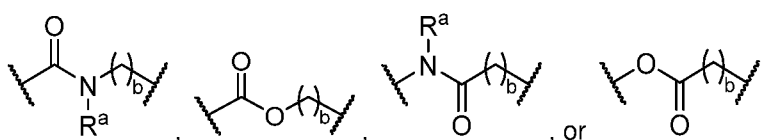
R^b is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl; and

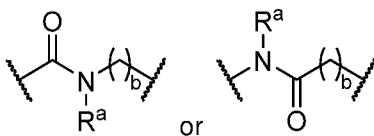
10 R^c is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl.

In some embodiments, E¹ is



In some embodiments, E¹ is





In some embodiments, E¹ is

or

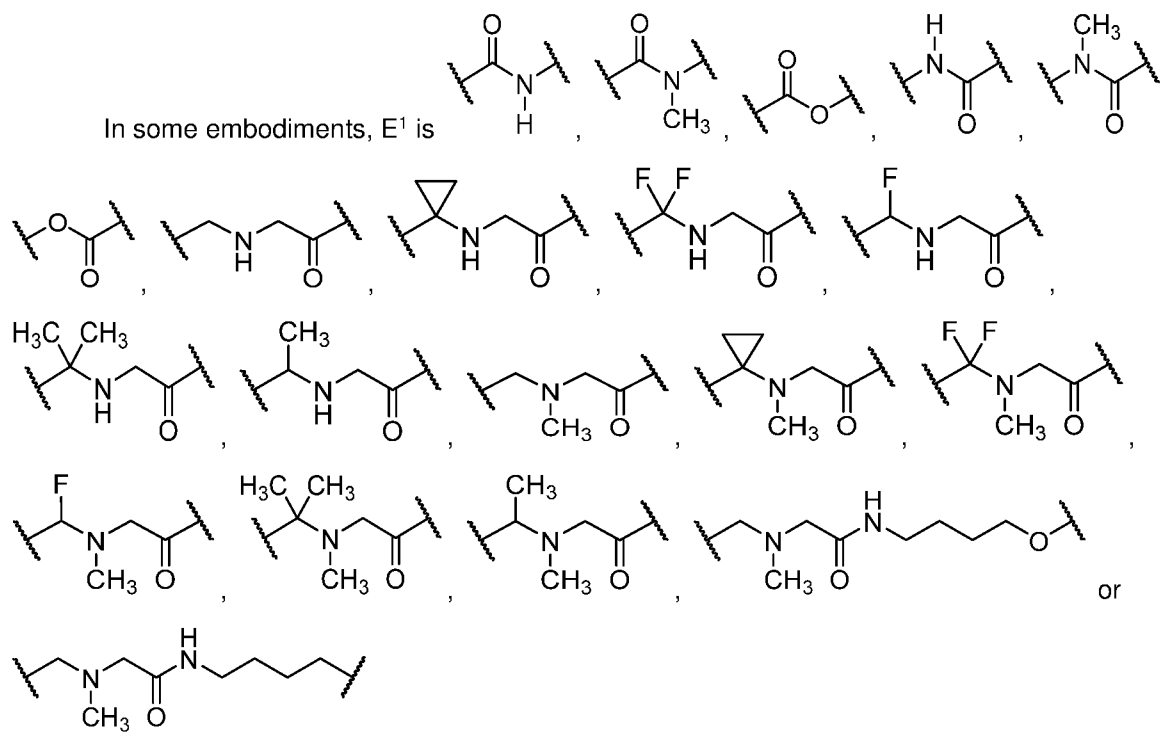
In some embodiments, R^a is H or optionally substituted C₁-C₆ alkyl. In some embodiments, R^b is H or optionally substituted C₁-C₆ alkyl. In some embodiments, R^c is H or optionally substituted C₁-C₆ alkyl.

5 In some embodiments, R^a is H or methyl. In some embodiments, R^b is H or methyl. In some embodiments, R^c is H or methyl.

In some embodiments, b is 0, 1, 2, or 3. In some embodiments, b is 0. In some embodiments, b is 1. In some embodiments, b is 2. In some embodiments, b is 3.

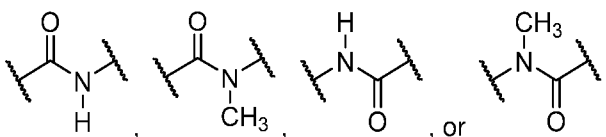
10

In some embodiments, E¹ is

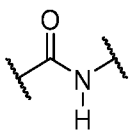


15

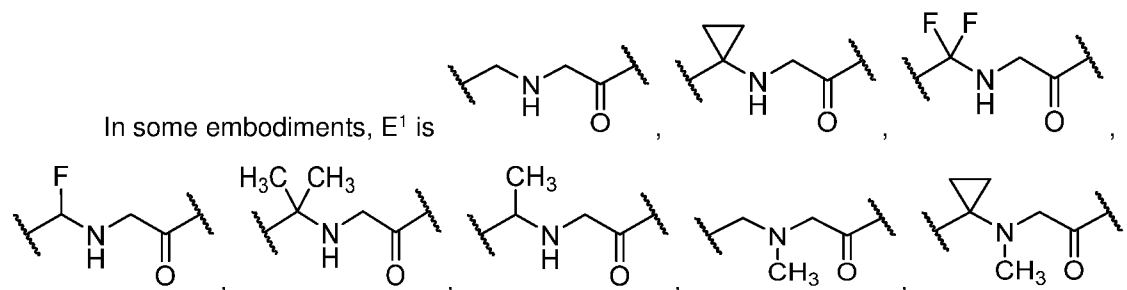
In some embodiments, E¹ is

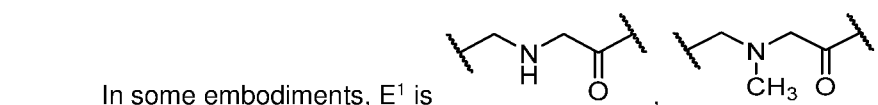
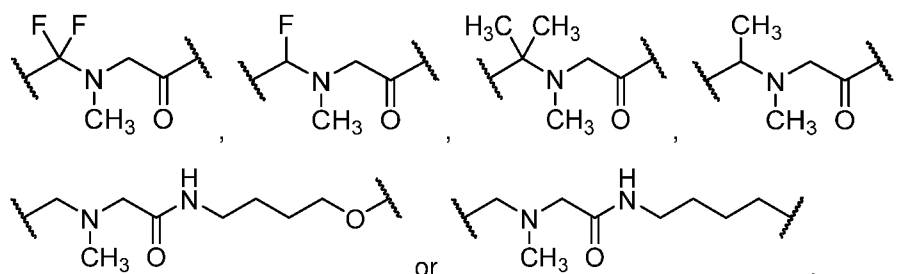


In some embodiments, E¹ is

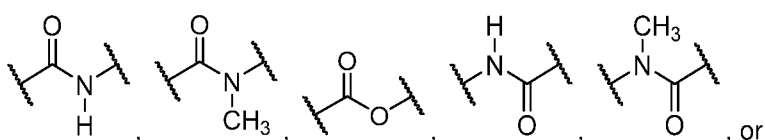
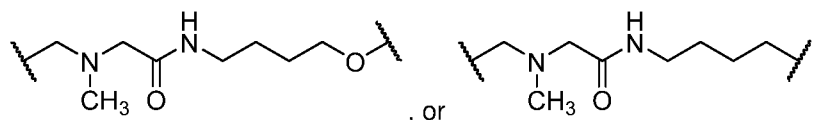


In some embodiments, E¹ is

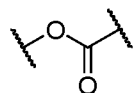




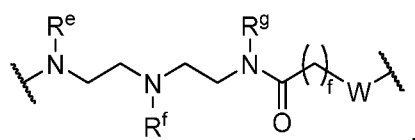
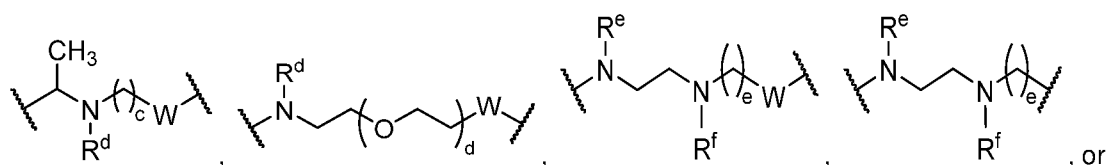
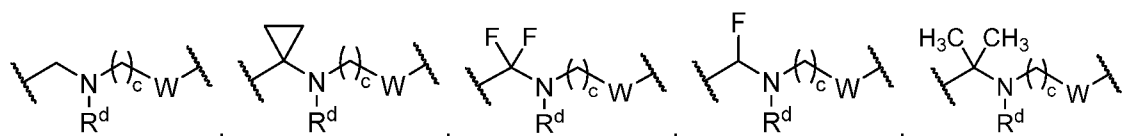
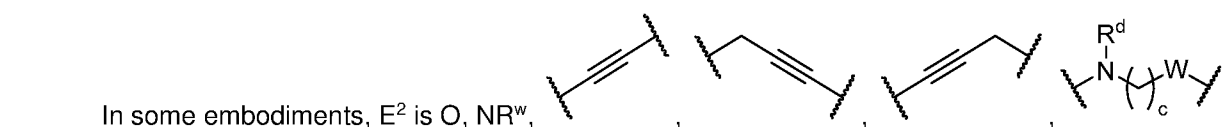
In some embodiments, E^1 is



In some embodiments, E^1 is



In some embodiments, E^2 is O, NR^w ,



wherein

c is 0, 1, 2, 3, 4, 5, 6, 7, or 8;

d is 0, 1, 2, or 3;

e is 0, 1, 2, 3, 4, 5, or 6:

f is 0, 1, 2, 3, or 4;

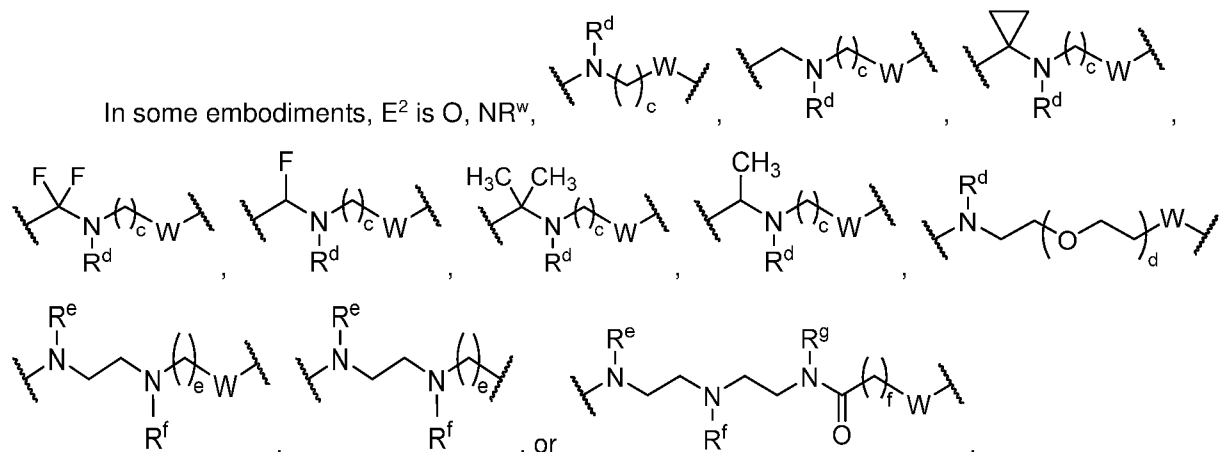
R^d is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl;

R^e is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl;

R¹ is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl;

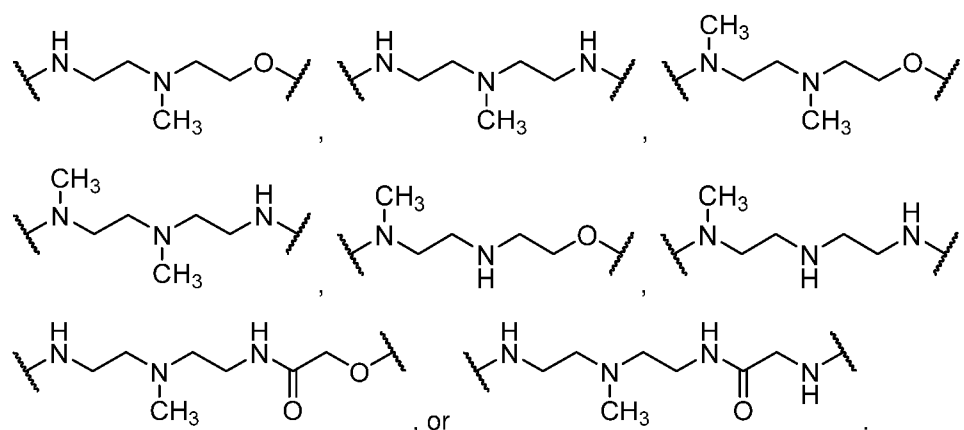
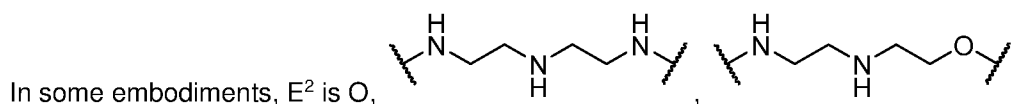
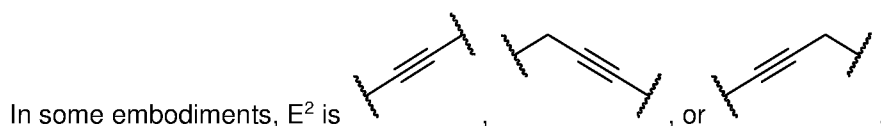
R⁹ is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl; and

5 W is O or NR^w, wherein R^w is H or optionally substituted C₁-C₆ alkyl.



In some embodiments, R^d is H or optionally substituted C₁-C₆ alkyl. In some embodiments, R^e is
 10 H or optionally substituted C₁-C₆ alkyl. In some embodiments, R^f is H or optionally substituted C₁-C₆
 alkyl. In some embodiments, R^g is H or optionally substituted C₁-C₆ alkyl. In some embodiments, R^w is H
 or optionally substituted C₁-C₆ alkyl.

In some embodiments, R^d is H or methyl. In some embodiments, R^e is H or methyl. In some
embodiments, R^f is H or methyl. In some embodiments, R^g is H or methyl. In some embodiments, R^w is
15 H or methyl.

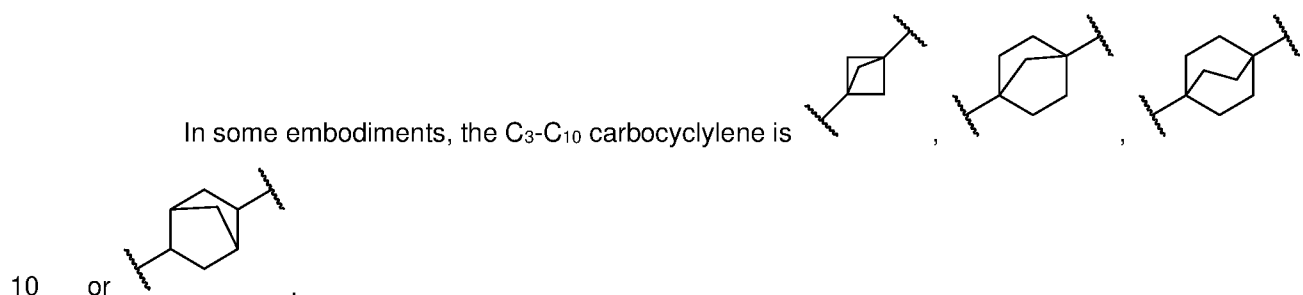
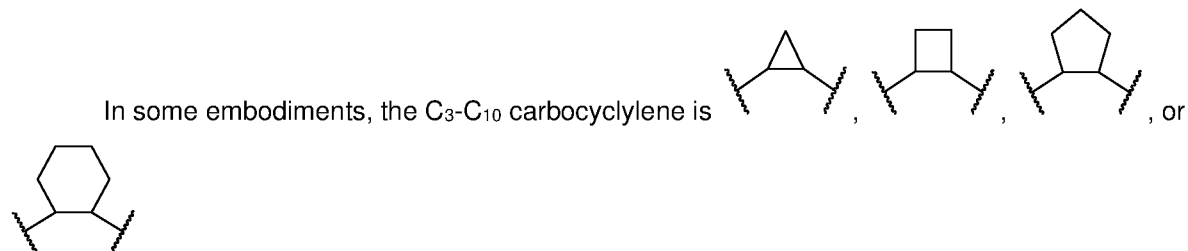


In some embodiments, each of F¹, F², or F³ is, independently, optionally substituted C₃-C₁₀ carbocyclylene.

In some embodiments, the C₃-C₁₀ carbocyclylene is monocyclic. In some embodiments, the C₃-C₁₀ carbocyclylene is polycyclic.

In some embodiments, the C₃-C₁₀ carbocyclylene is bicyclic.

In some embodiments, the C₃-C₁₀ carbocyclylene is bridged. In some embodiments, the C₃-C₁₀ carbocyclylene is fused. In some embodiments, the C₃-C₁₀ carbocyclylene is spirocyclic.



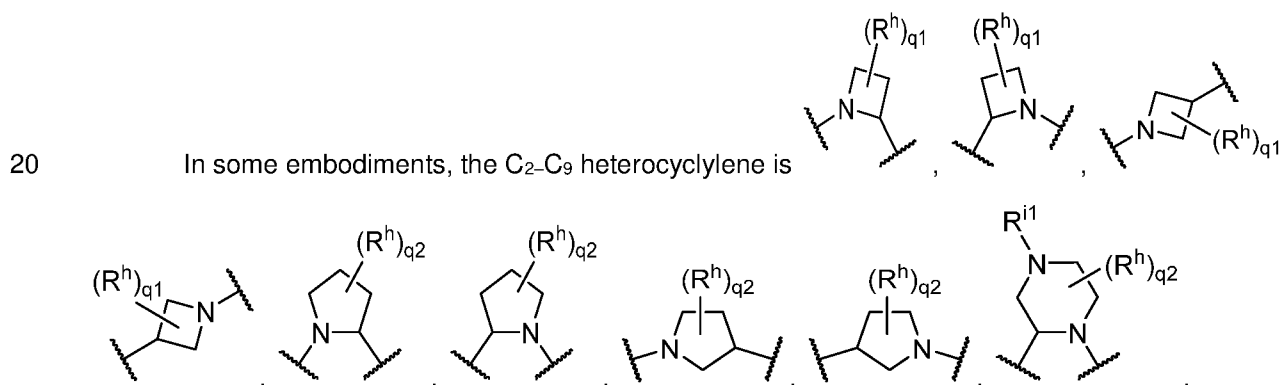
In some embodiments, each of F¹, F², or F³ is, independently, optionally substituted C₂-C₉ heterocyclylene.

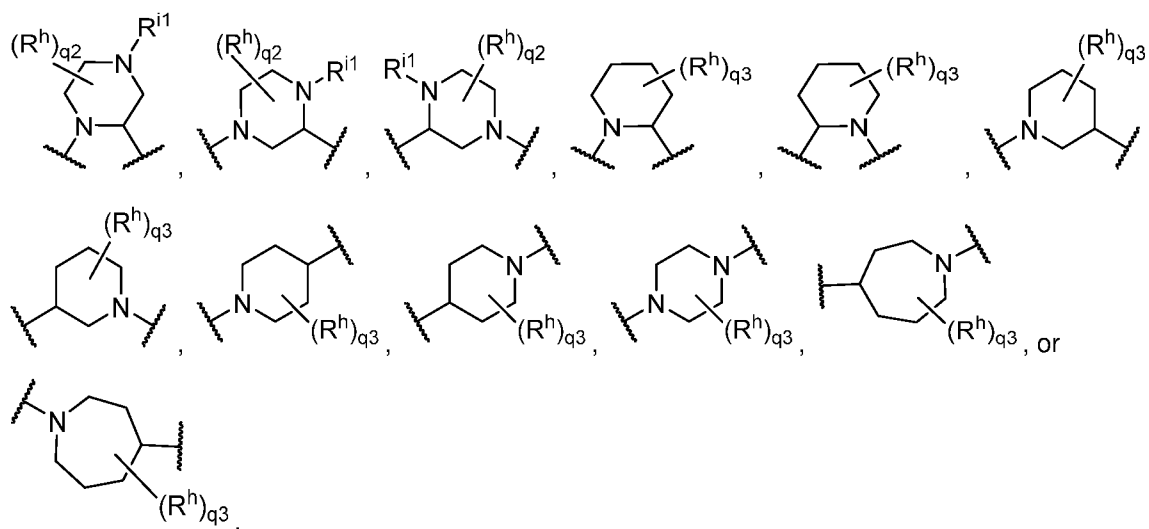
In some embodiments, the C₂-C₉ heterocyclylene is monocyclic. In some embodiments, the C₂-C₉ heterocyclylene is polycyclic.

In some embodiments, the C₂-C₉ heterocyclylene is bicyclic.

In some embodiments, the C₂-C₉ heterocyclylene is bridged. In some embodiments, the C₂-C₉ heterocyclylene is fused. In some embodiments, the C₂-C₉ heterocyclylene is spirocyclic.

In some embodiments, the C₂-C₉ heterocyclylene includes a quaternary amine.





where

5 q_1 is 0, 1, 2, 3, or 4;

q_2 is 0, 1, 2, 3, 4, 5, or 6;

q_3 is 0, 1, 2, 3, 4, 5, 6, 7, or 8;

each R^h is, independently, ^2H , halogen, optionally substituted C_1 - C_6 alkyl, OR^{i2} , or $NR^{i3}R^{i4}$; or two R^h groups, together with the carbon atom to which each is attached, combine to form optionally substituted C_3 - C_{10} carbocyclyl or optionally substituted C_2 - C_9 heterocyclyl; or two R^h groups, together with the carbon atoms to which each is attached, combine to form optionally substituted C_3 - C_{10} carbocyclyl or optionally substituted C_2 - C_9 heterocyclyl;

R^{i1} is H or optionally substituted C_1 - C_6 alkyl;

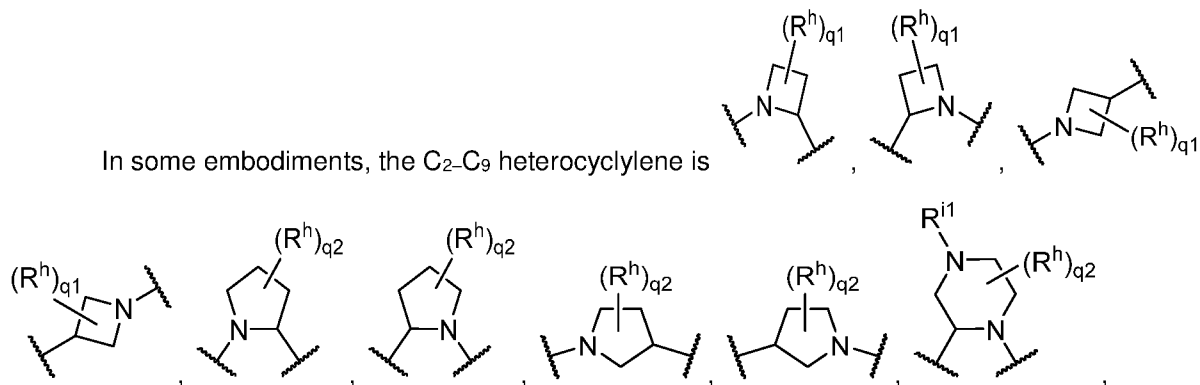
15 R^{i2} is H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, or optionally substituted C_3 - C_6 carbocyclyl;

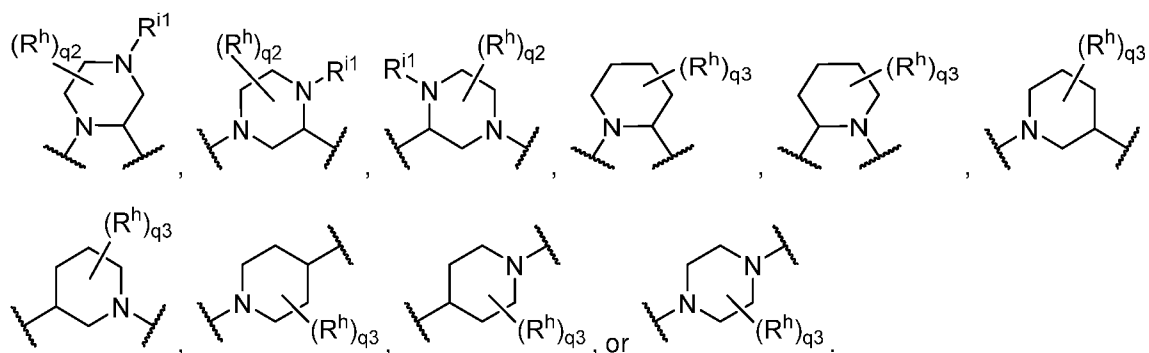
R^{i3} is H or optionally substituted C_1 - C_6 alkyl; and

R^{i4} is H or optionally substituted C_1 - C_6 alkyl.

In some embodiments, each R^h is, independently, halogen, optionally substituted C_1 - C_6 alkyl, OR^{i2} , or $NR^{i3}R^{i4}$. In some embodiments, R^{i1} is H or optionally substituted C_1 - C_6 alkyl. In some
20 embodiments, R^{i2} is H or optionally substituted C_1 - C_6 alkyl. In some embodiments, R^{i3} is H or optionally substituted C_1 - C_6 alkyl. In some embodiments, R^{i4} is H or optionally substituted C_1 - C_6 alkyl.

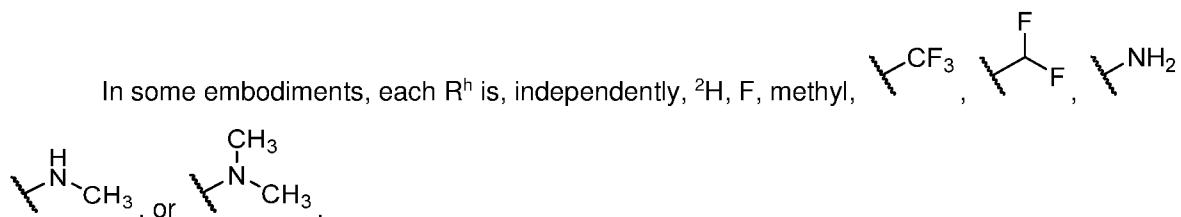
In some embodiments, the C_2 - C_9 heterocyclylene is





In some embodiments, each R^h is, independently, halogen, optionally substituted C_1 - C_6 alkyl, OR^{i2} , or $NR^{i3}R^{i4}$. In some embodiments, each R^h is, independently, halogen, optionally substituted C_1 - C_6 alkyl, or $NR^{i3}R^{i4}$.

In some embodiments, each R^h is, independently, ^2H , halogen, cyano, optionally substituted C_1 - C_6 alkyl, OR^{i2} , or $NR^{i3}R^{i4}$. In some embodiments, two R^h groups, together with the carbon atom to which each is attached, combine to form optionally substituted C_3 - C_{10} carbocyclyl or optionally substituted C_2 - C_9 heterocyclyl. In some embodiments, two R^h groups, together with the carbon atoms to which each is attached, combine to form optionally substituted C_3 - C_{10} carbocyclyl or optionally substituted C_2 - C_9 heterocyclyl.

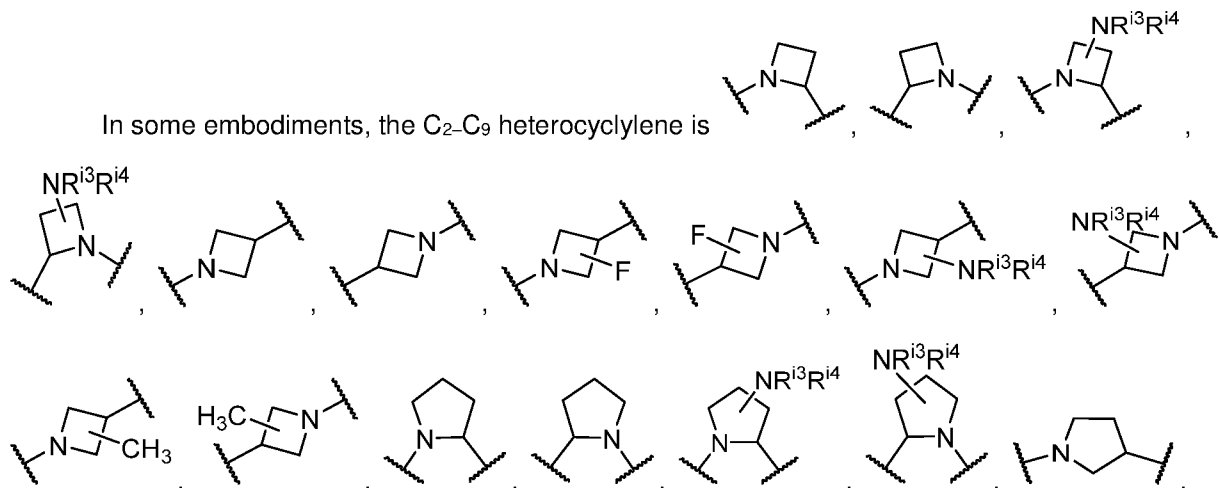


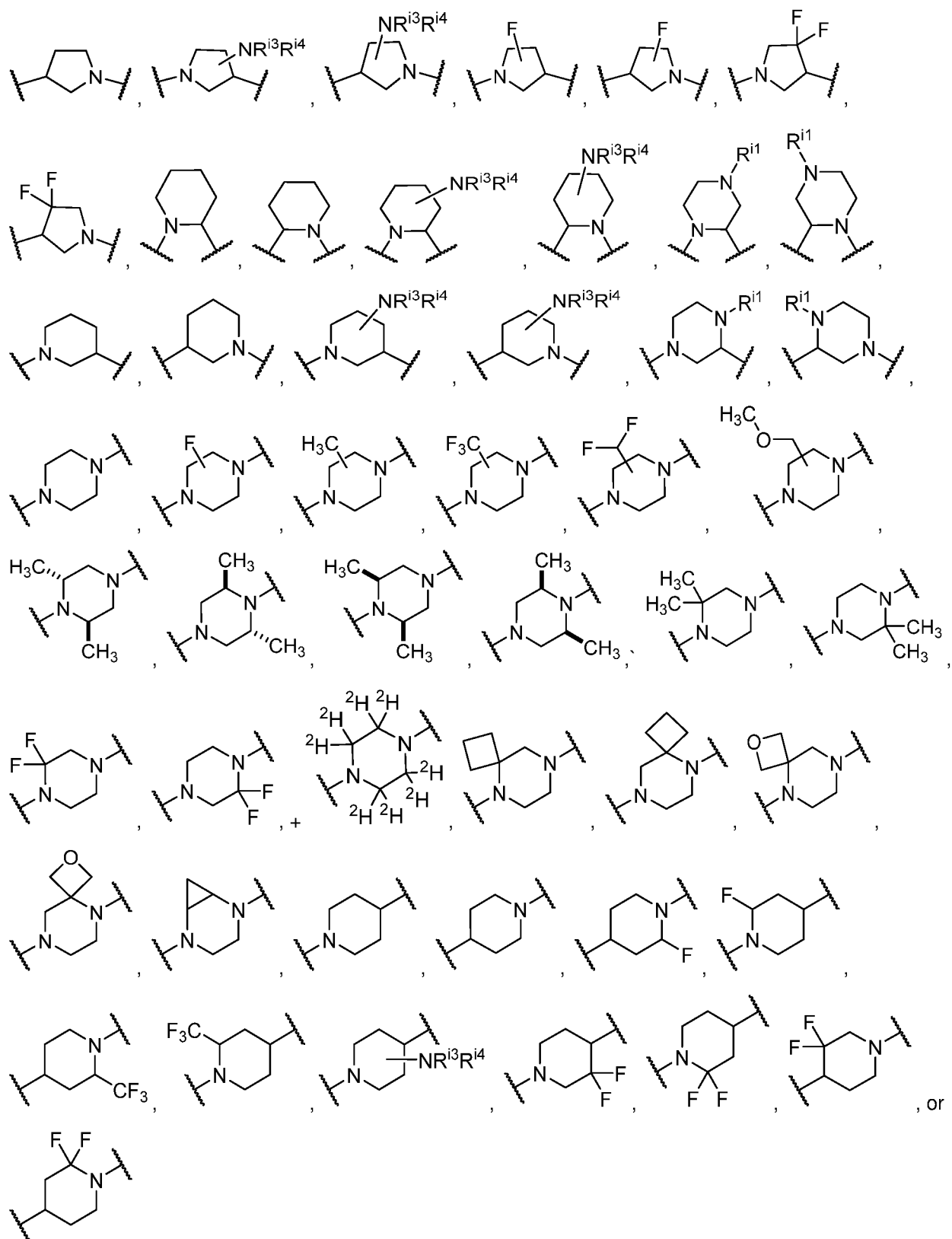
In some embodiments, each R^h is, independently, F, methyl, or $NR^{i3}R^{i4}$.

In some embodiments, q_1 is 0, 1, or 2. In some embodiments, q_1 is 0. In some embodiments, q_1 is 1. In some embodiments, q_1 is 2.

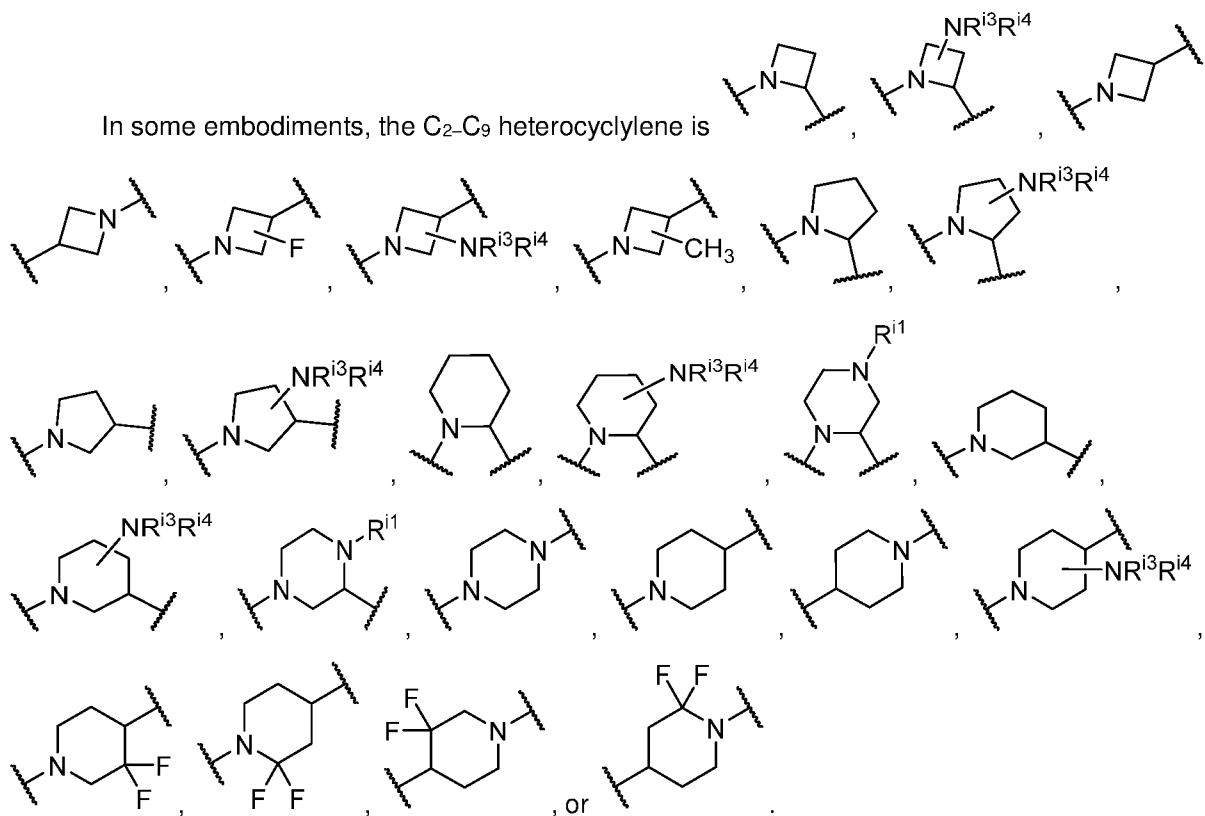
In some embodiments, q_2 is 0, 1, or 2. In some embodiments, q_2 is 0. In some embodiments, q_2 is 1. In some embodiments, q_2 is 2.

In some embodiments, q_3 is 0, 1, or 2. In some embodiments, q_3 is 0. In some embodiments, q_3 is 1. In some embodiments, q_3 is 2.

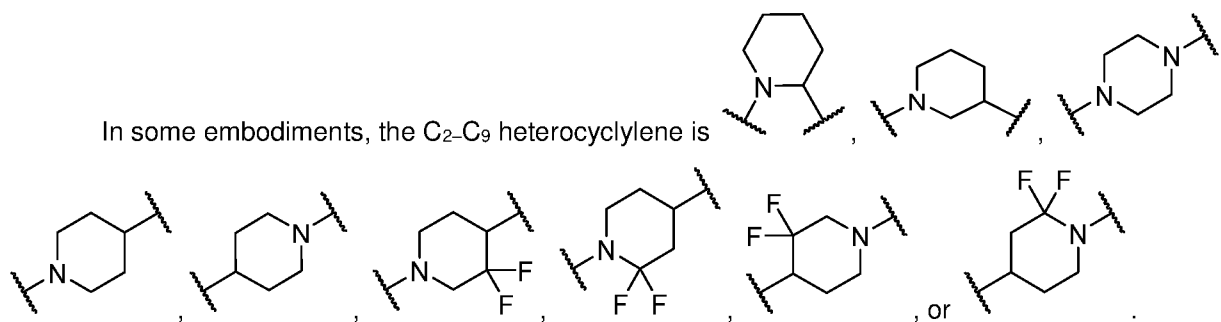




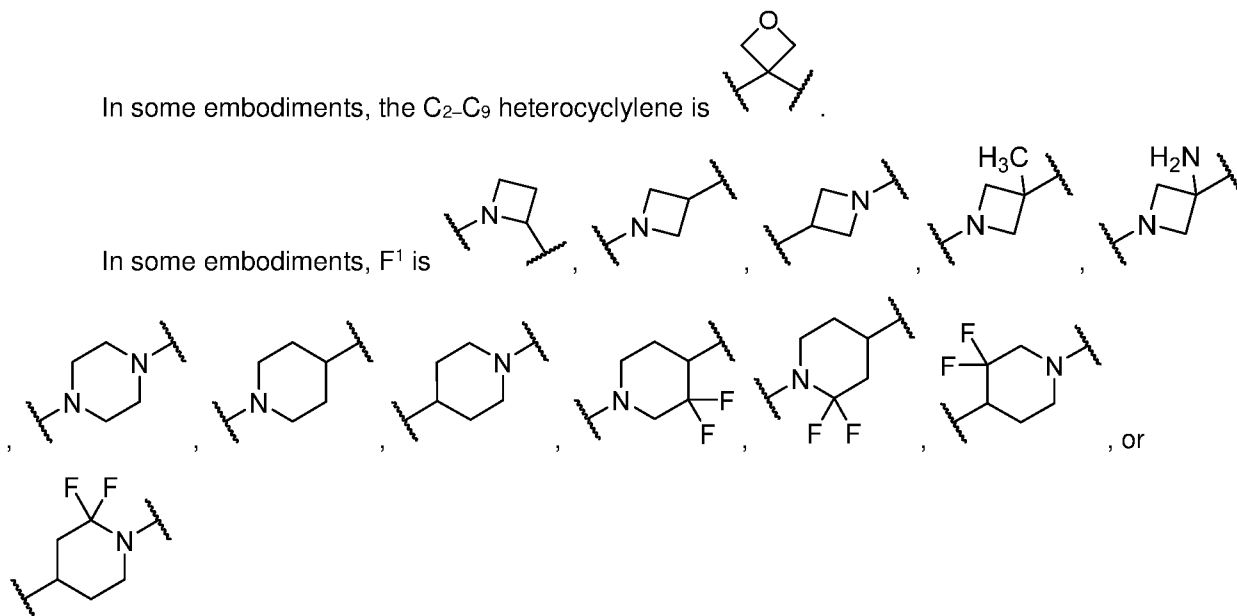
In some embodiments, the C₂-C₉ heterocyclylene is



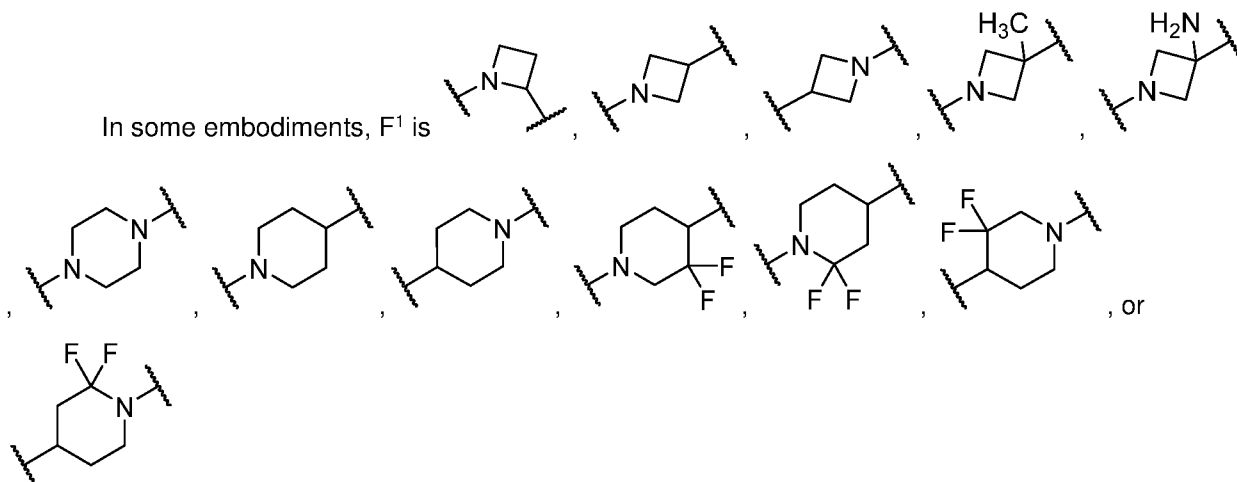
In some embodiments, the C₂-C₉ heterocyclylene is



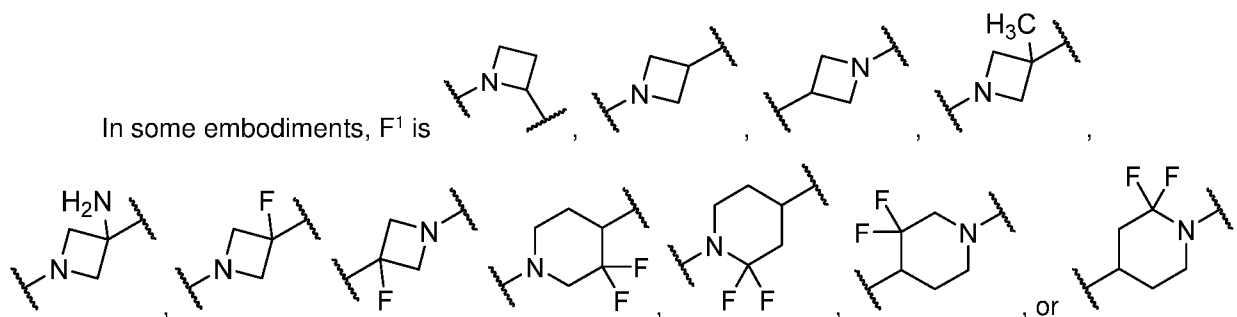
In some embodiments, the C₂-C₉ heterocyclylene is



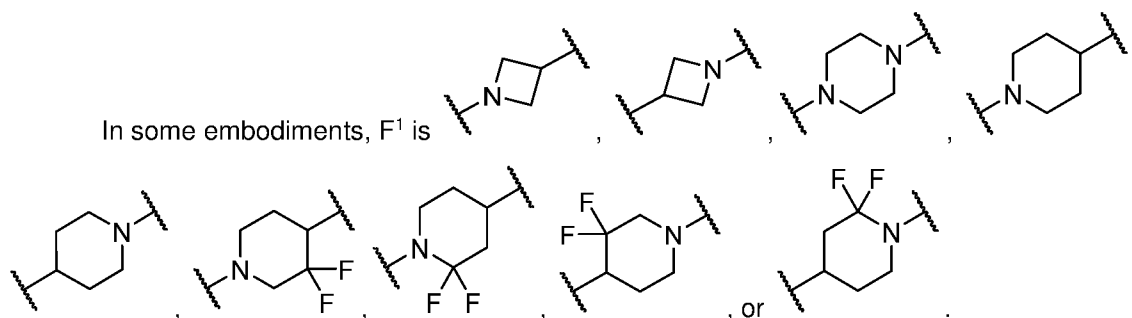
In some embodiments, F¹ is



In some embodiments, F¹ is

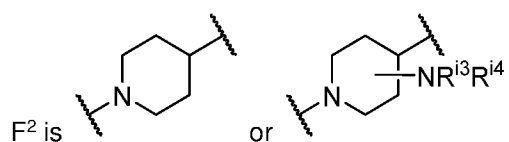
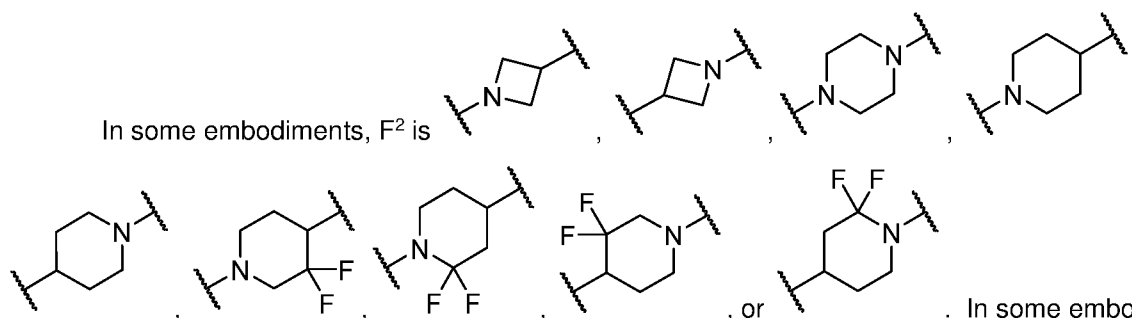


In some embodiments, F¹ is

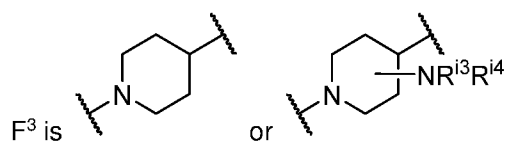
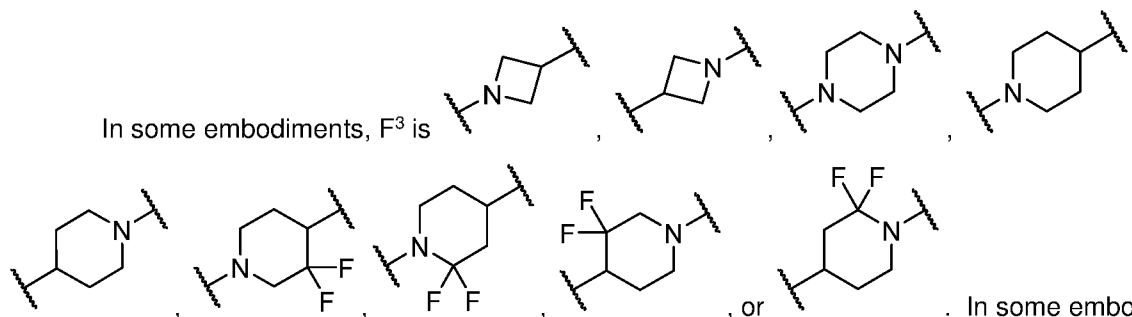


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In some embodiments, F² is



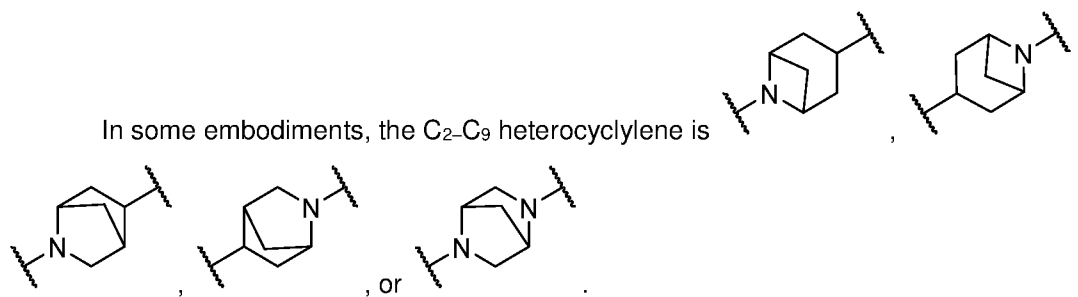
In some embodiments, F³ is



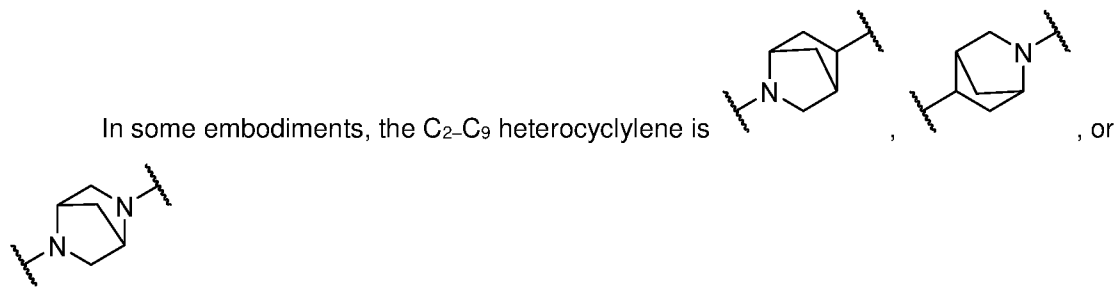
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In some embodiments, Rⁱ¹ is H or methyl. In some embodiments, Rⁱ² is H or methyl. In some embodiments, Rⁱ³ is H or methyl. In some embodiments, Rⁱ⁴ is H or methyl.

In some embodiments, the C₂-C₉ heterocyclylene is

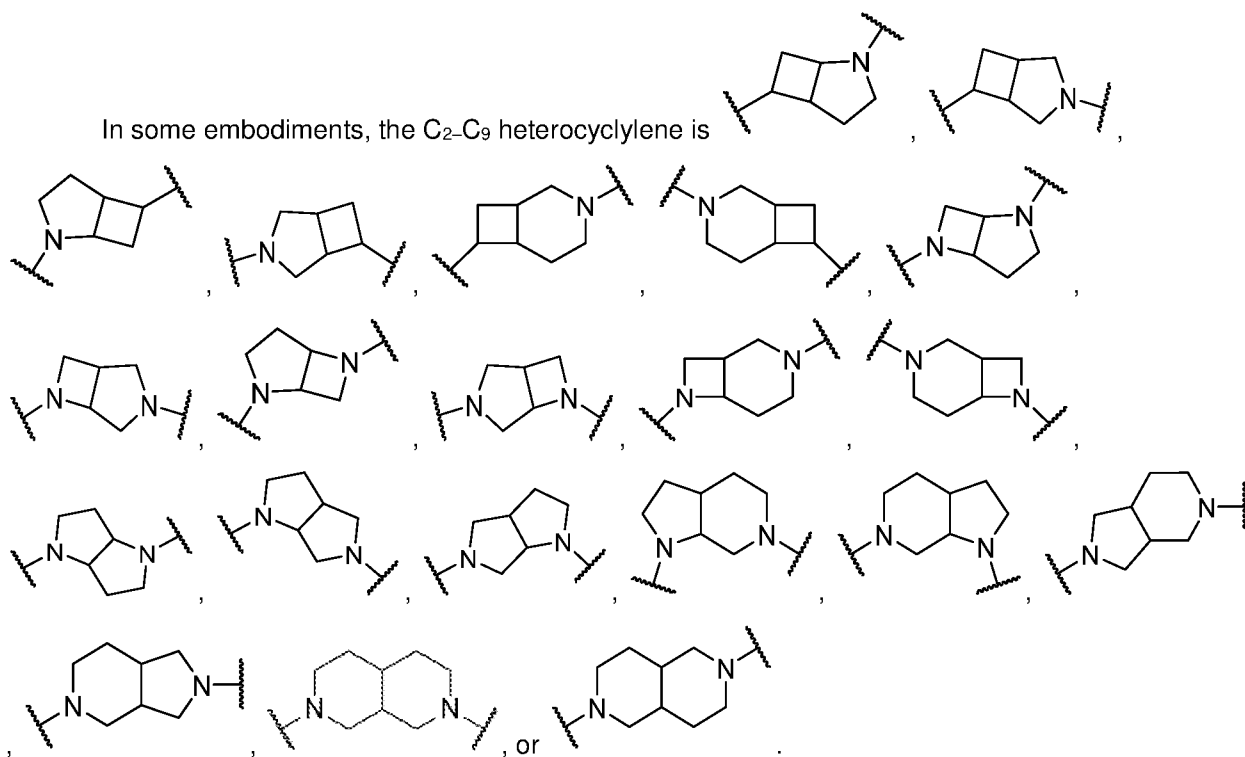


In some embodiments, the C₂-C₉ heterocyclylene is



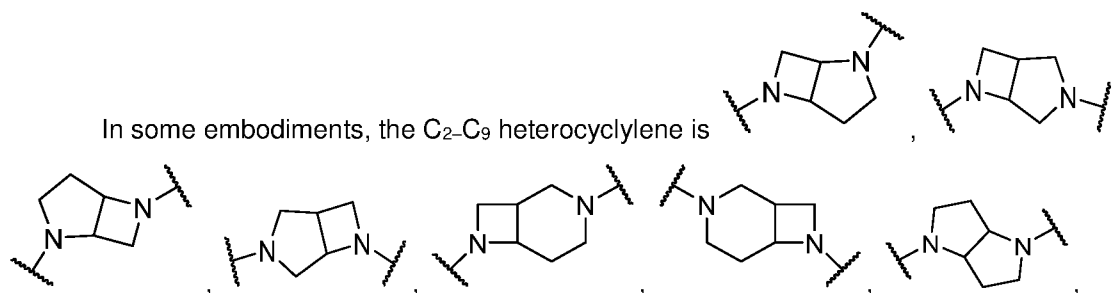
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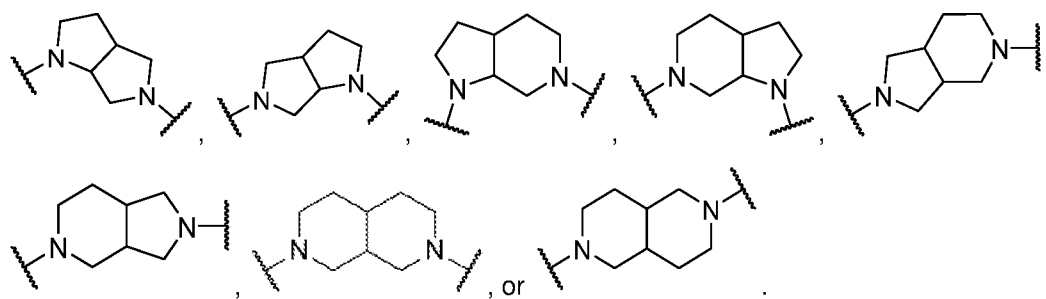
In some embodiments, the C₂-C₉ heterocyclylene is



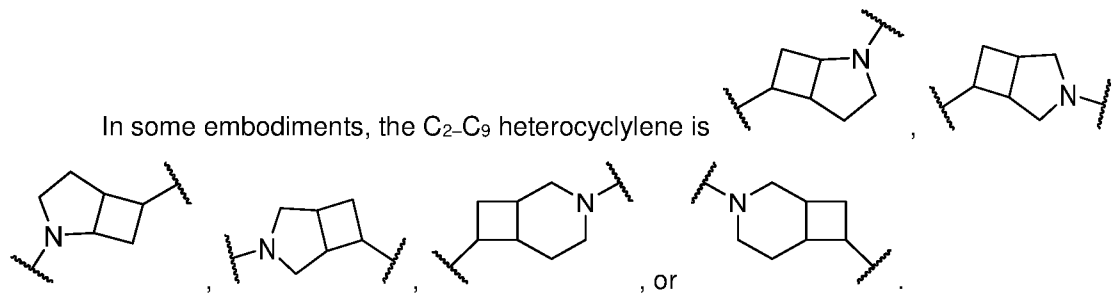
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In some embodiments, the C₂-C₉ heterocyclylene is



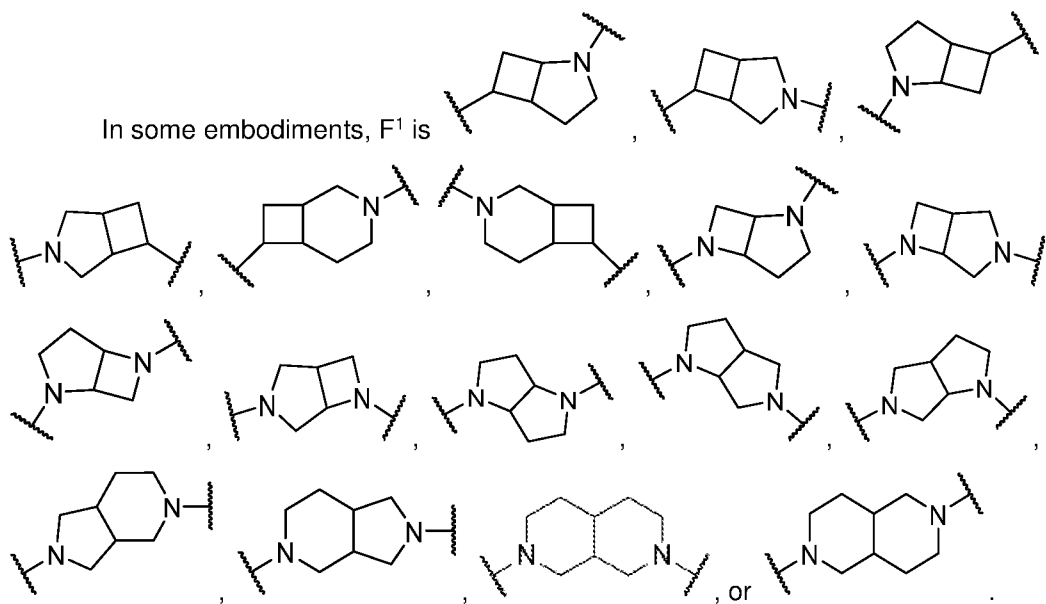


In some embodiments, the C₂-C₉ heterocyclene is

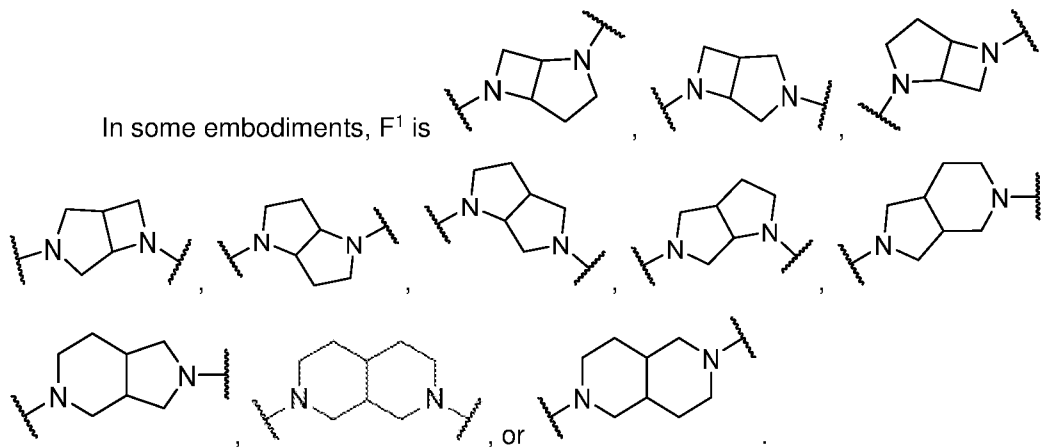


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In some embodiments, F¹ is

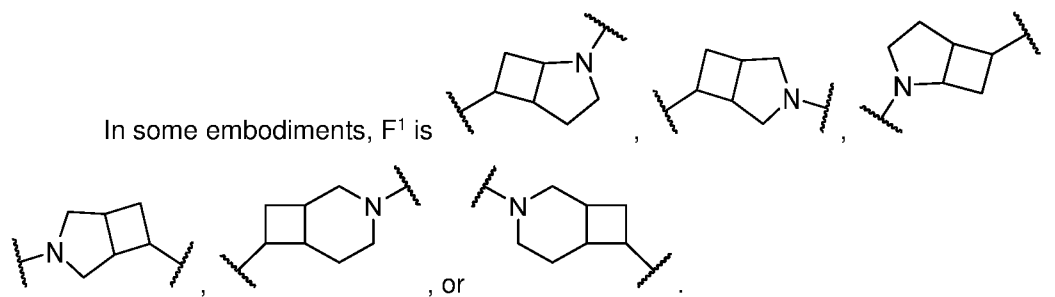


In some embodiments, F¹ is

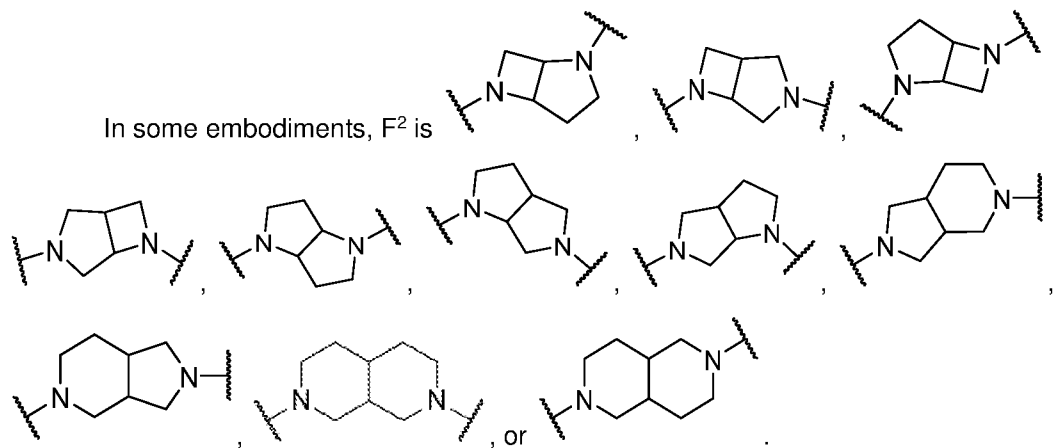


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In some embodiments, F¹ is

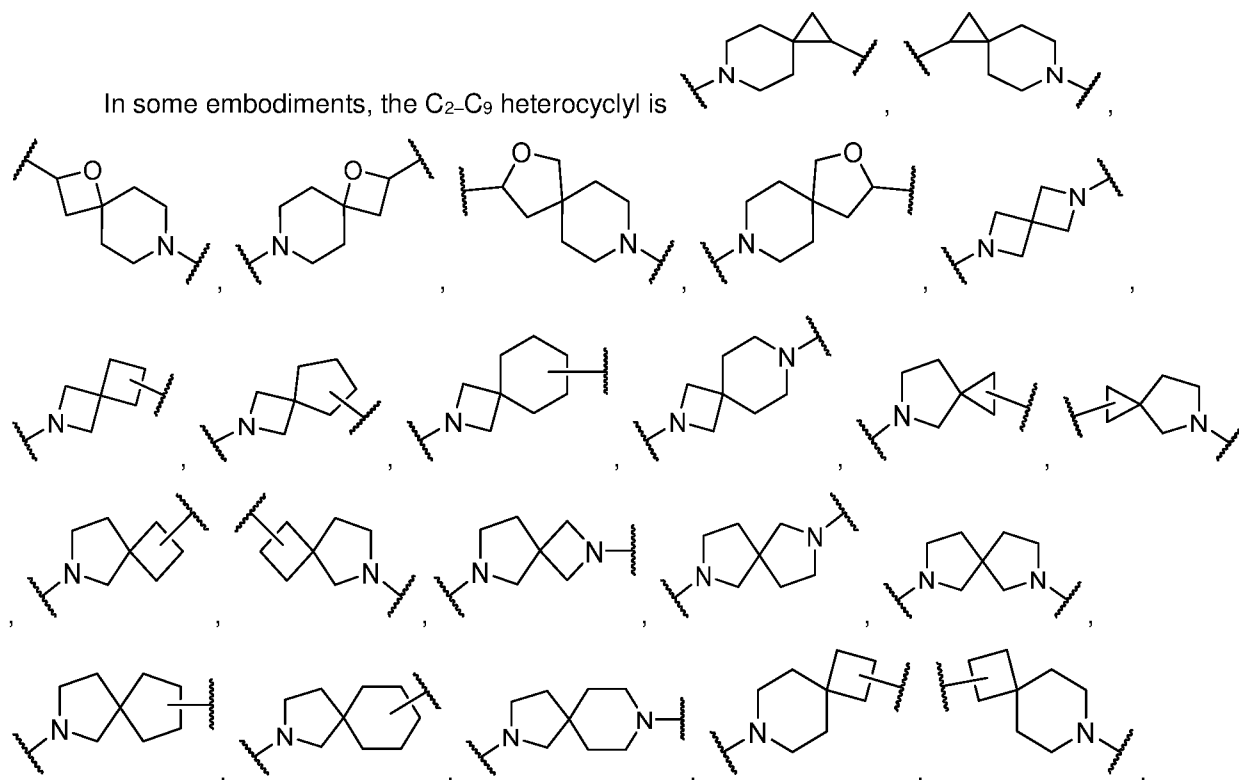


In some embodiments, F² is

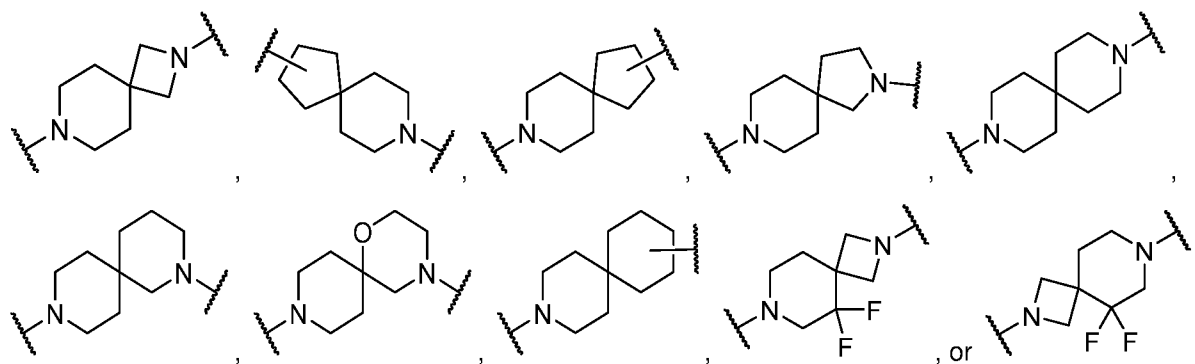


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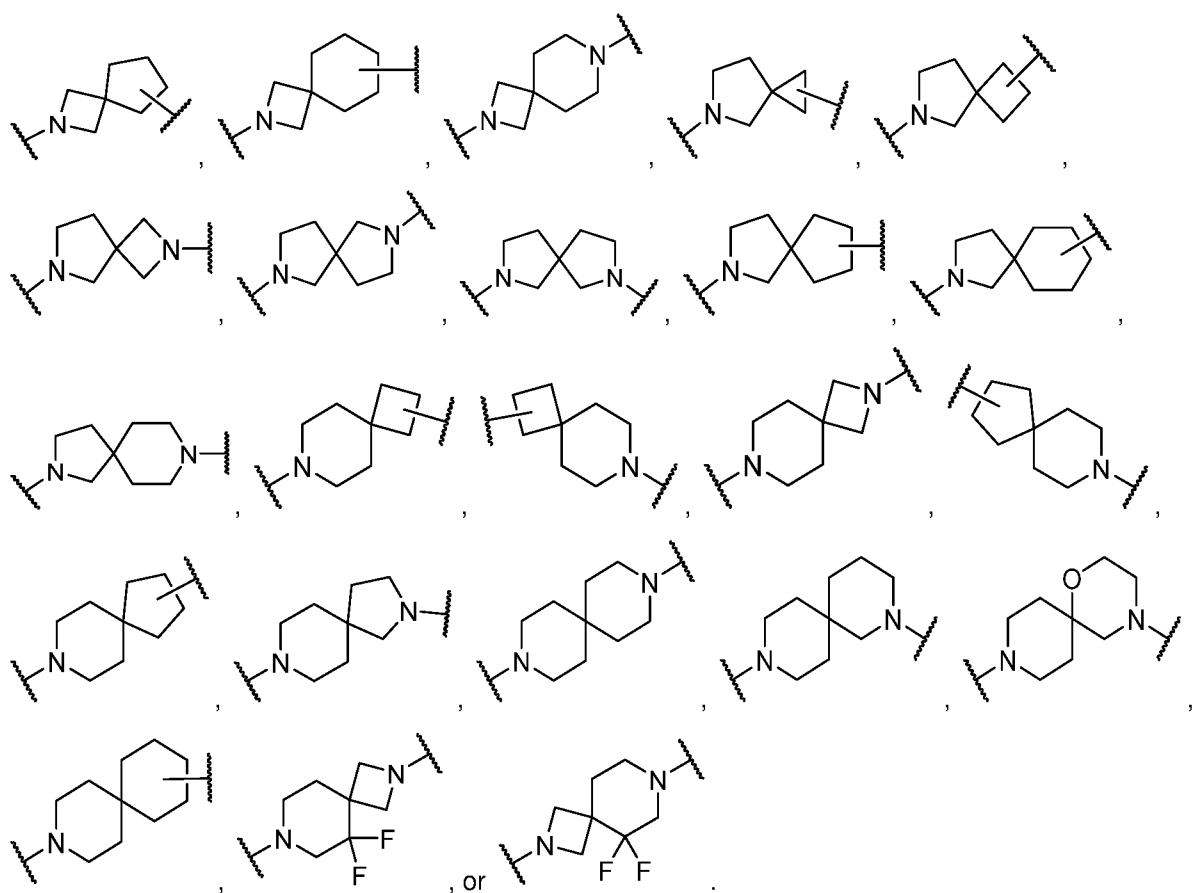
In some embodiments, the C₂-C₉ heterocyclyl is



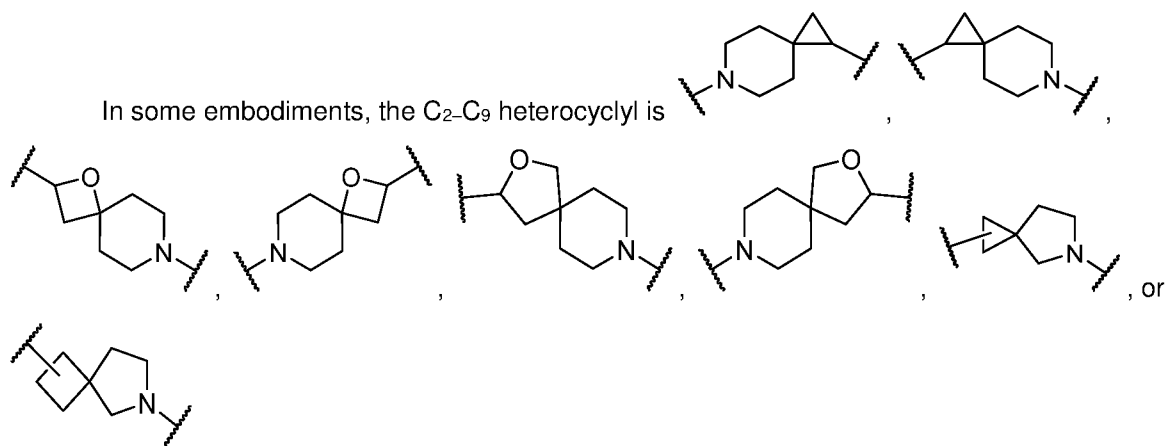
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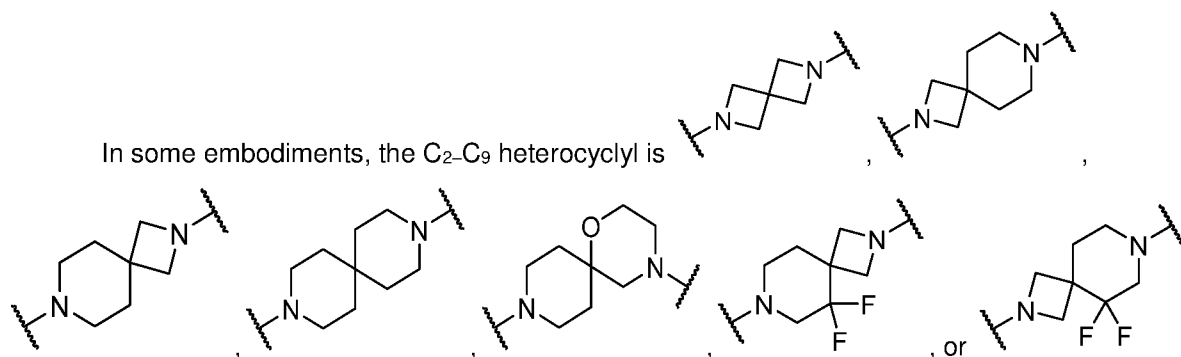
In some embodiments, the C₂-C₉ heterocyclyl is



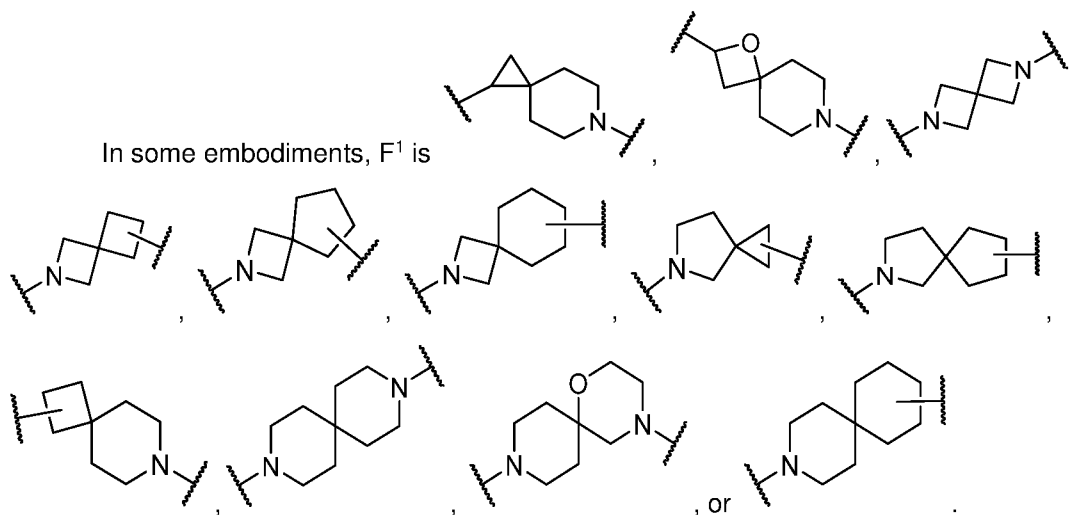
In some embodiments, the C₂-C₉ heterocyclyl is



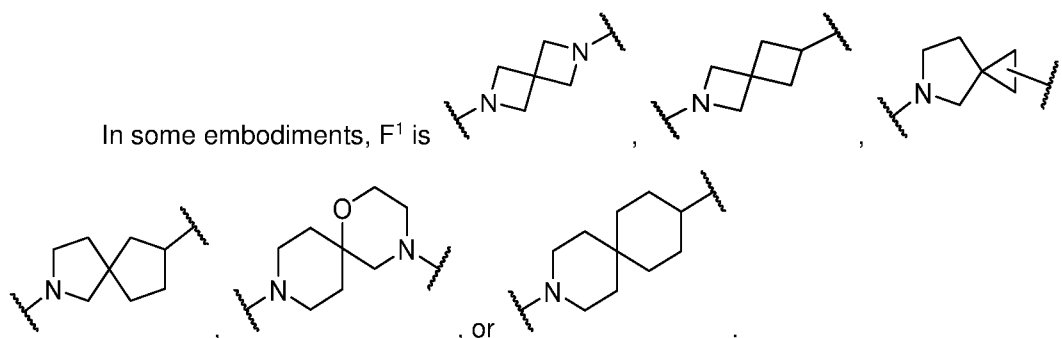
In some embodiments, the C₂-C₉ heterocyclyl is



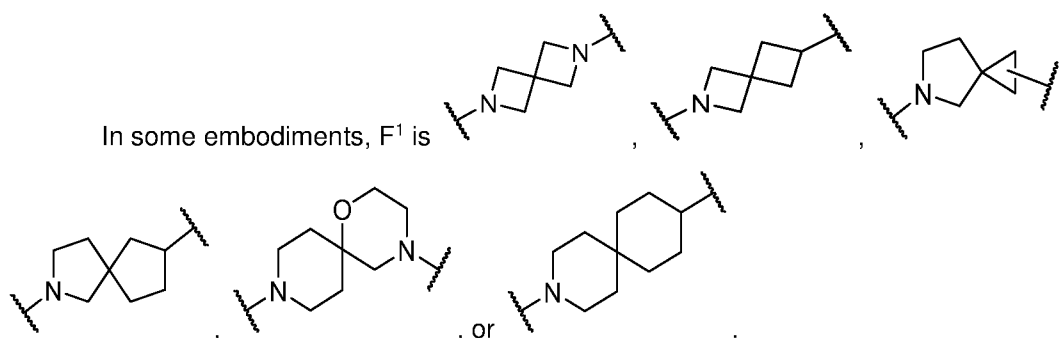
In some embodiments, F¹ is



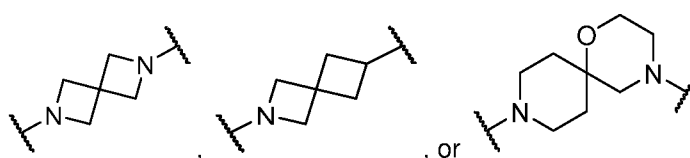
In some embodiments, F¹ is



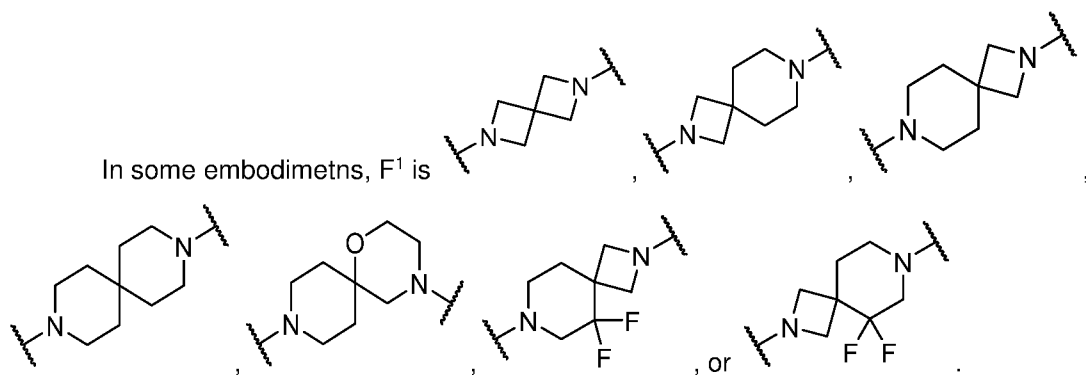
In some embodiments, F¹ is



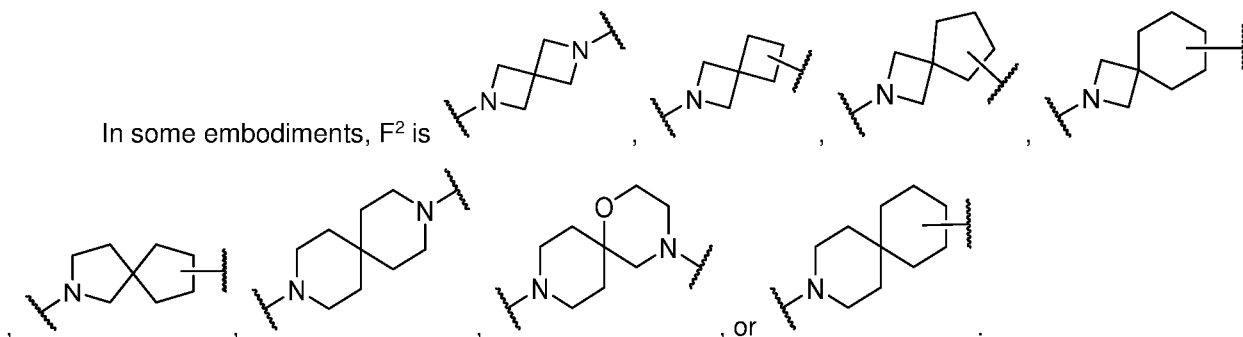
In some embodiments, F¹ is



In some embodiments, F¹ is

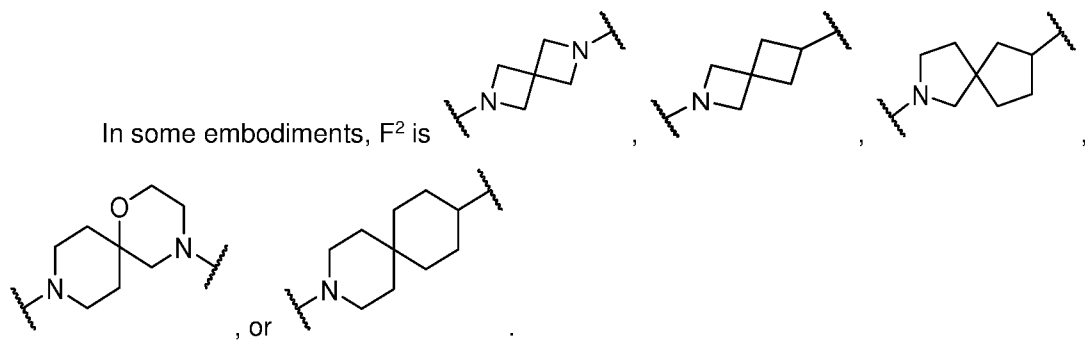


In some embodiments, F² is

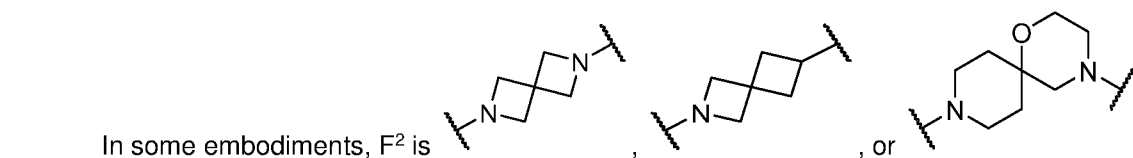


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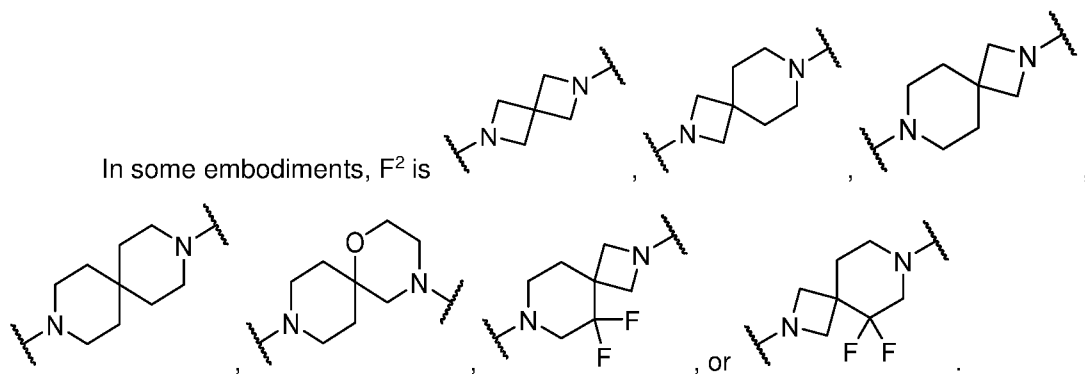
In some embodiments, F² is



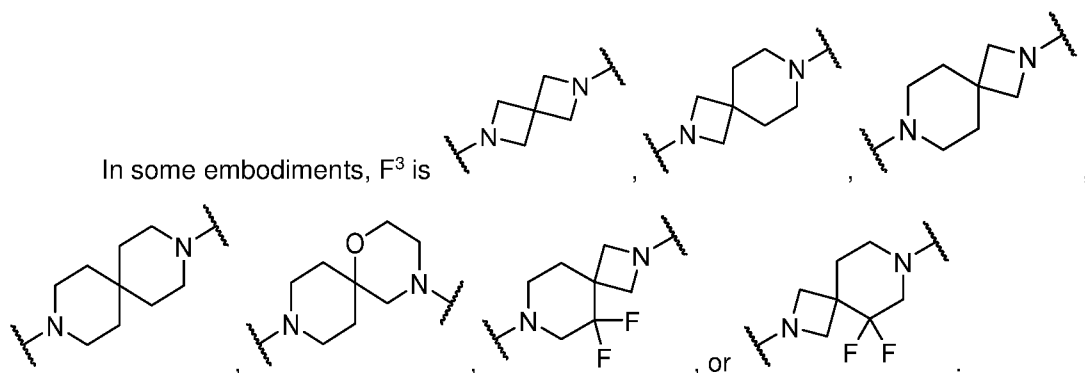
In some embodiments, F² is



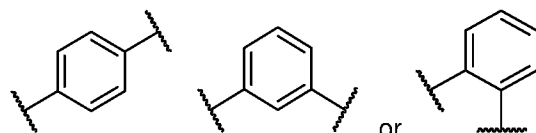
In some embodiments, F² is



In some embodiments, F^3 is



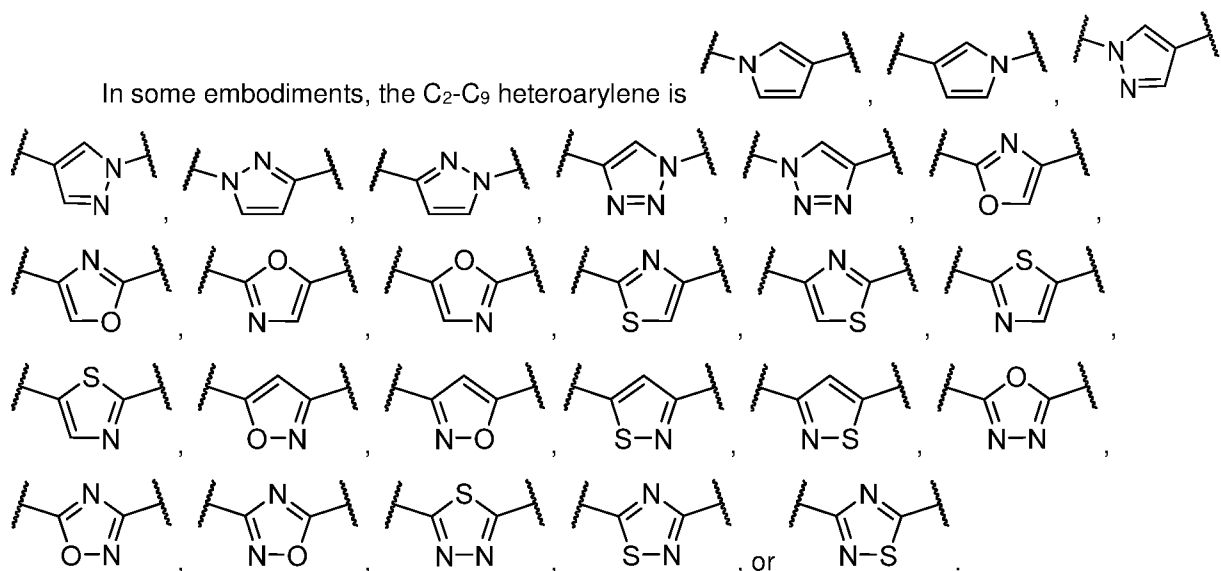
In some embodiments, each of F^1 , F^2 , or F^3 is, independently, optionally substituted C_6 - C_{10} arylene.



5 In some embodiments, the C_6 - C_{10} arylene is

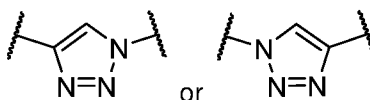
In some embodiments, each of F^1 , F^2 , or F^3 is, independently, optionally substituted C_2 - C_9 heteroarylene.

In some embodiments, the C_2 - C_9 heteroarylene is



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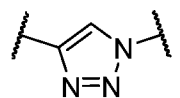
In some embodiments, F^2 is



or

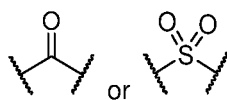
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In some embodiments, F^2 is



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In some embodiments, C^3 is



or

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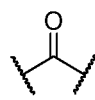
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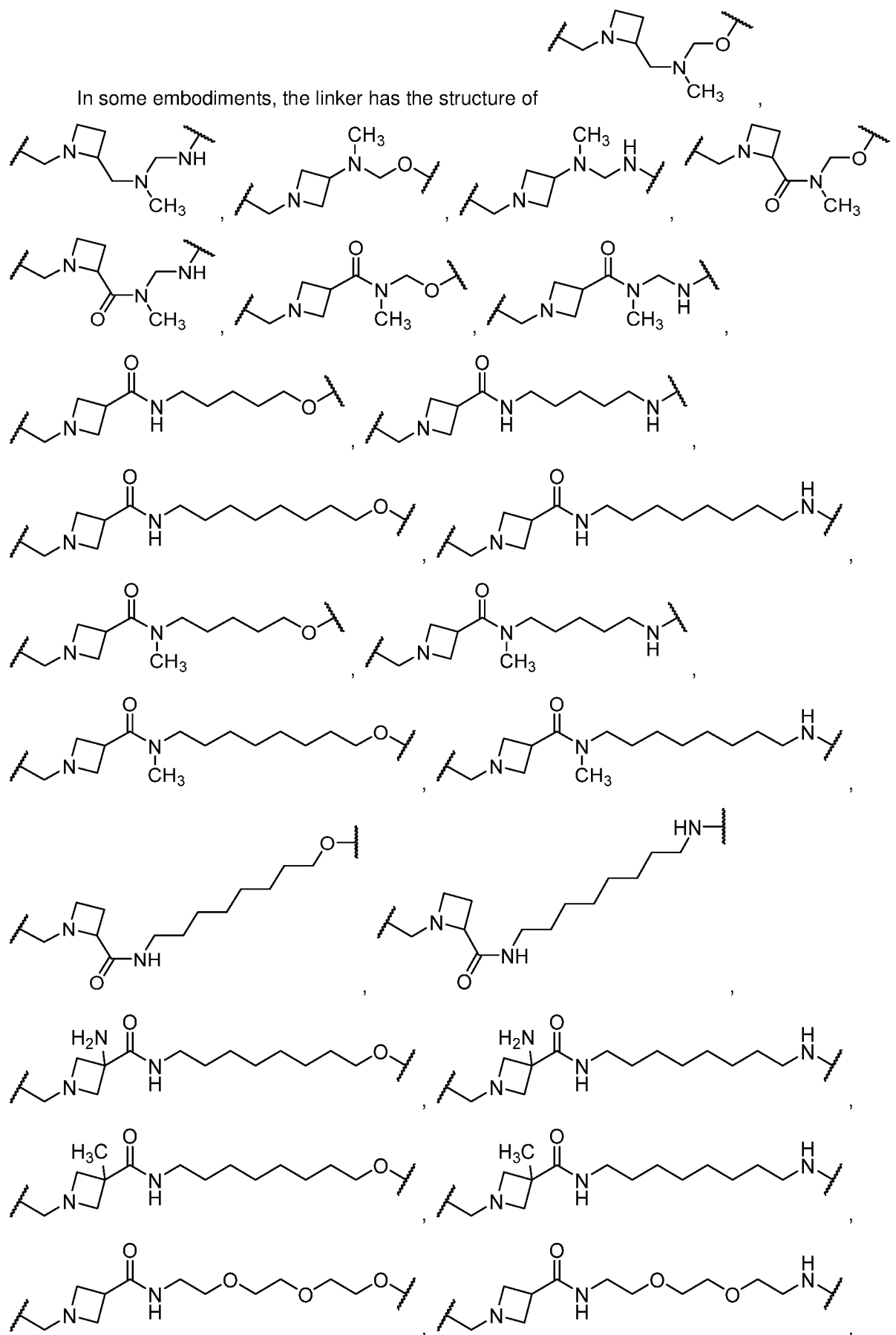
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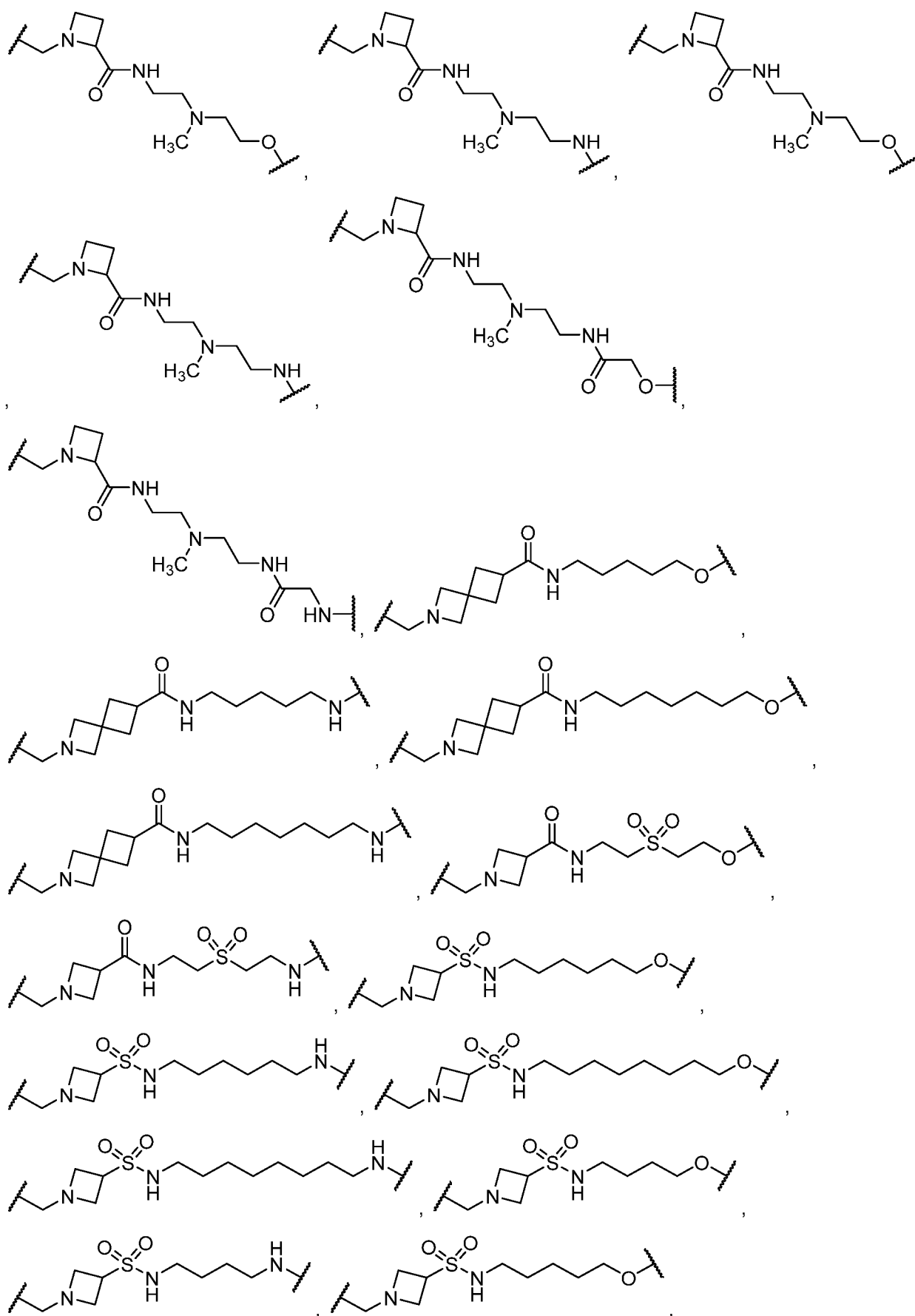
In some embodiments, C^3 is

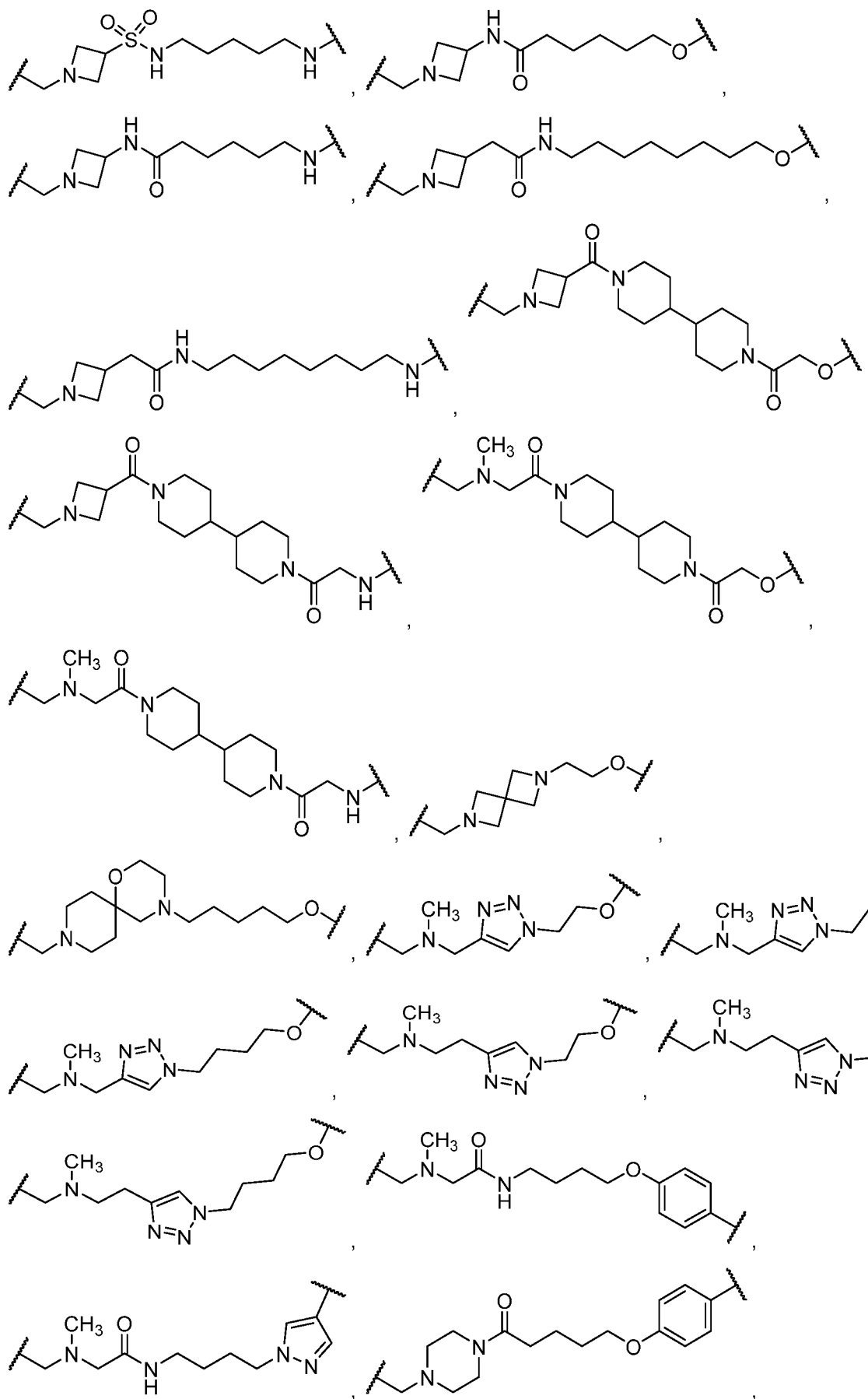


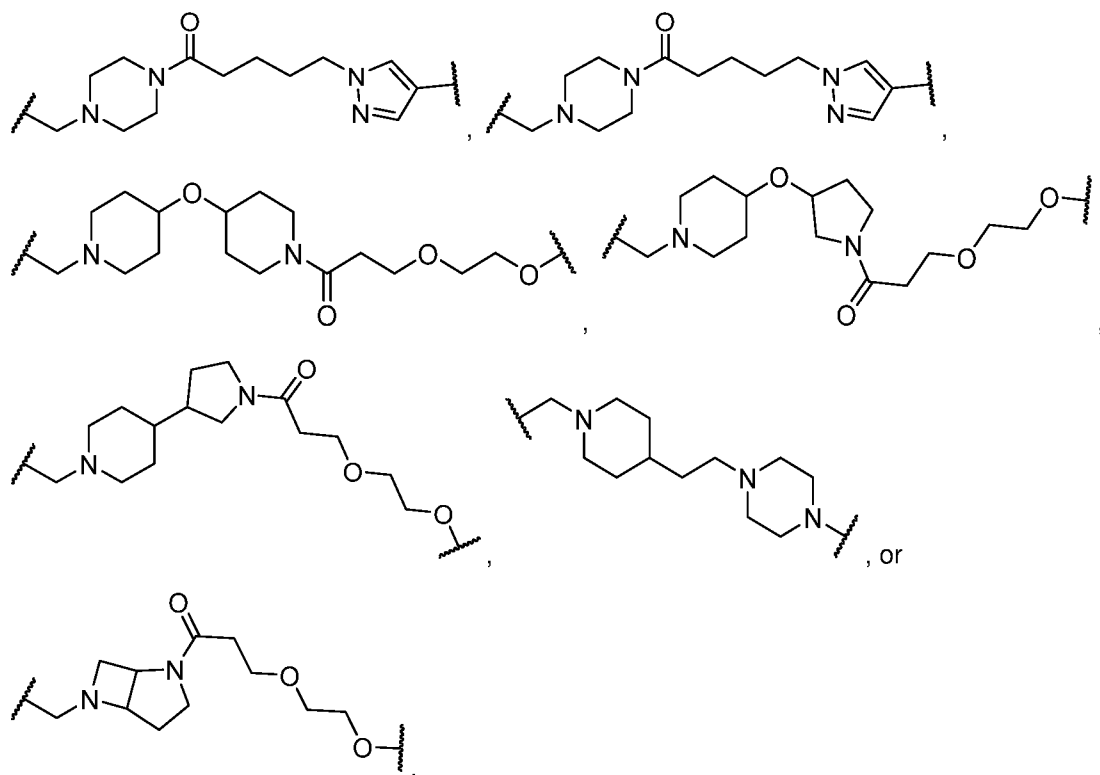
In some embodiments, m is 1. In some embodiments, p is 1.

In some embodiments, the linker has the structure of

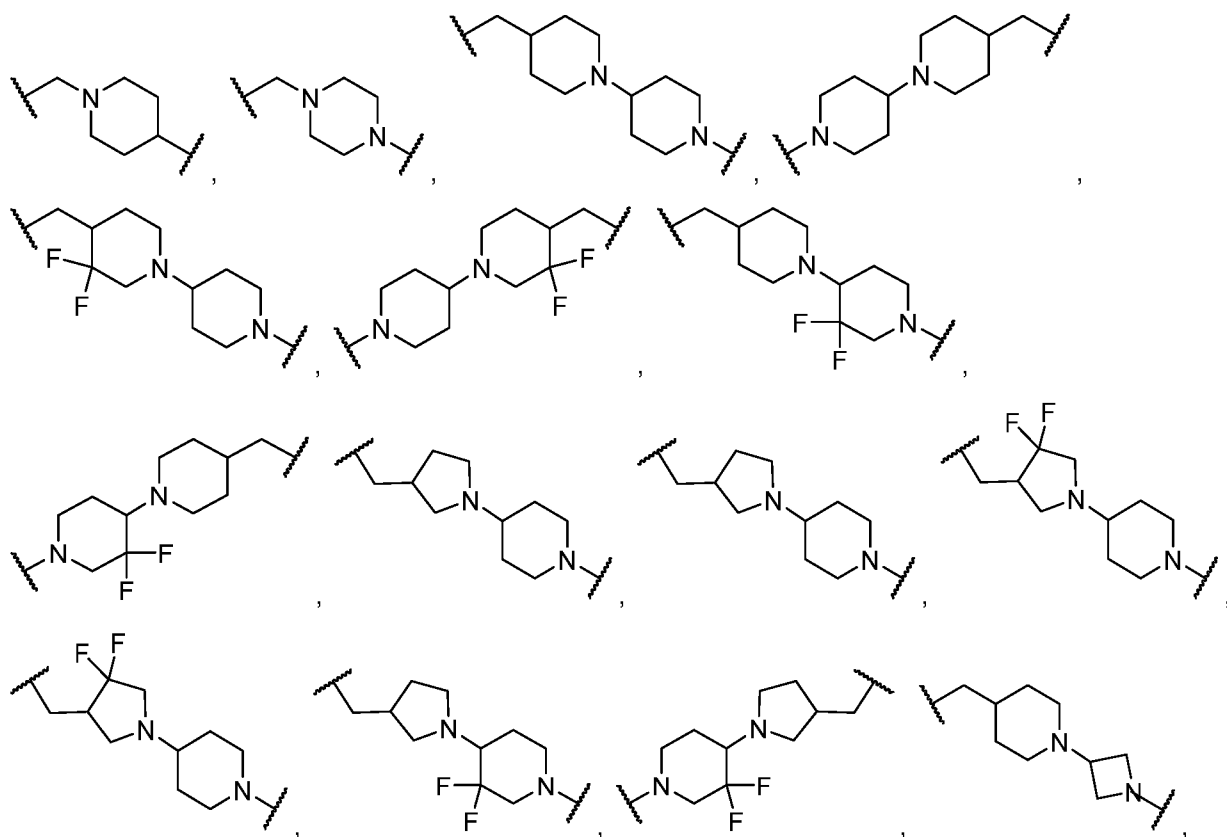
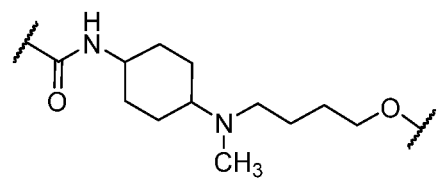




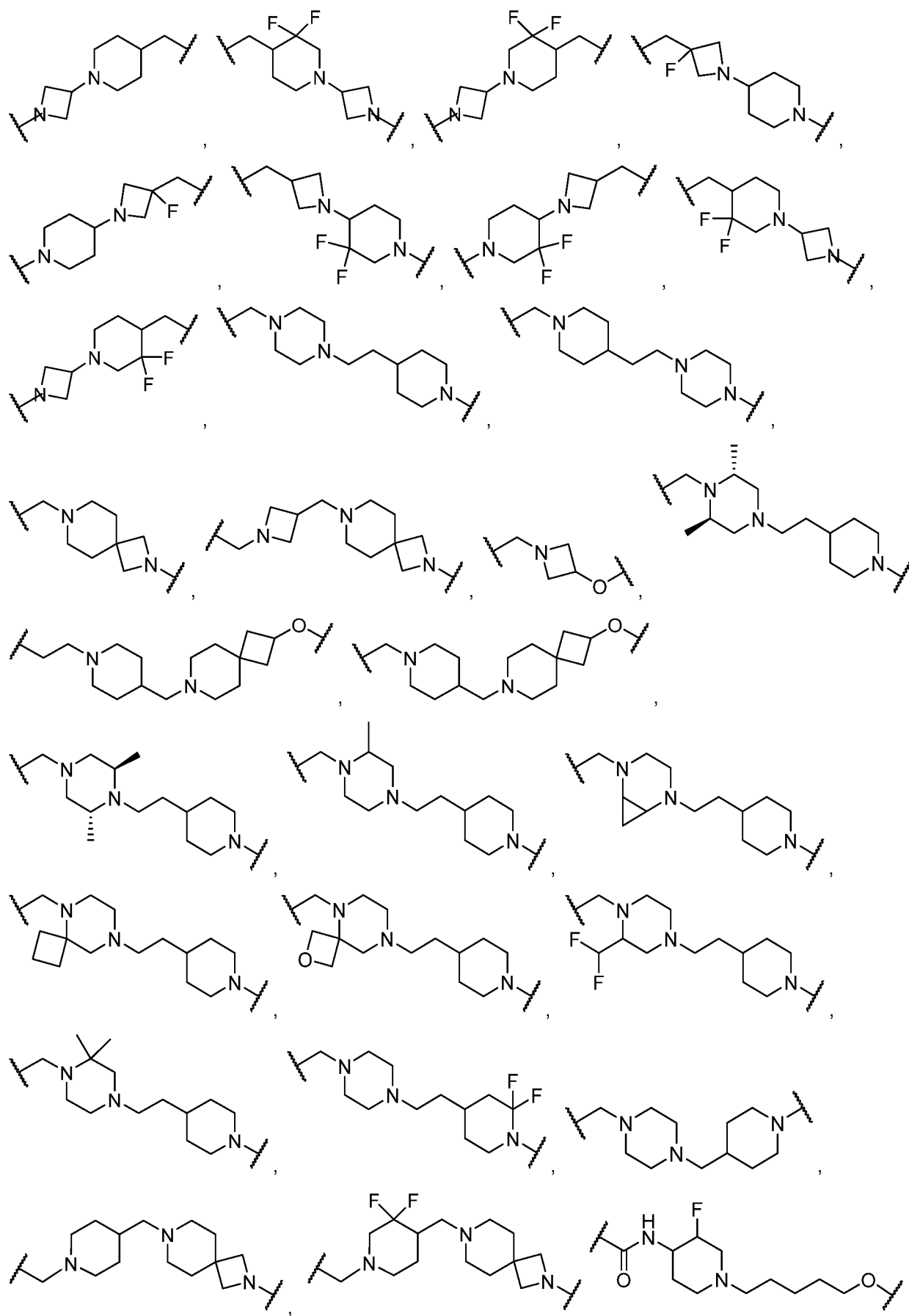


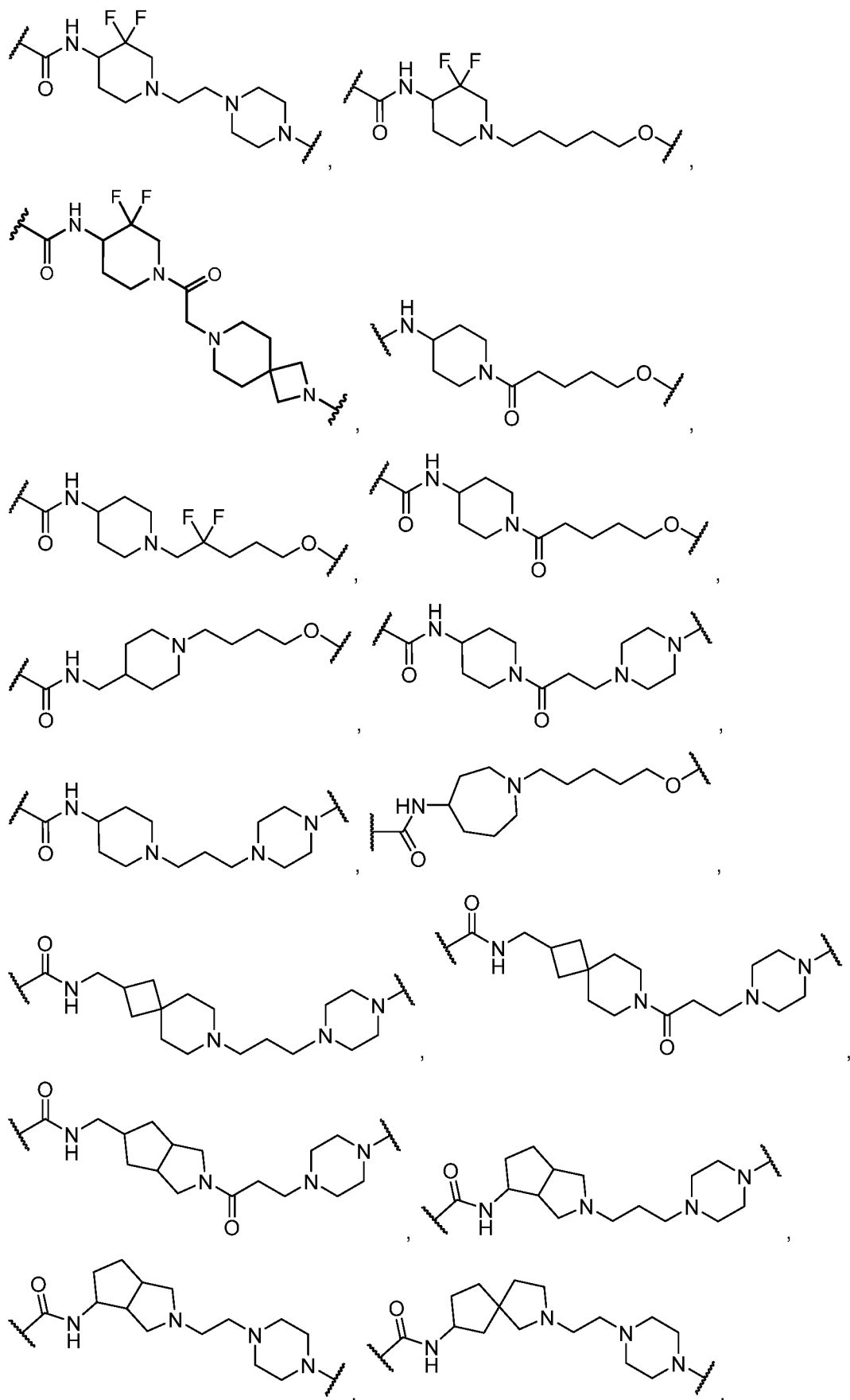


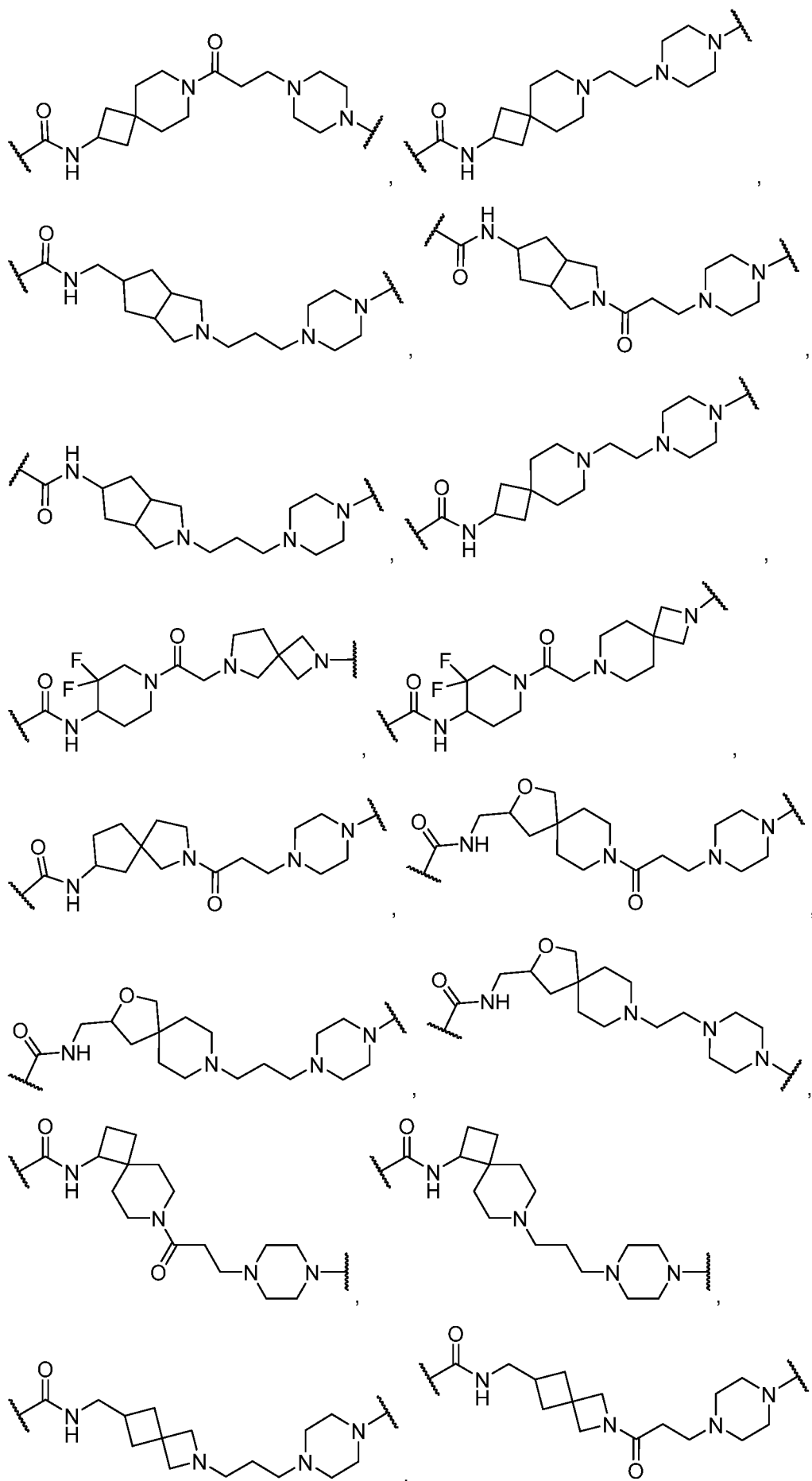
5 In some embodiments, the linker has the structure of

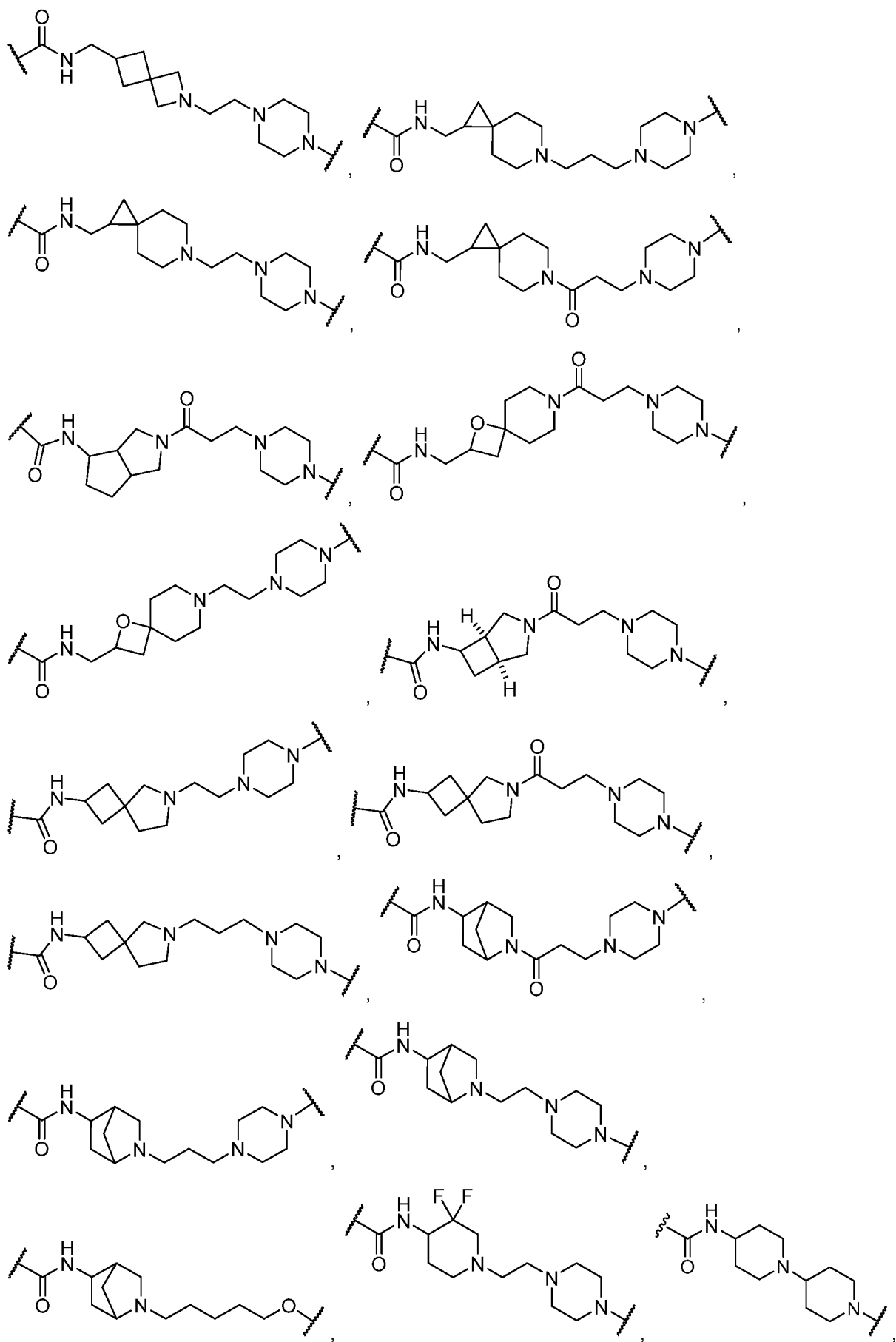


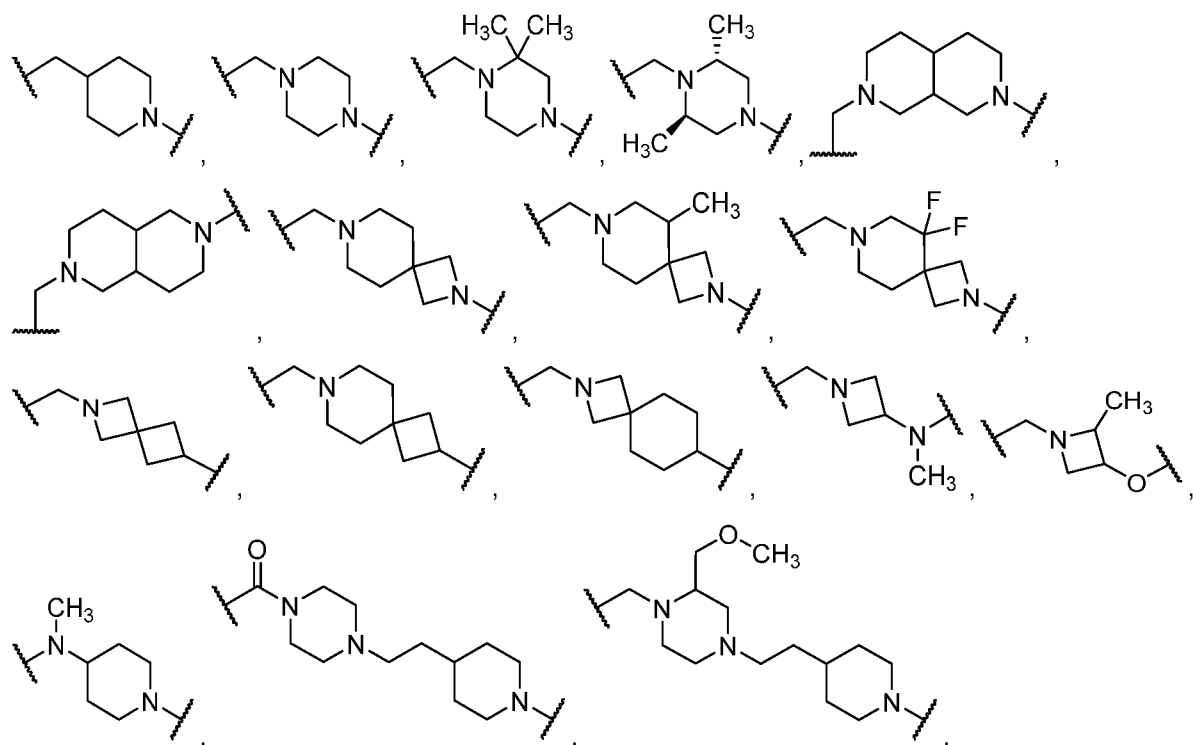
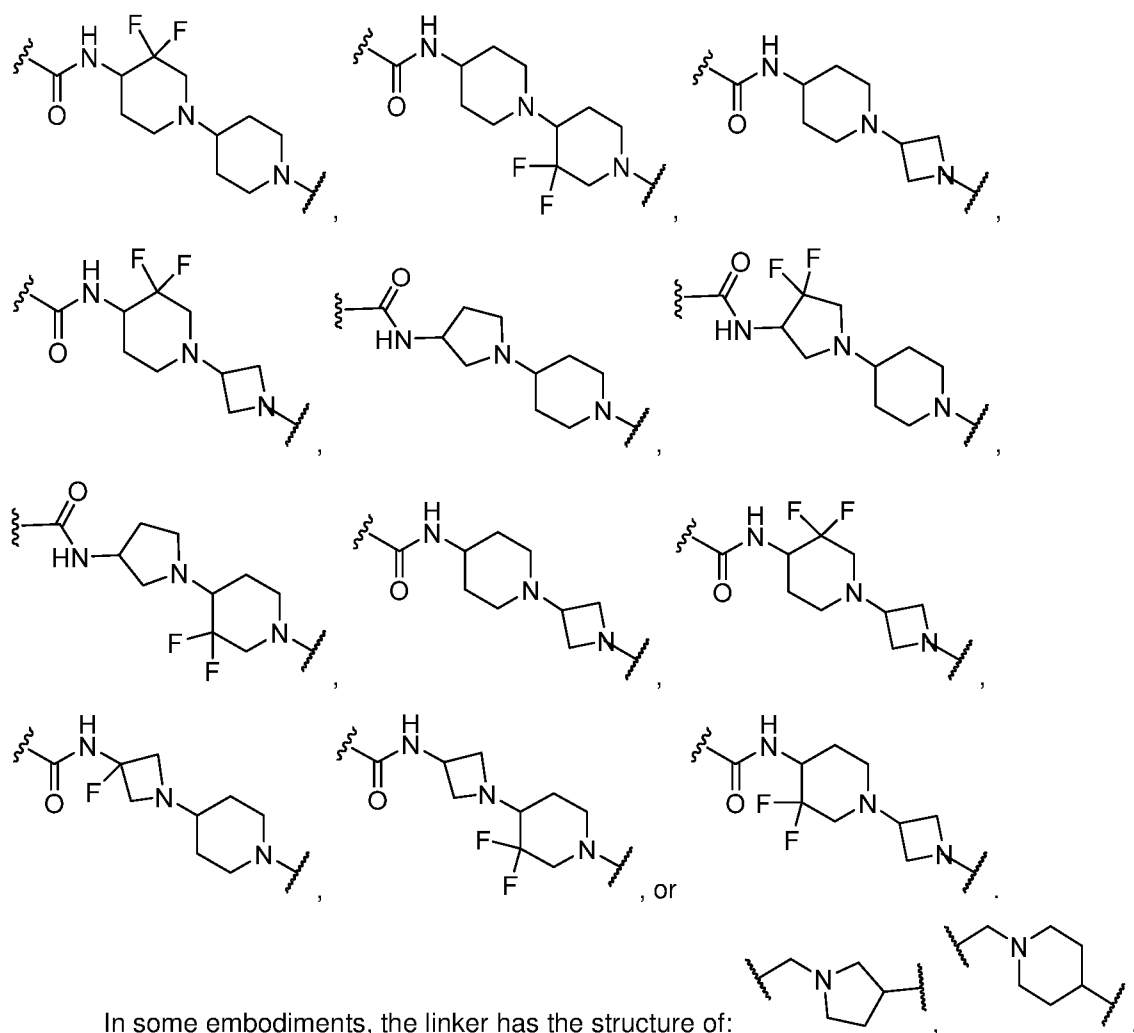
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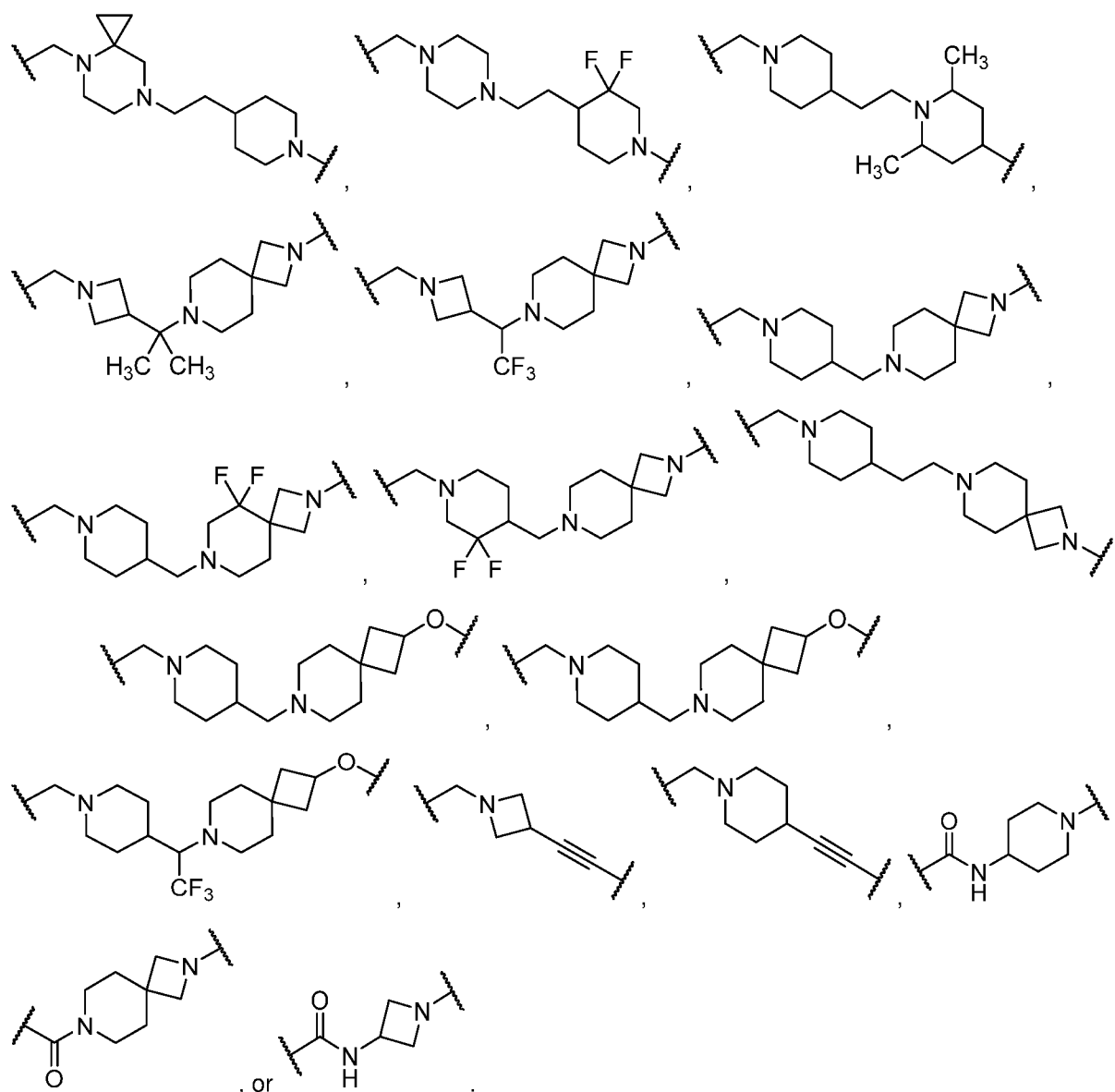












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In some embodiments, the linker is absent.

In some embodiments, the linker is optionally substituted C_3 - C_{10} carbocyclylene, optionally substituted C_{2-10} heterocyclylene, optionally substituted C_6 - C_{10} arylene, or optionally substituted C_2 - C_9 heteroarylene.

In some embodiments, the linker is optionally substituted C_3 - C_{10} carbocyclylene or optionally substituted C_{2-10} heterocyclylene. In some embodiments, the linker is optionally substituted C_6 - C_{10} arylene or optionally substituted C_2 - C_9 heteroarylene.

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In some embodiments, the linker is optionally substituted C_{2-10} heterocyclylene.

In some embodiments, the C_2 - C_9 heterocyclylene is monocyclic. In some embodiments, the C_2 - C_9 heterocyclylene is polycyclic.

In some embodiments, the C_2 - C_9 heterocyclylene is bicyclic.

In some embodiments, the C_2 - C_9 heterocyclylene is bridged. In some embodiments, the C_2 - C_9 heterocyclylene is fused. In some embodiments, the C_2 - C_9 heterocyclylene is spirocyclic.

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In some embodiments, the linker has the structure of 

In some embodiments, the linker has the structure of , , , or .

In some embodiments, the compound has the structure of any one of compounds D1-D15 in Table 2A, or a pharmaceutically acceptable salt thereof. In some embodiments, the compound has the structure of any one of compounds D16-D90 in Table 2B, or a pharmaceutically acceptable salt thereof. In some embodiments, the compound has the structure of any one of compounds D91-D220 in Table 2C, or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound has the structure of any one of compounds D3, D10, D12, D13, and D15 in Table 2A, or a pharmaceutically acceptable salt thereof. In some embodiments, the compound has the structure of any one of compounds D16-D29, D33, D35-D43, D46, D49, D50, D57, D60, D65, D66, D70, D72-D75, D77-D79, D83-D87, D89, and D90 in Table 2B, or a pharmaceutically acceptable salt thereof. In some embodiments, the compound has the structure of any one of compounds D96-D101-D123-D136, D138-D141, D144, D146, D147, D149-D170, and D173-D219 in Table 2C, or a pharmaceutically acceptable salt thereof.

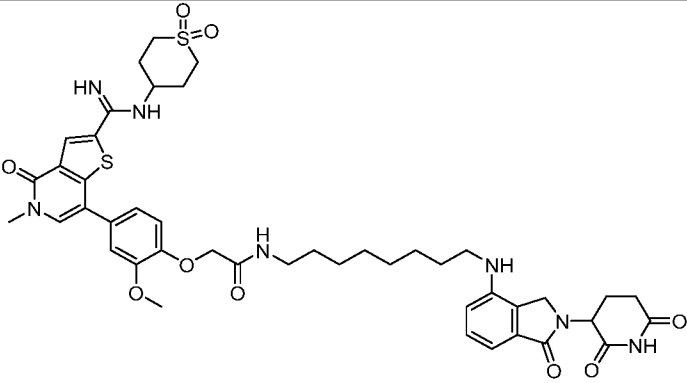
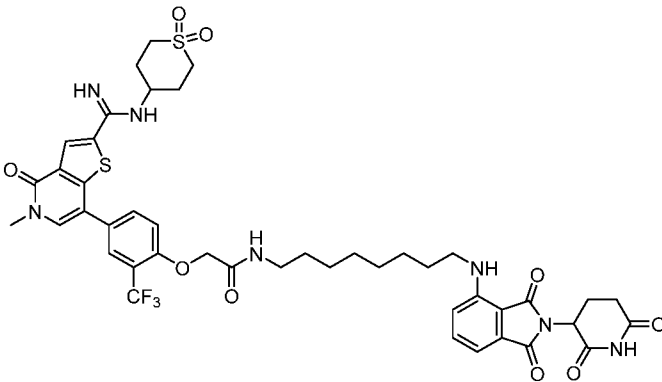
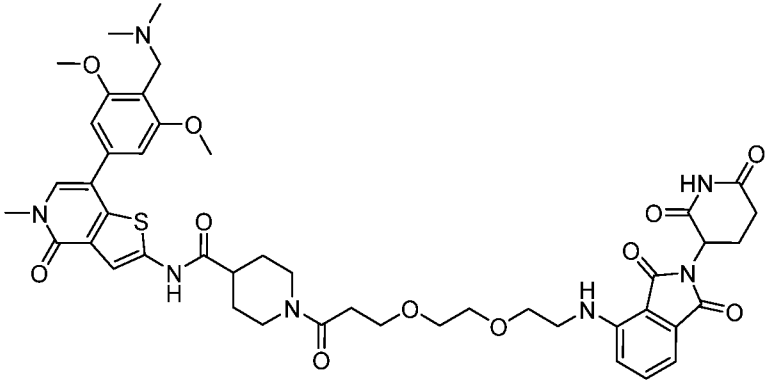
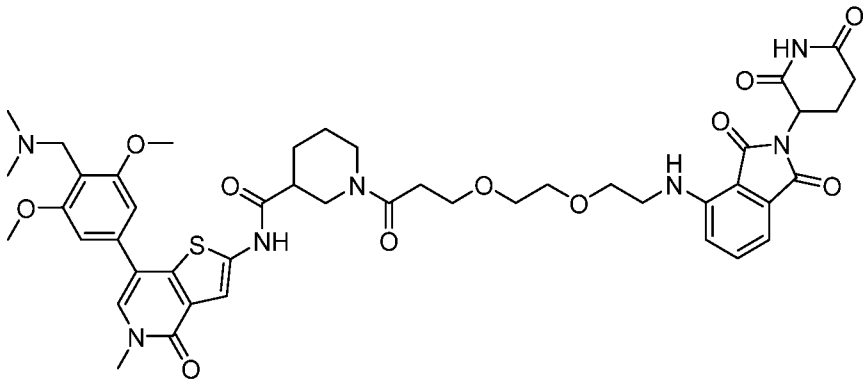
In an aspect, the disclosure features a compound having the structure of any one of compounds D1-D15 in Table 2A, or a pharmaceutically acceptable salt thereof.

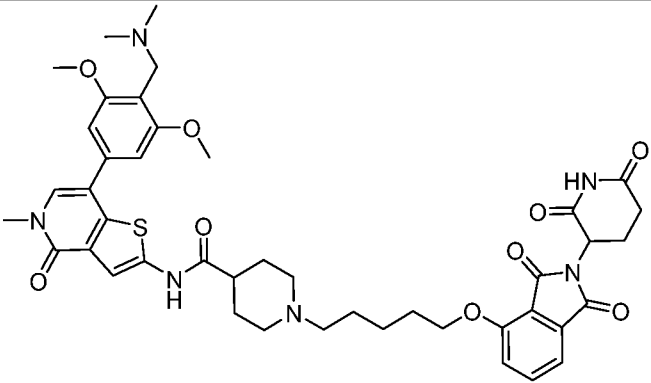
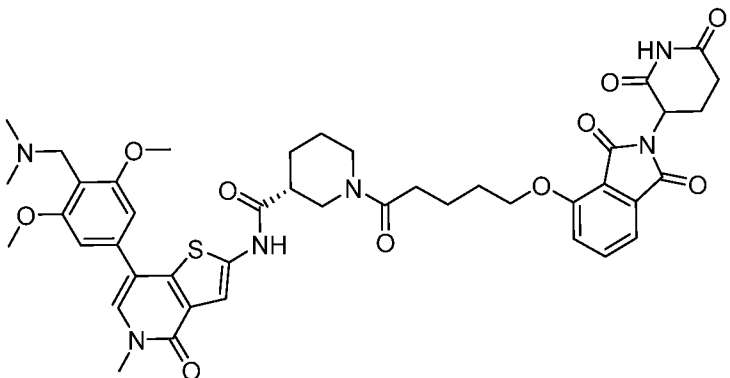
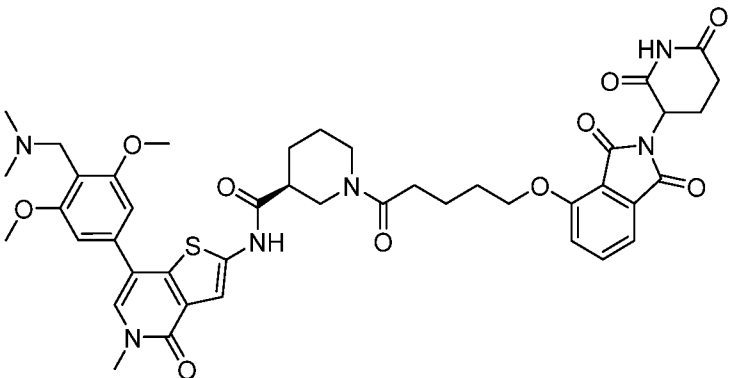
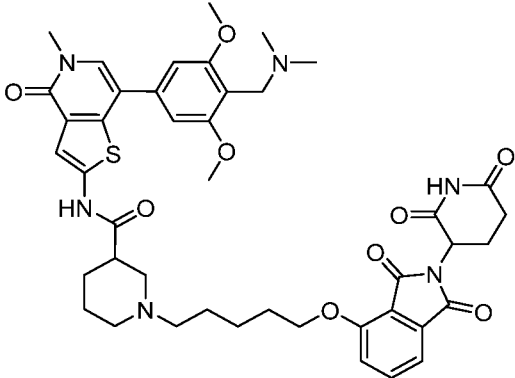
In an aspect, the disclosure features a compound having the structure of any one of compounds D16-D90 in Table 2B, or a pharmaceutically acceptable salt thereof.

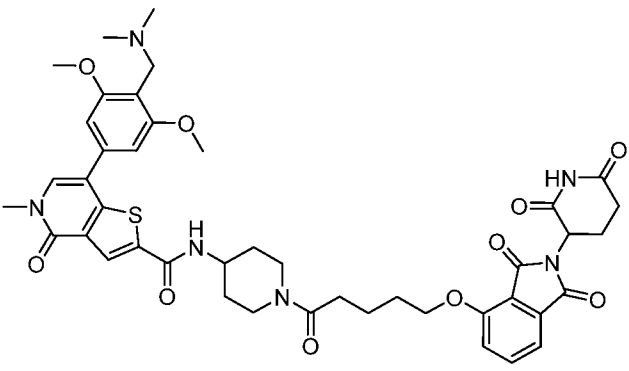
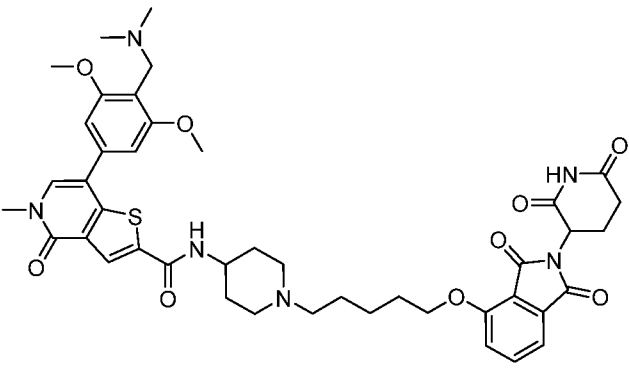
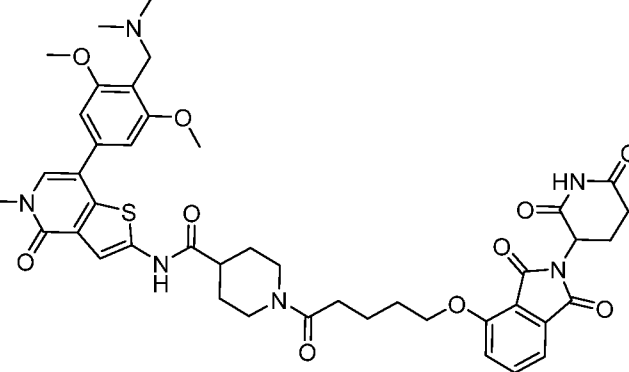
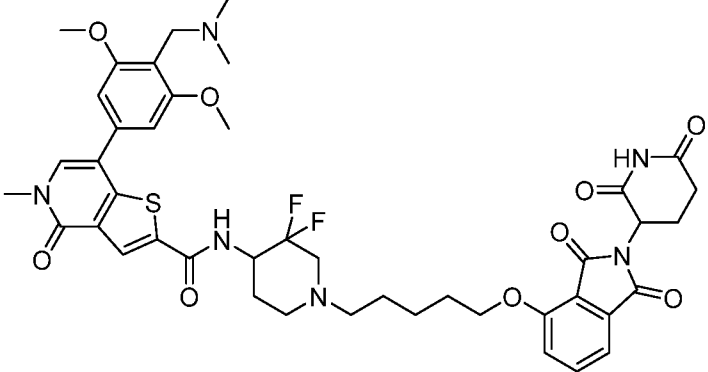
In an aspect, the disclosure features a compound having the structure of any one of compounds D91-D220 in Table 2C, or a pharmaceutically acceptable salt thereof.

Table 2A. Compounds D1-D15 of the Disclosure

Compound No.	Structure
D1	

Compound No.	Structure
D2	 Chemical structure of compound D2: A thienopyridine core substituted with a methyl group at the 4-position, a 1-methyl-1H-thiazol-2-yl group at the 5-position, and a 4-methoxyphenyl group at the 6-position. The 4-methoxyphenyl group is linked via an ester bond to a 7-((8-oxo-8,9-dihydro-1H-benz[5,6]cyclohepta[1,2-b]pyridin-3-yl)amino)heptan-1-yl group. The thiazol-2-yl group is linked via an imine bond to a 1,4-dithiane-1,1-dioxide group.
D3	 Chemical structure of compound D3: A thienopyridine core substituted with a methyl group at the 4-position, a 1-methyl-1H-thiazol-2-yl group at the 5-position, and a 4-(trifluoromethyl)phenyl group at the 6-position. The 4-(trifluoromethyl)phenyl group is linked via an ester bond to a 7-((8-oxo-8,9-dihydro-1H-benz[5,6]cyclohepta[1,2-b]pyridin-3-yl)amino)heptan-1-yl group. The thiazol-2-yl group is linked via an imine bond to a 1,4-dithiane-1,1-dioxide group.
D4	 Chemical structure of compound D4: A thienopyridine core substituted with a methyl group at the 4-position, a 4-methoxy-2-(dimethylamino)phenyl group at the 5-position, and a 1-methyl-1H-thiazol-2-yl group at the 6-position. The 1-methyl-1H-thiazol-2-yl group is linked via an amide bond to a 4-((2-((8-oxo-8,9-dihydro-1H-benz[5,6]cyclohepta[1,2-b]pyridin-3-yl)amino)ethoxy)ethyl)pyrrolidine-1-carboxylate group.
D5	 Chemical structure of compound D5: A thienopyridine core substituted with a methyl group at the 4-position, a 4-methoxy-2-(dimethylamino)phenyl group at the 5-position, and a 1-methyl-1H-thiazol-2-yl group at the 6-position. The 1-methyl-1H-thiazol-2-yl group is linked via an amide bond to a 4-((2-((8-oxo-8,9-dihydro-1H-benz[5,6]cyclohepta[1,2-b]pyridin-3-yl)amino)ethoxy)ethyl)pyrrolidine-1-carboxylate group.

Compound No.	Structure
D6	 Chemical structure of compound D6: A thienopyridine core substituted with a 3,4,5-trimethoxybenzyl group and a dimethylaminomethyl group. The thienopyridine is linked via an amide bond to a piperidine ring, which is further connected through a hexamethylene chain to an indole-1,3-dione moiety.
D7	 Chemical structure of compound D7: A thienopyridine core substituted with a 3,4,5-trimethoxybenzyl group and a dimethylaminomethyl group. The thienopyridine is linked via an amide bond to a piperidine ring, which is further connected through a hexamethylene chain to an indole-1,3-dione moiety. The stereochemistry at the amide bond is (S).
D8	 Chemical structure of compound D8: A thienopyridine core substituted with a 3,4,5-trimethoxybenzyl group and a dimethylaminomethyl group. The thienopyridine is linked via an amide bond to a piperidine ring, which is further connected through a hexamethylene chain to an indole-1,3-dione moiety. The stereochemistry at the amide bond is (R).
D9	 Chemical structure of compound D9: A thienopyridine core substituted with a 3,4,5-trimethoxybenzyl group and a dimethylaminomethyl group. The thienopyridine is linked via an amide bond to a piperidine ring, which is further connected through a hexamethylene chain to an indole-1,3-dione moiety.

Compound No.	Structure
D10	 Chemical structure of compound D10: A thienopyridine core substituted with a 3,4,5-trimethoxybenzyl group and a methyl group. The thienopyridine is linked via an amide bond to a piperidine ring, which is further linked via an amide bond to a hexyl chain. The hexyl chain is connected via an ether linkage to a benzimidazole moiety.
D11	 Chemical structure of compound D11: A thienopyridine core substituted with a 3,4,5-trimethoxybenzyl group and a methyl group. The thienopyridine is linked via an amide bond to a piperidine ring, which is further linked via an amide bond to a hexyl chain. The hexyl chain is connected via an ether linkage to a benzimidazole moiety.
D12	 Chemical structure of compound D12: A thienopyridine core substituted with a 3,4,5-trimethoxybenzyl group and a methyl group. The thienopyridine is linked via an amide bond to a piperidine ring, which is further linked via an amide bond to a hexyl chain. The hexyl chain is connected via an ether linkage to a benzimidazole moiety.
D13	 Chemical structure of compound D13: A thienopyridine core substituted with a 3,4,5-trimethoxybenzyl group and a methyl group. The thienopyridine is linked via an amide bond to a piperidine ring, which is further linked via an amide bond to a hexyl chain. The hexyl chain is connected via an ether linkage to a benzimidazole moiety.

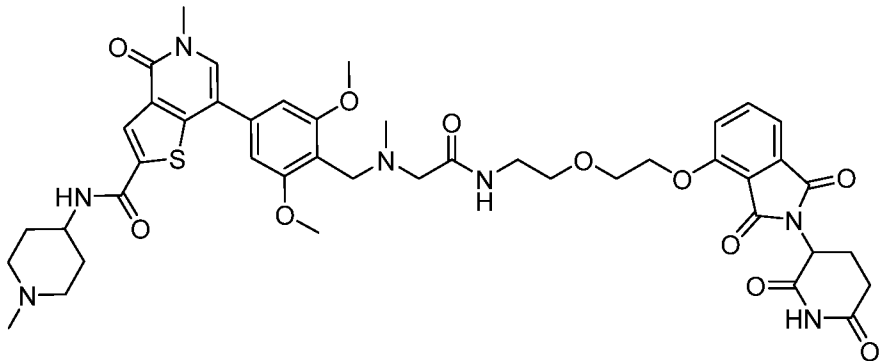
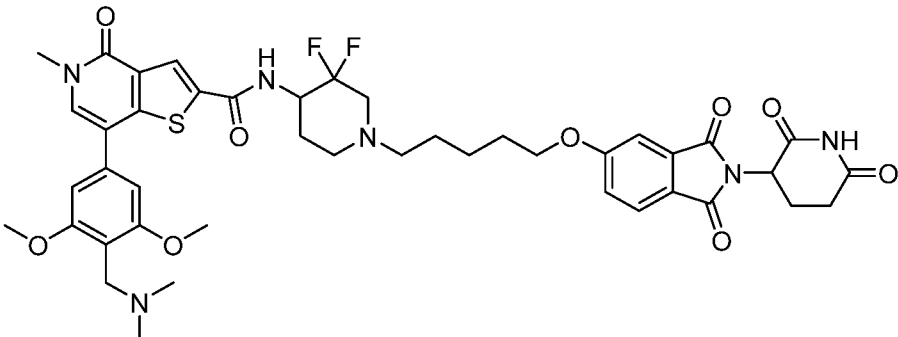
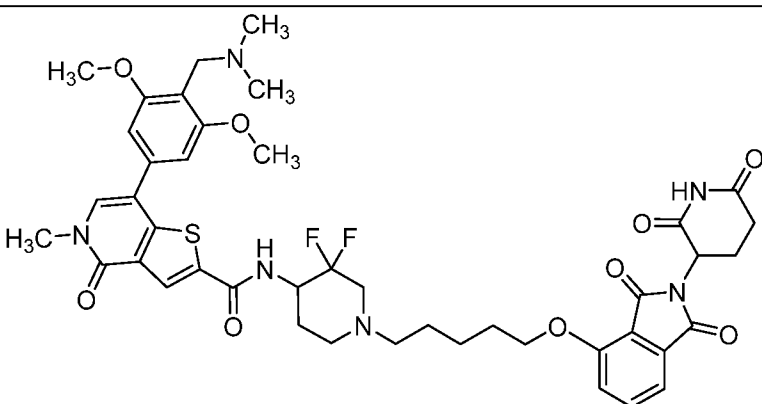
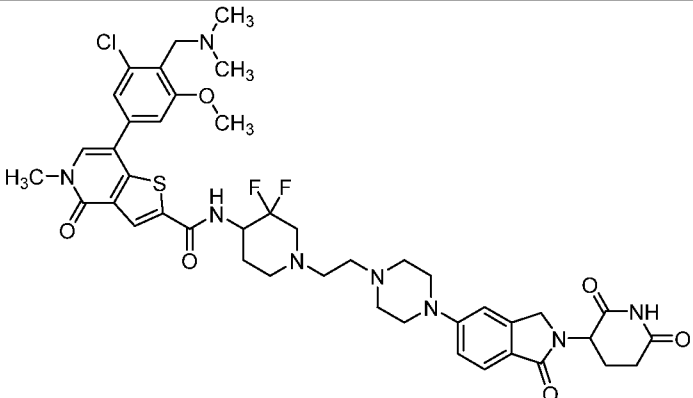
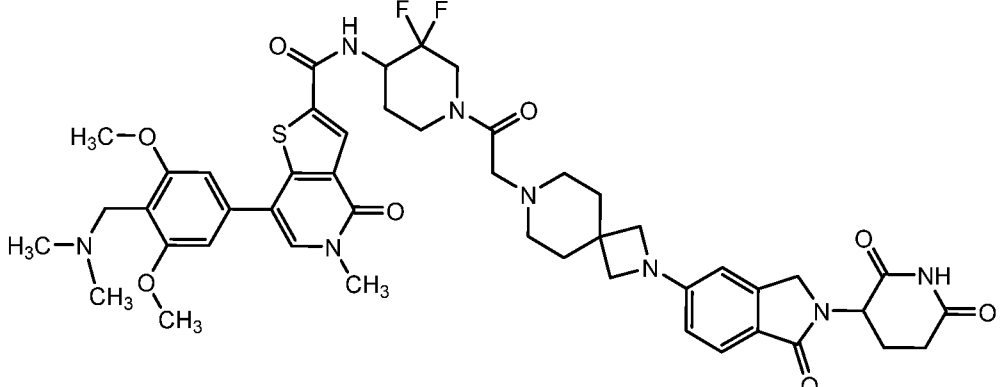
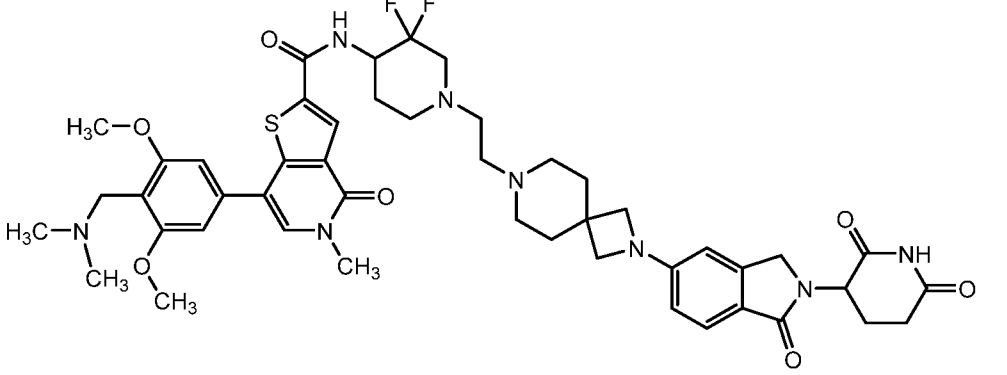
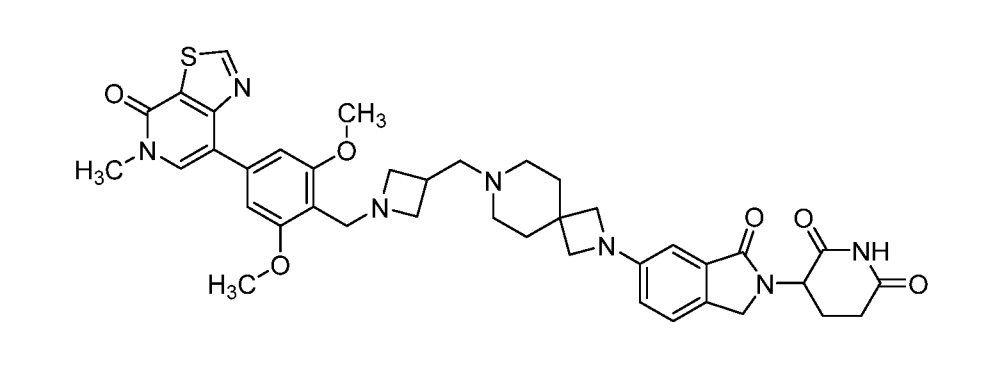
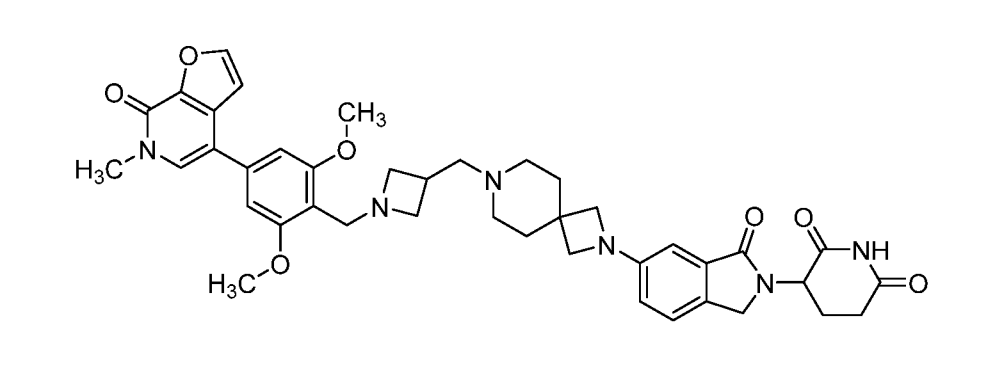
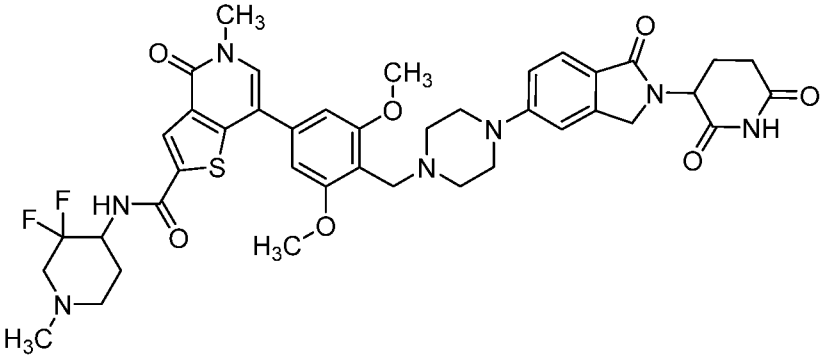
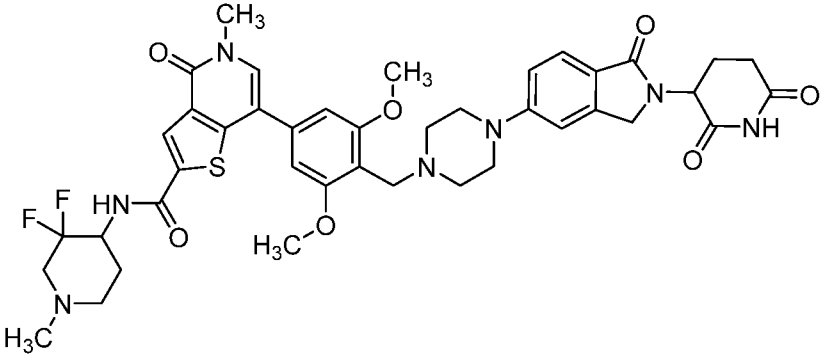
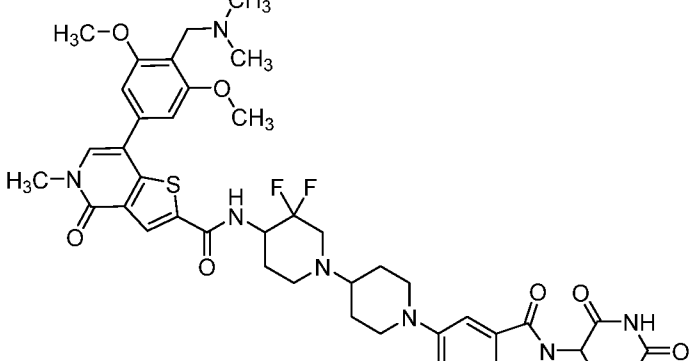
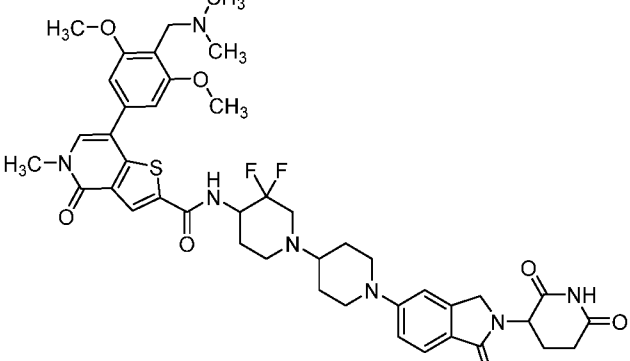
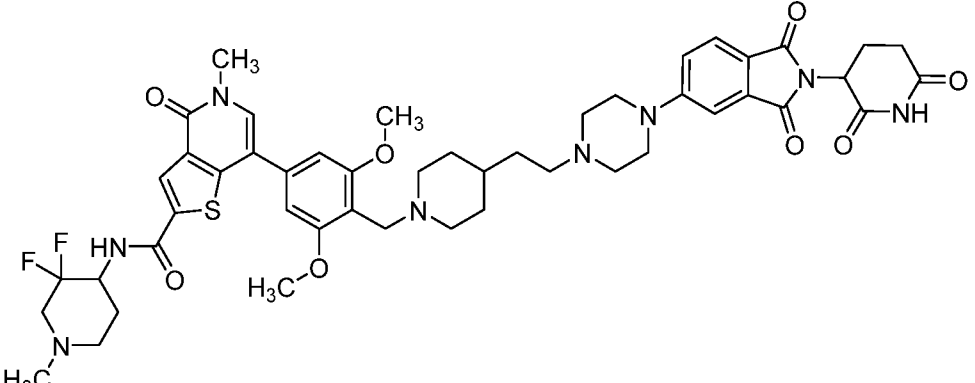
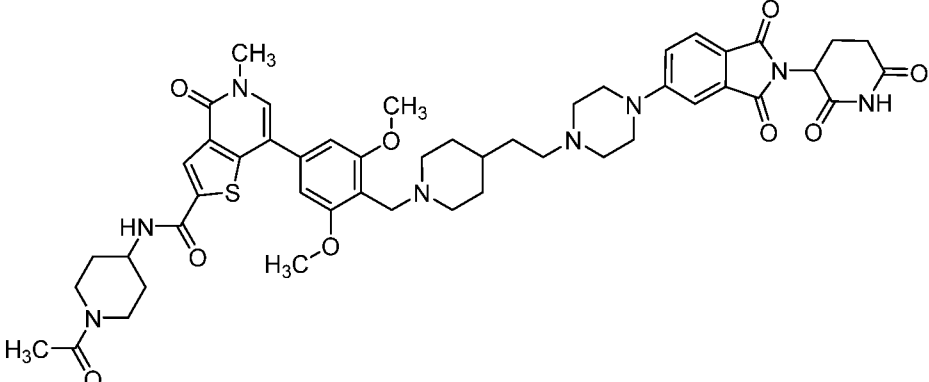
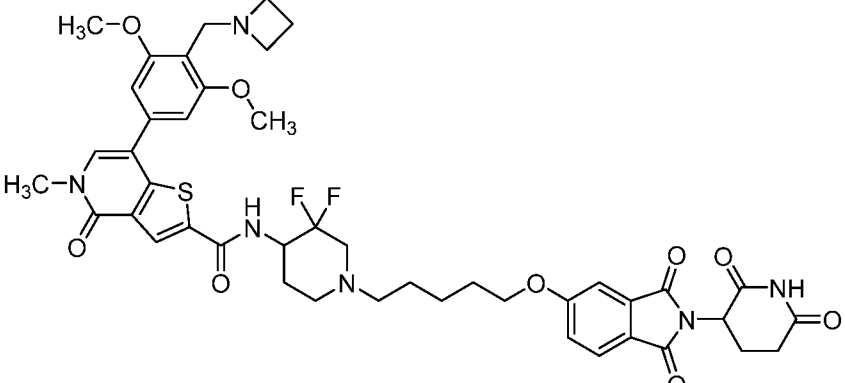
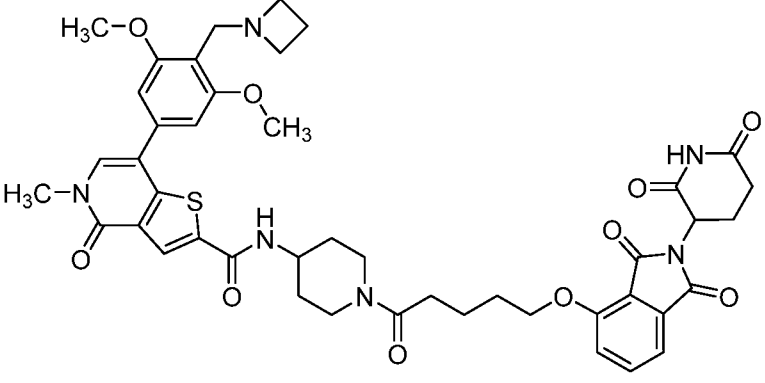
Compound No.	Structure
D14	
D15	

Table 2B. Compounds D16-D90 of the Disclosure

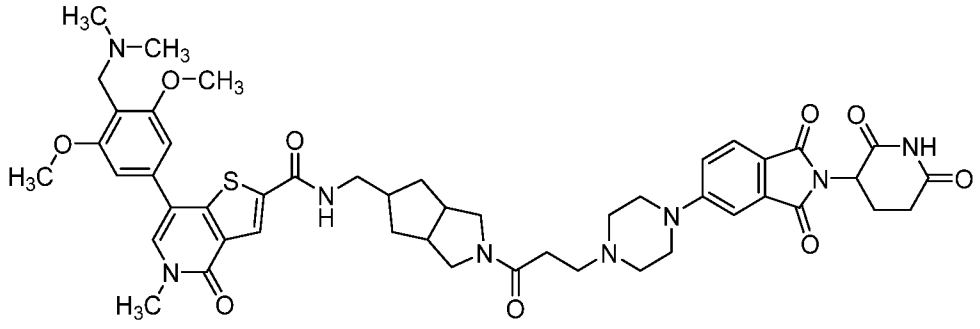
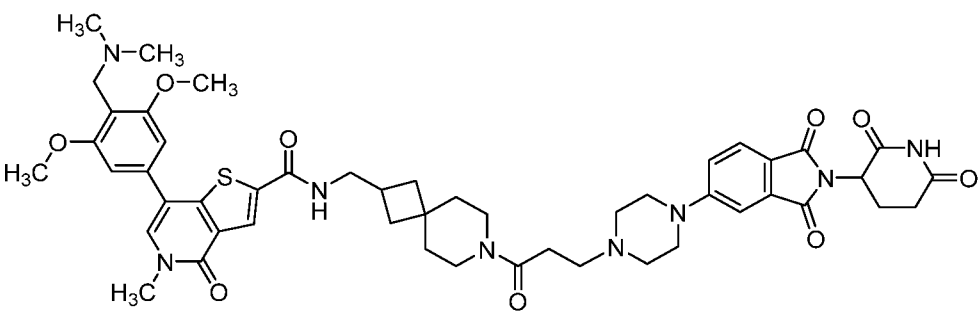
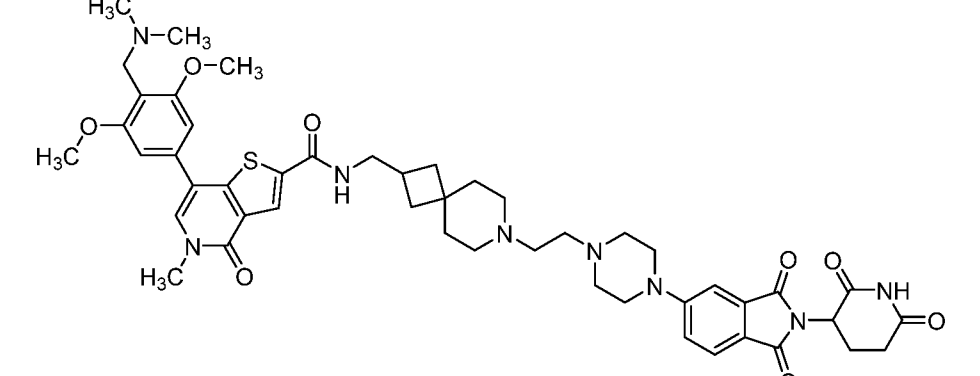
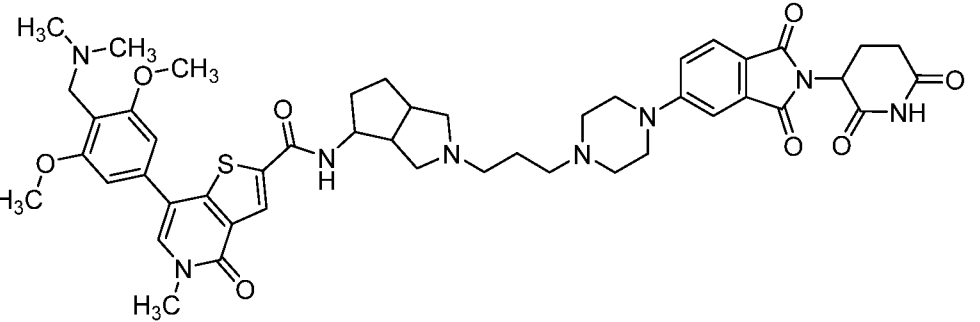
Compound No.	Structure
D16	
D17	

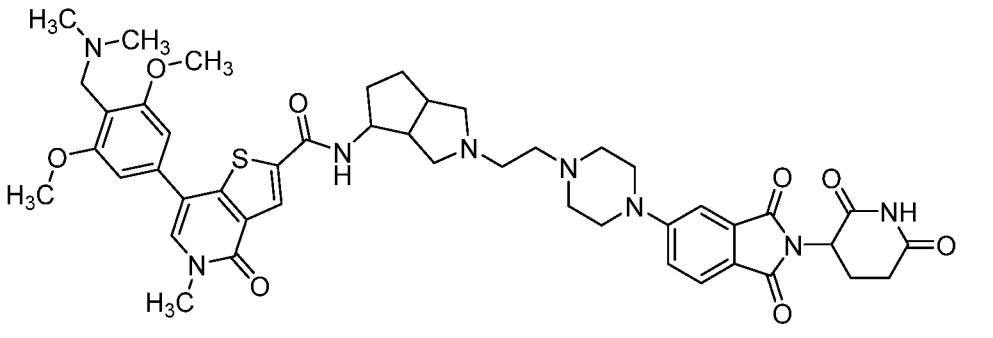
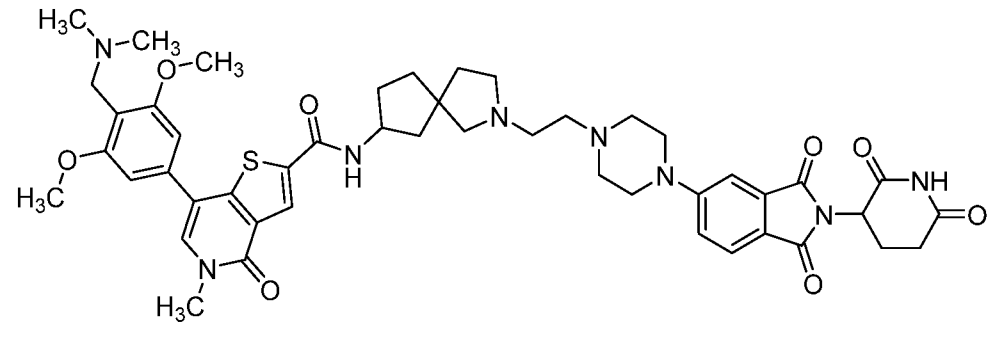
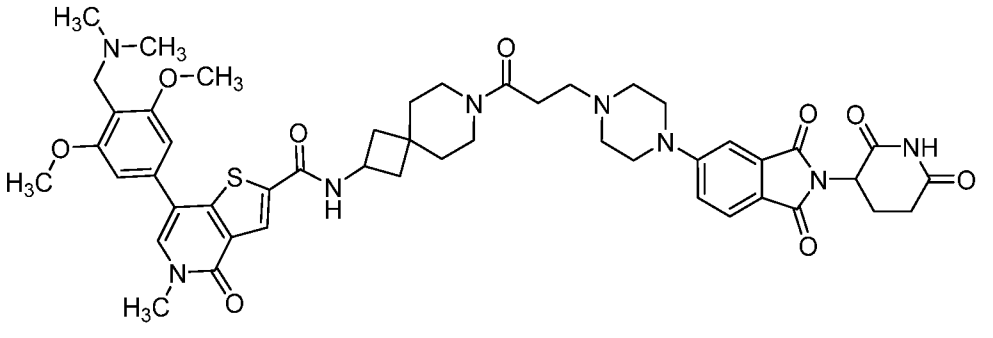
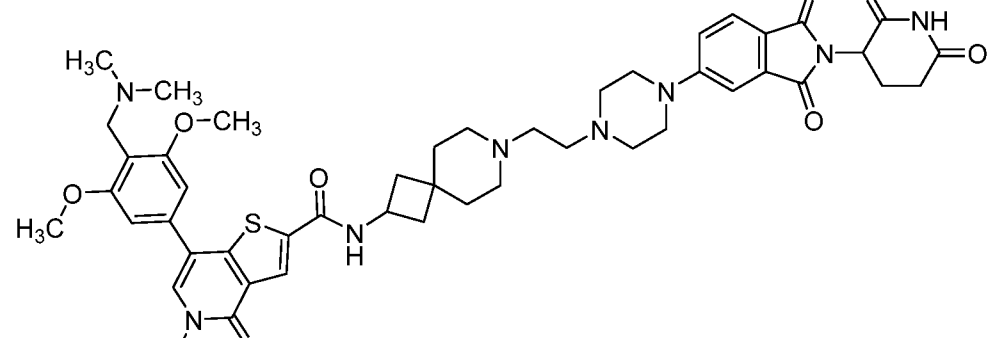
Compound No.	Structure
D18	 Chemical structure of compound D18. It features a central pyrimidine-2,4-dione core. At position 6, there is a 3,4-dimethoxyphenyl group substituted with a (dimethylamino)methyl group. At position 5, there is a thienyl group substituted with a (2,2-difluoroethyl)carbamoyl group. At position 4, there is a side chain consisting of a carbonyl group linked to a piperidine ring, which is further connected via a methylene group to a bicyclic system (a piperidine ring fused to a cyclopropane ring). This bicyclic system is substituted with a 1,2,3,4-tetrahydronaphthalen-1-yl group, which is in turn linked to a 2,6-pyridinedione moiety.
D19	 Chemical structure of compound D19. It is similar to D18, but the side chain at position 4 of the pyrimidine core is extended by an additional methylene group before connecting to the bicyclic system.
D20	 Chemical structure of compound D20. It features a central pyrimidine-2,4-dione core. At position 6, there is a 3,4-dimethoxyphenyl group substituted with a (dimethylamino)methyl group. At position 5, there is a thiazolyl group substituted with a carbonyl group. At position 4, there is a side chain consisting of a methylene group linked to a cyclopropyl ring, which is further connected via a methylene group to a bicyclic system (a piperidine ring fused to a cyclopropane ring). This bicyclic system is substituted with a 1,2,3,4-tetrahydronaphthalen-1-yl group, which is in turn linked to a 2,6-pyridinedione moiety.
D21	 Chemical structure of compound D21. It is similar to D20, but the thiazolyl group at position 5 is replaced by a furanyl group.

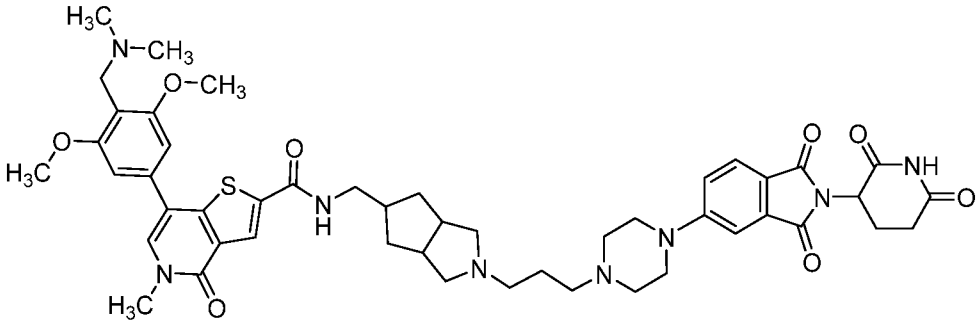
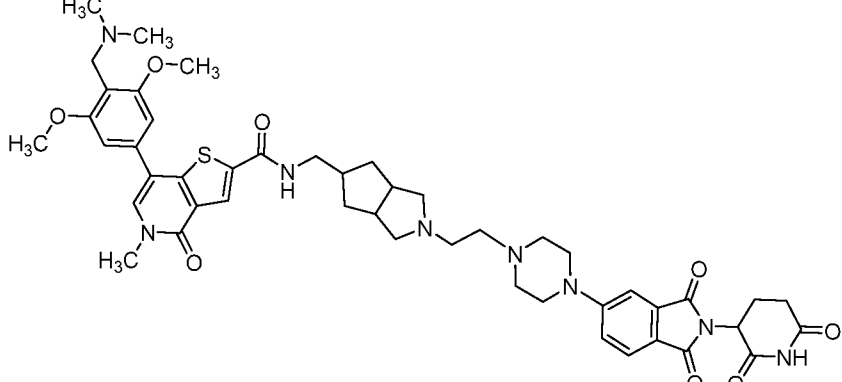
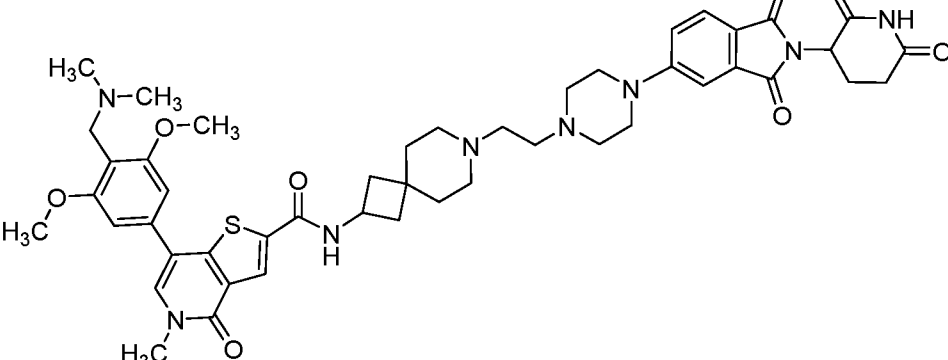
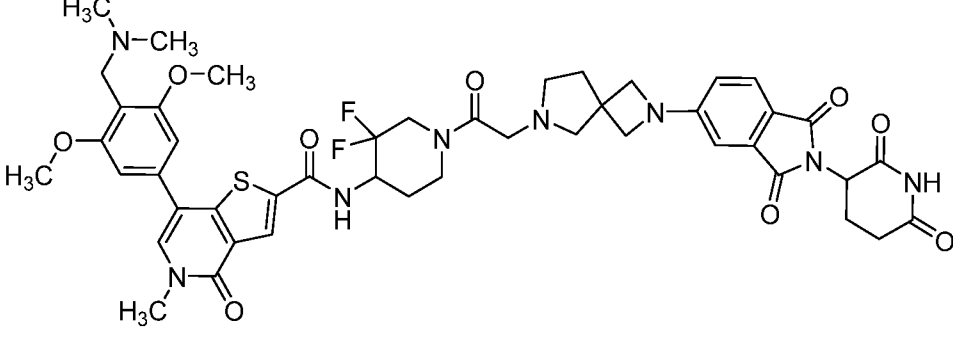
Compound No.	Structure
D22	 Chemical structure of compound D22: A complex molecule featuring a central benzene ring substituted with a methoxy group (H₃C-O-), a methylthio group (-SCH₃), and a methylthio group (-SCH₃). The benzene ring is connected to a thiazole ring, which is further substituted with a methylthio group (-SCH₃) and a methylthio group (-SCH₃). The thiazole ring is also connected to a piperidine ring, which is substituted with a methylthio group (-SCH₃) and a methylthio group (-SCH₃). The piperidine ring is further connected to a benzimidazole ring, which is substituted with a methylthio group (-SCH₃) and a methylthio group (-SCH₃). The benzimidazole ring is also connected to a piperidine ring, which is substituted with a methylthio group (-SCH₃) and a methylthio group (-SCH₃).
D23	 Chemical structure of compound D23: A complex molecule featuring a central benzene ring substituted with a methoxy group (H₃C-O-), a methylthio group (-SCH₃), and a methylthio group (-SCH₃). The benzene ring is connected to a thiazole ring, which is further substituted with a methylthio group (-SCH₃) and a methylthio group (-SCH₃). The thiazole ring is also connected to a piperidine ring, which is substituted with a methylthio group (-SCH₃) and a methylthio group (-SCH₃). The piperidine ring is further connected to a benzimidazole ring, which is substituted with a methylthio group (-SCH₃) and a methylthio group (-SCH₃). The benzimidazole ring is also connected to a piperidine ring, which is substituted with a methylthio group (-SCH₃) and a methylthio group (-SCH₃).
D24	 Chemical structure of compound D24: A complex molecule featuring a central benzene ring substituted with a methoxy group (H₃C-O-), a methylthio group (-SCH₃), and a methylthio group (-SCH₃). The benzene ring is connected to a thiazole ring, which is further substituted with a methylthio group (-SCH₃) and a methylthio group (-SCH₃). The thiazole ring is also connected to a piperidine ring, which is substituted with a methylthio group (-SCH₃) and a methylthio group (-SCH₃). The piperidine ring is further connected to a benzimidazole ring, which is substituted with a methylthio group (-SCH₃) and a methylthio group (-SCH₃). The benzimidazole ring is also connected to a piperidine ring, which is substituted with a methylthio group (-SCH₃) and a methylthio group (-SCH₃).
D25	 Chemical structure of compound D25: A complex molecule featuring a central benzene ring substituted with a methoxy group (H₃C-O-), a methylthio group (-SCH₃), and a methylthio group (-SCH₃). The benzene ring is connected to a thiazole ring, which is further substituted with a methylthio group (-SCH₃) and a methylthio group (-SCH₃). The thiazole ring is also connected to a piperidine ring, which is substituted with a methylthio group (-SCH₃) and a methylthio group (-SCH₃). The piperidine ring is further connected to a benzimidazole ring, which is substituted with a methylthio group (-SCH₃) and a methylthio group (-SCH₃). The benzimidazole ring is also connected to a piperidine ring, which is substituted with a methylthio group (-SCH₃) and a methylthio group (-SCH₃).

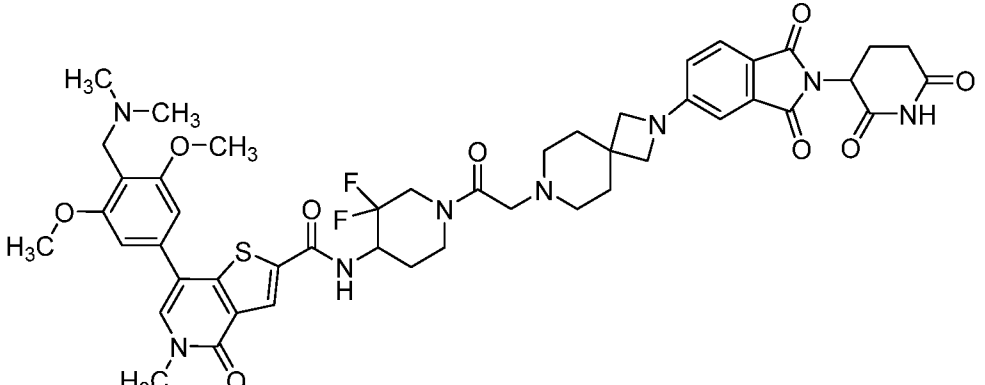
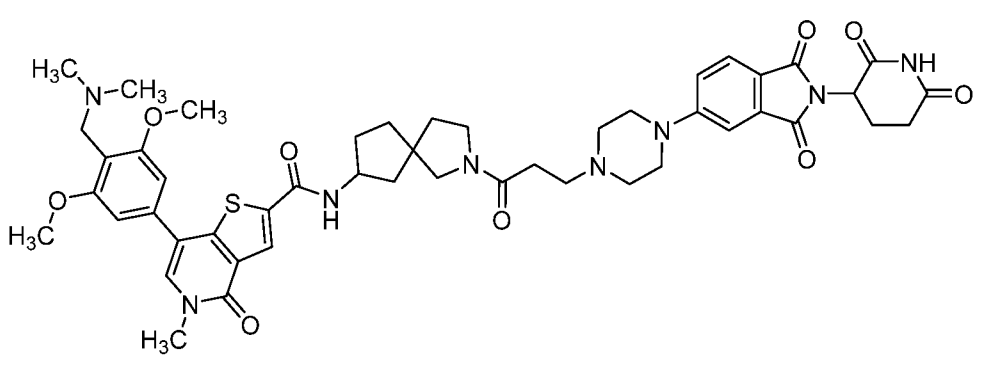
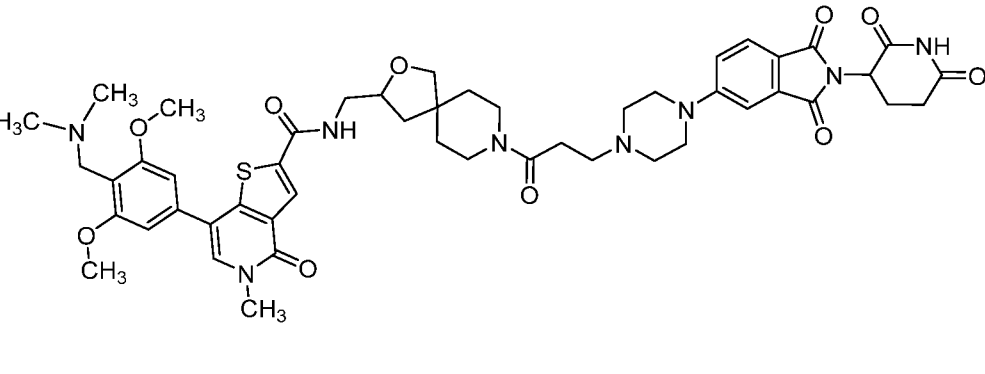
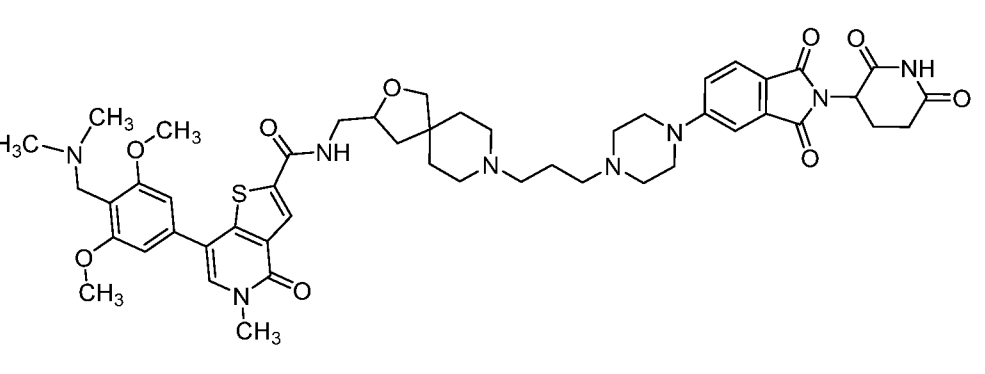
Compound No.	Structure
D26	 Chemical structure of compound D26: A complex molecule featuring a central benzene ring substituted with a 4-methoxyphenyl group, a 2-methoxyphenyl group, and a 4-methoxyphenyl group. The central benzene ring is also substituted with a 4-methoxyphenyl group. The molecule includes a thiazole ring, a pyridine ring, and a piperidine ring, all connected by various linkers including amide bonds and ether linkages. The structure is highly symmetrical and contains multiple functional groups.
D27	 Chemical structure of compound D27: A complex molecule featuring a central benzene ring substituted with a 4-methoxyphenyl group, a 2-methoxyphenyl group, and a 4-methoxyphenyl group. The central benzene ring is also substituted with a 4-methoxyphenyl group. The molecule includes a thiazole ring, a pyridine ring, and a piperidine ring, all connected by various linkers including amide bonds and ether linkages. The structure is highly symmetrical and contains multiple functional groups.
D28	 Chemical structure of compound D28: A complex molecule featuring a central benzene ring substituted with a 4-methoxyphenyl group, a 2-methoxyphenyl group, and a 4-methoxyphenyl group. The central benzene ring is also substituted with a 4-methoxyphenyl group. The molecule includes a thiazole ring, a pyridine ring, and a piperidine ring, all connected by various linkers including amide bonds and ether linkages. The structure is highly symmetrical and contains multiple functional groups.
D29	 Chemical structure of compound D29: A complex molecule featuring a central benzene ring substituted with a 4-methoxyphenyl group, a 2-methoxyphenyl group, and a 4-methoxyphenyl group. The central benzene ring is also substituted with a 4-methoxyphenyl group. The molecule includes a thiazole ring, a pyridine ring, and a piperidine ring, all connected by various linkers including amide bonds and ether linkages. The structure is highly symmetrical and contains multiple functional groups.

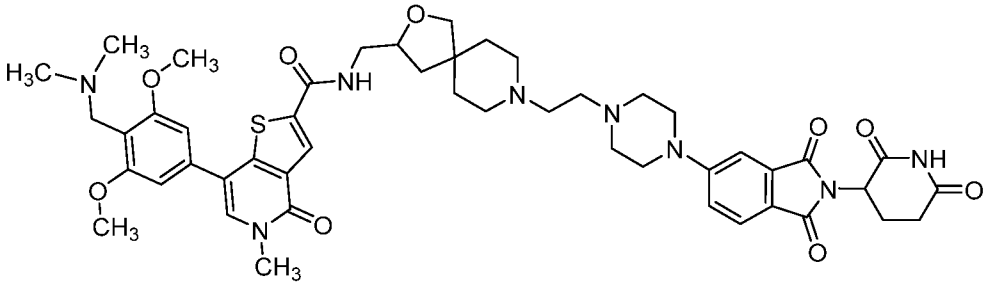
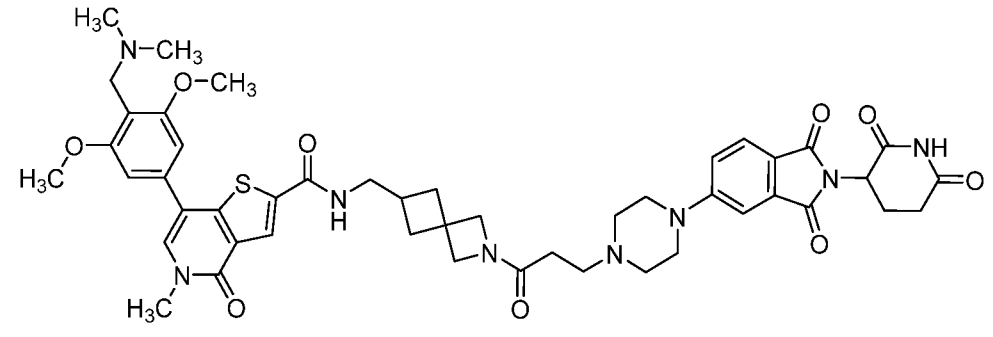
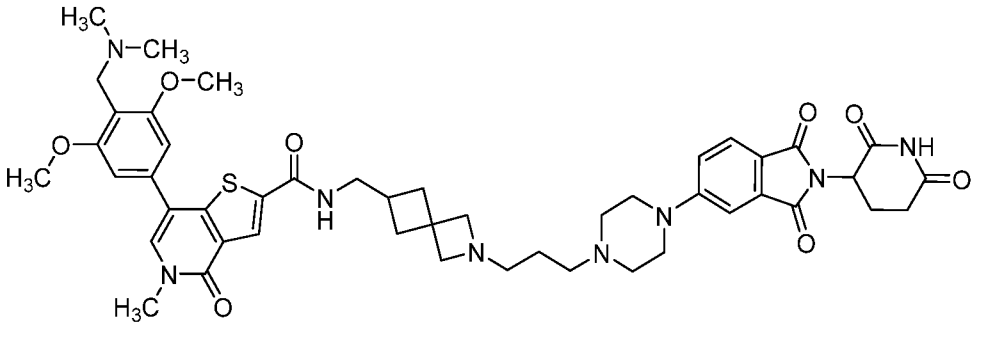
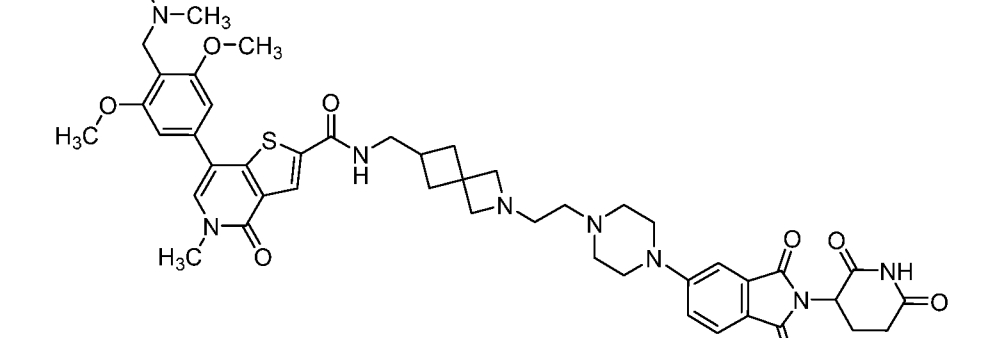
Compound No.	Structure
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D31	
D32	
D33	

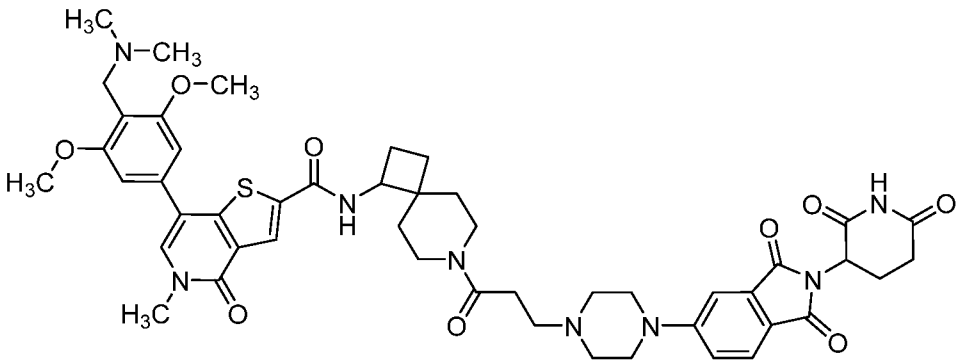
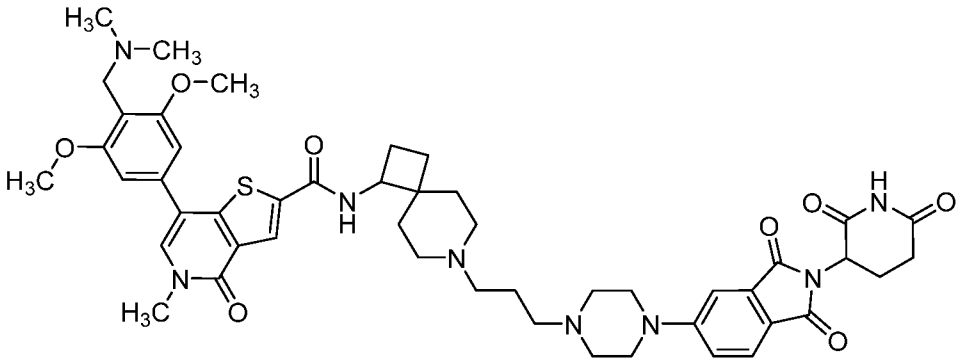
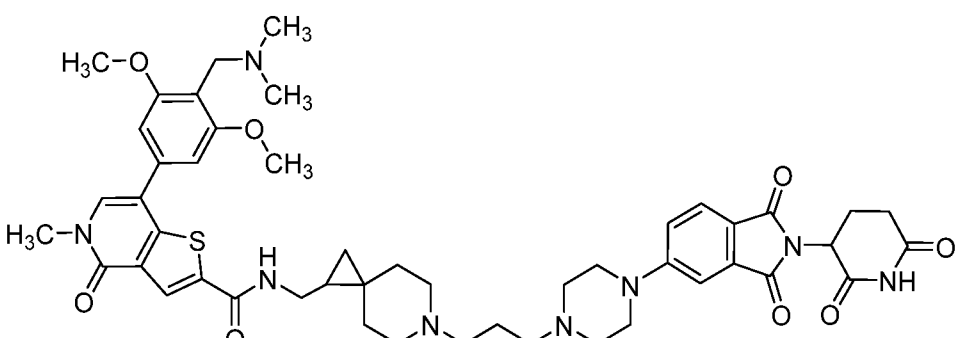
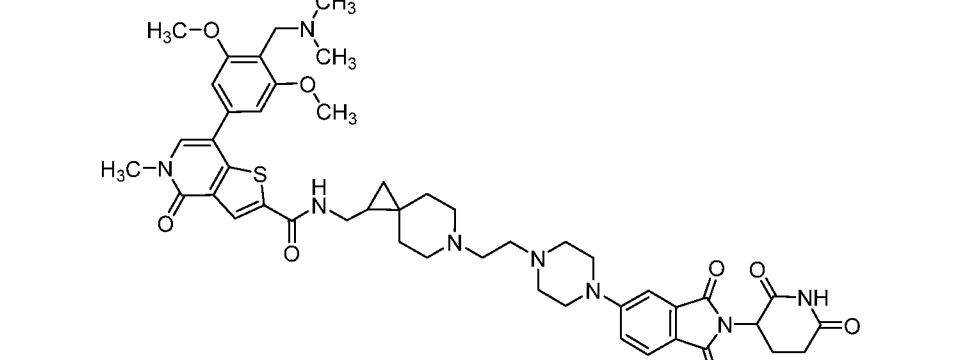
Compound No.	Structure
D34	 Chemical structure of D34: A complex molecule featuring a 4-(dimethylamino)-2-methoxyphenyl group attached to a thiophene ring. The thiophene ring is also substituted with a methyl group and a carbonyl group. The carbonyl group is linked via an amide bond to a bicyclic system (a cyclopentane ring fused to a pyrrolidine ring). This bicyclic system is further linked via an amide bond to a piperazine ring, which is connected to a benzimidazole system. The benzimidazole system is substituted with a methyl group and a carbonyl group.
D35	 Chemical structure of D35: A complex molecule featuring a 4-(dimethylamino)-2-methoxyphenyl group attached to a thiophene ring. The thiophene ring is also substituted with a methyl group and a carbonyl group. The carbonyl group is linked via an amide bond to a bicyclic system (a cyclopentane ring fused to a piperidine ring). This bicyclic system is further linked via an amide bond to a piperazine ring, which is connected to a benzimidazole system. The benzimidazole system is substituted with a methyl group and a carbonyl group.
D36	 Chemical structure of D36: A complex molecule featuring a 4-(dimethylamino)-2-methoxyphenyl group attached to a thiophene ring. The thiophene ring is also substituted with a methyl group and a carbonyl group. The carbonyl group is linked via an amide bond to a bicyclic system (a cyclopentane ring fused to a piperidine ring). This bicyclic system is further linked via an amide bond to a piperazine ring, which is connected to a benzimidazole system. The benzimidazole system is substituted with a methyl group and a carbonyl group.
D37	 Chemical structure of D37: A complex molecule featuring a 4-(dimethylamino)-2-methoxyphenyl group attached to a thiophene ring. The thiophene ring is also substituted with a methyl group and a carbonyl group. The carbonyl group is linked via an amide bond to a bicyclic system (a cyclopentane ring fused to a pyrrolidine ring). This bicyclic system is further linked via an amide bond to a piperazine ring, which is connected to a benzimidazole system. The benzimidazole system is substituted with a methyl group and a carbonyl group.

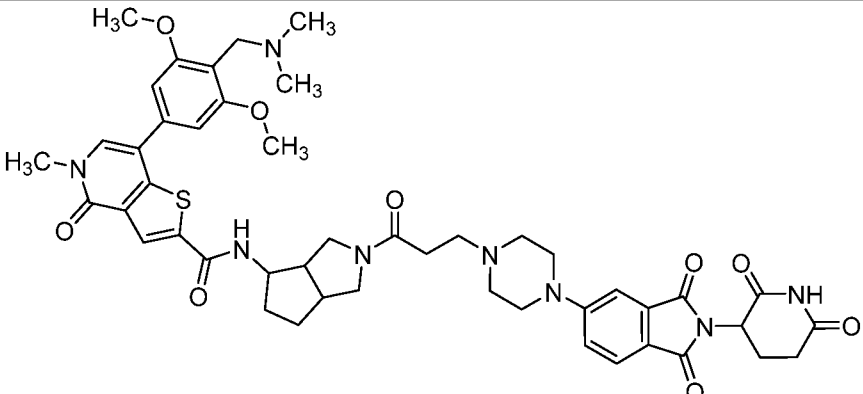
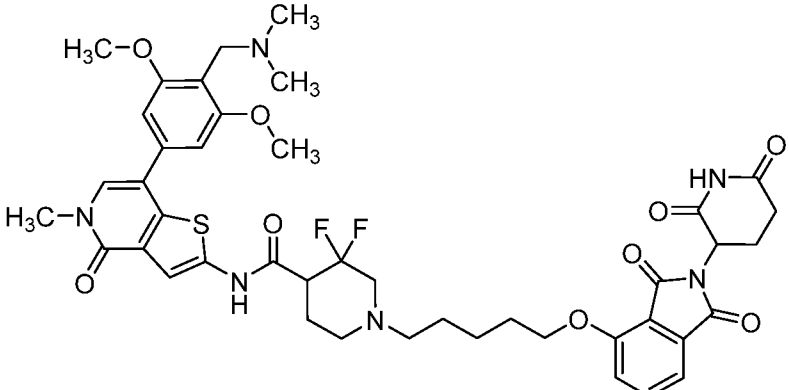
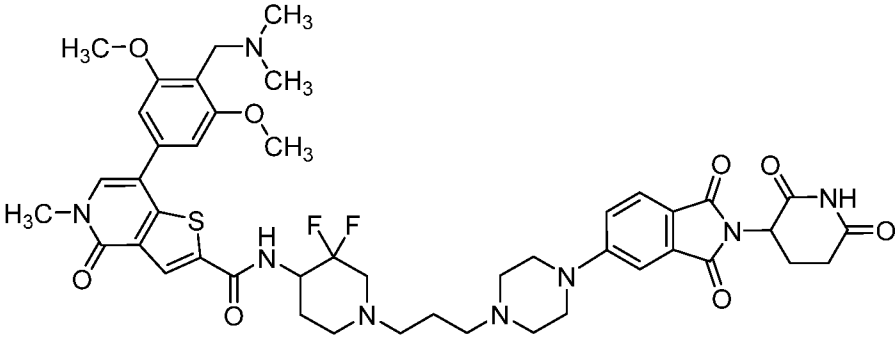
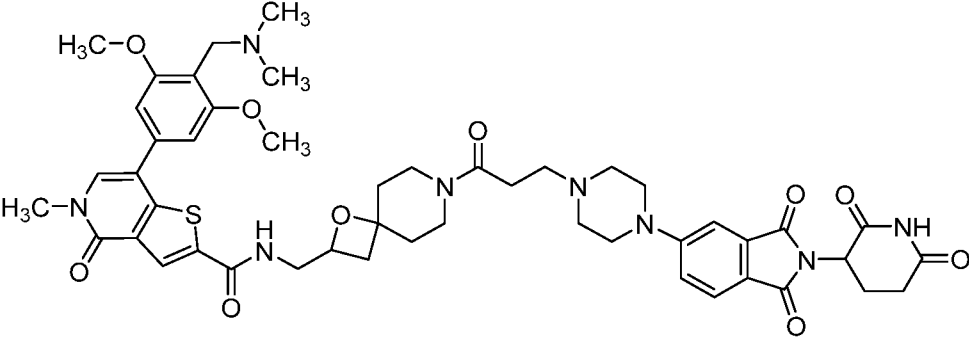
Compound No.	Structure
D38	 Chemical structure of compound D38. It features a 4-methoxy-2-(dimethylmethoxymethyl)phenyl group attached to a 2-methyl-4-thienylpyridine-3-carboxamide moiety. The amide nitrogen is connected to a bicyclic system (cyclopentane fused to a pyrrolidine ring). This system is further linked via a methylene group to a piperazine ring, which is connected to a 4-oxo-4,5-dihydro-1H-benzodisole-3-carboxamide moiety.
D39	 Chemical structure of compound D39. It features a 4-methoxy-2-(dimethylmethoxymethyl)phenyl group attached to a 2-methyl-4-thienylpyridine-3-carboxamide moiety. The amide nitrogen is connected to a bicyclic system (cyclopentane fused to a pyrrolidine ring). This system is further linked via a methylene group to a piperazine ring, which is connected to a 4-oxo-4,5-dihydro-1H-benzodisole-3-carboxamide moiety.
D40	 Chemical structure of compound D40. It features a 4-methoxy-2-(dimethylmethoxymethyl)phenyl group attached to a 2-methyl-4-thienylpyridine-3-carboxamide moiety. The amide nitrogen is connected to a bicyclic system (cyclopentane fused to a piperidine ring). This system is further linked via a methylene group to a piperazine ring, which is connected to a 4-oxo-4,5-dihydro-1H-benzodisole-3-carboxamide moiety.
D41	 Chemical structure of compound D41. It features a 4-methoxy-2-(dimethylmethoxymethyl)phenyl group attached to a 2-methyl-4-thienylpyridine-3-carboxamide moiety. The amide nitrogen is connected to a bicyclic system (cyclopentane fused to a piperidine ring). This system is further linked via a methylene group to a piperazine ring, which is connected to a 4-oxo-4,5-dihydro-1H-benzodisole-3-carboxamide moiety.

Compound No.	Structure
D42	
D43	
D44	
D45	

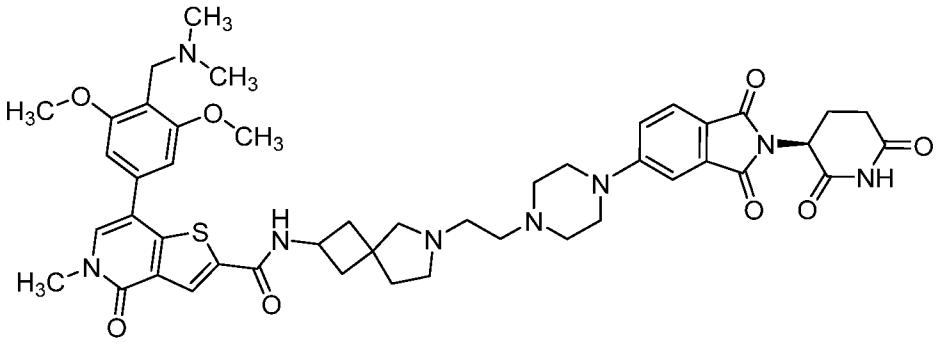
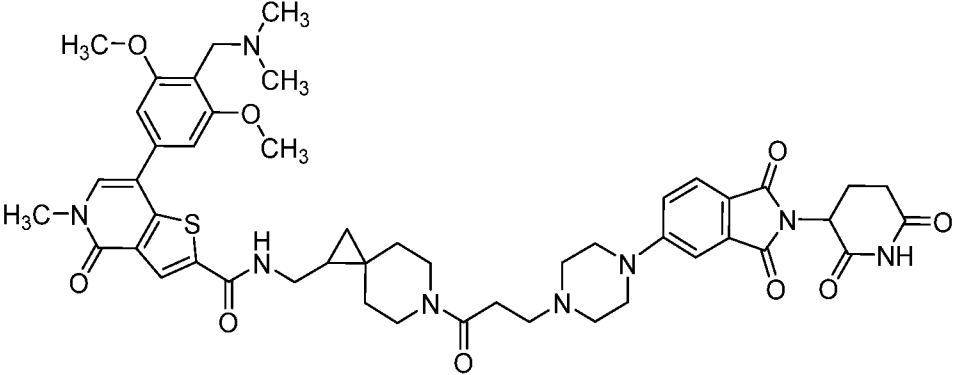
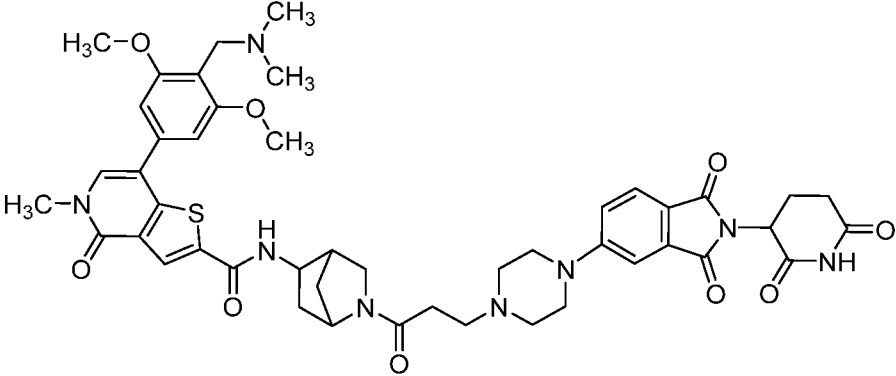
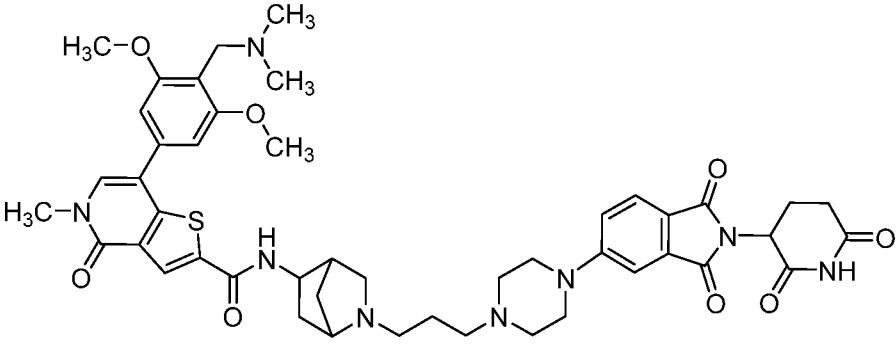
Compound No.	Structure
D46	 Chemical structure of D46: A complex molecule featuring a 4-methoxy-2-(dimethylamino)phenyl group attached to a thienopyridine core. The thienopyridine core is substituted with a methyl group on the nitrogen and a thioether linkage to a piperidine ring. The piperidine ring is further substituted with a fluorine atom and a carbonyl group, which is linked to a piperazine ring. The piperazine ring is connected to a benzimidazole system, which is further substituted with a carbonyl group and a piperidine ring.
D47	 Chemical structure of D47: A complex molecule featuring a 4-methoxy-2-(dimethylamino)phenyl group attached to a thienopyridine core. The thienopyridine core is substituted with a methyl group on the nitrogen and a thioether linkage to a piperidine ring. The piperidine ring is further substituted with a carbonyl group, which is linked to a piperazine ring. The piperazine ring is connected to a benzimidazole system, which is further substituted with a carbonyl group and a piperidine ring.
D48	 Chemical structure of D48: A complex molecule featuring a 4-methoxy-2-(dimethylamino)phenyl group attached to a thienopyridine core. The thienopyridine core is substituted with a methyl group on the nitrogen and a thioether linkage to a piperidine ring. The piperidine ring is further substituted with a carbonyl group, which is linked to a piperazine ring. The piperazine ring is connected to a benzimidazole system, which is further substituted with a carbonyl group and a piperidine ring.
D49	 Chemical structure of D49: A complex molecule featuring a 4-methoxy-2-(dimethylamino)phenyl group attached to a thienopyridine core. The thienopyridine core is substituted with a methyl group on the nitrogen and a thioether linkage to a piperidine ring. The piperidine ring is further substituted with a carbonyl group, which is linked to a piperazine ring. The piperazine ring is connected to a benzimidazole system, which is further substituted with a carbonyl group and a piperidine ring.

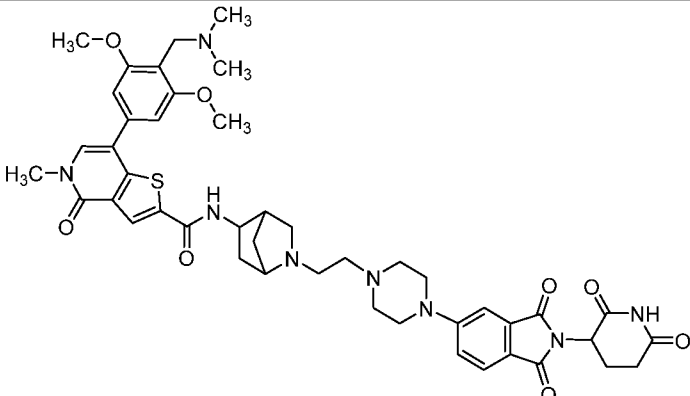
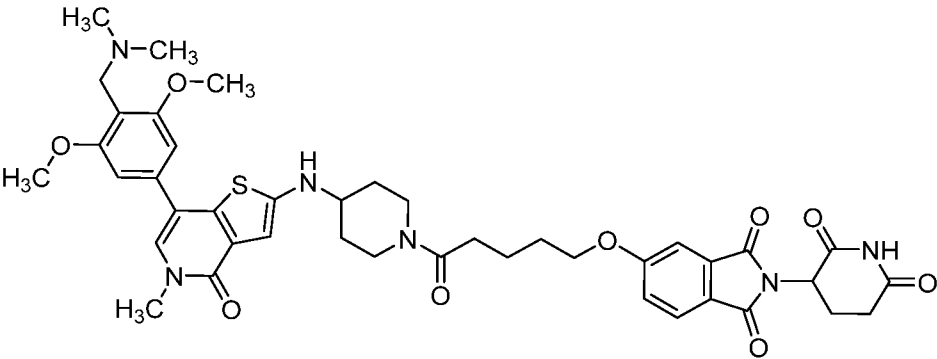
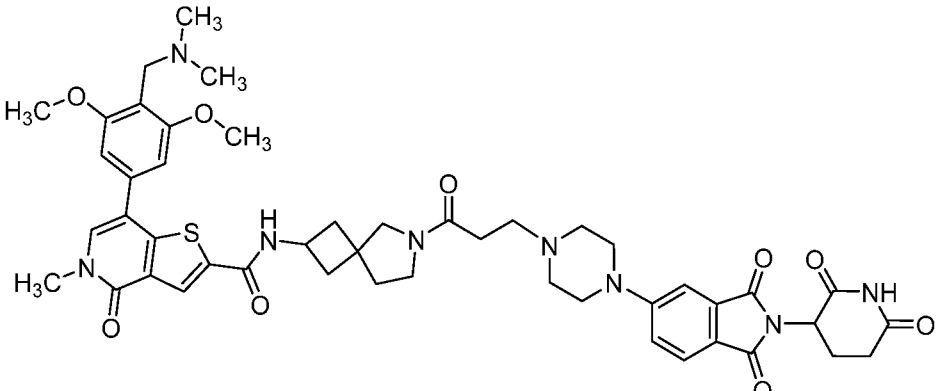
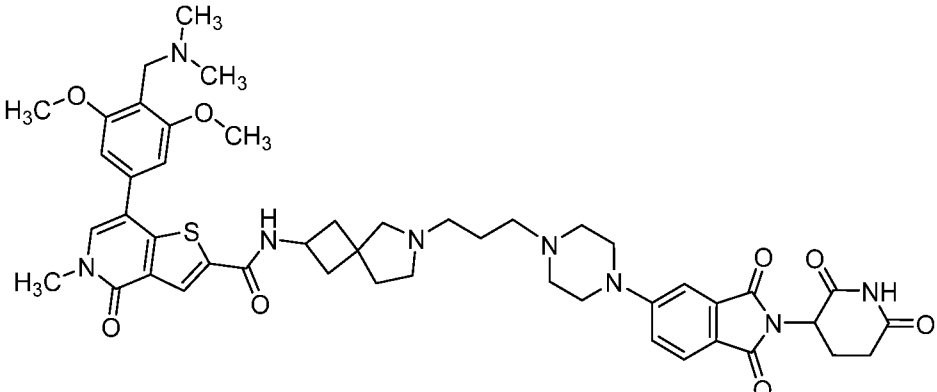
Compound No.	Structure
D50	 Chemical structure of compound D50: A thienopyridine core substituted with a 3,4,5-trimethoxy-2-(dimethylamino)phenyl group and a methyl group on the pyridine nitrogen. The thiophene ring is linked via an amide bond to a 4-(2-(4-(1,3-dioxolane-2-yl)ethyl)piperidin-1-yl)butyl chain, which is further connected to a 4-(1,3-dioxolane-2-yl)piperidine ring, and finally to a 4-(1,3-dioxolane-2-yl)piperidine ring.
D51	 Chemical structure of compound D51: A thienopyridine core substituted with a 3,4,5-trimethoxy-2-(dimethylamino)phenyl group and a methyl group on the pyridine nitrogen. The thiophene ring is linked via an amide bond to a 4-(2-(4-(1,3-dioxolane-2-yl)ethyl)piperidin-1-yl)butyl chain, which is further connected to a 4-(1,3-dioxolane-2-yl)piperidine ring, and finally to a 4-(1,3-dioxolane-2-yl)piperidine ring.
D52	 Chemical structure of compound D52: A thienopyridine core substituted with a 3,4,5-trimethoxy-2-(dimethylamino)phenyl group and a methyl group on the pyridine nitrogen. The thiophene ring is linked via an amide bond to a 4-(2-(4-(1,3-dioxolane-2-yl)ethyl)piperidin-1-yl)butyl chain, which is further connected to a 4-(1,3-dioxolane-2-yl)piperidine ring, and finally to a 4-(1,3-dioxolane-2-yl)piperidine ring.
D53	 Chemical structure of compound D53: A thienopyridine core substituted with a 3,4,5-trimethoxy-2-(dimethylamino)phenyl group and a methyl group on the pyridine nitrogen. The thiophene ring is linked via an amide bond to a 4-(2-(4-(1,3-dioxolane-2-yl)ethyl)piperidin-1-yl)butyl chain, which is further connected to a 4-(1,3-dioxolane-2-yl)piperidine ring, and finally to a 4-(1,3-dioxolane-2-yl)piperidine ring.

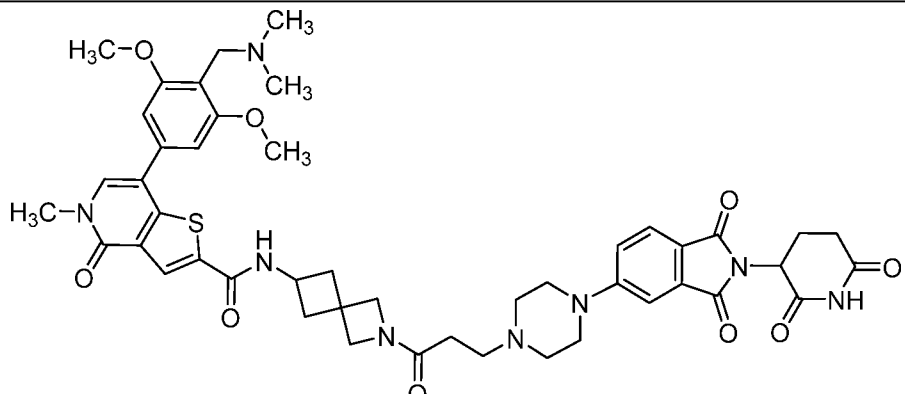
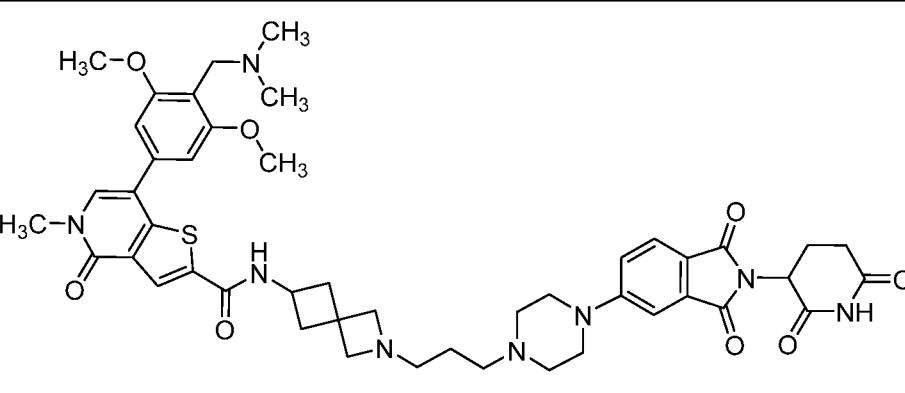
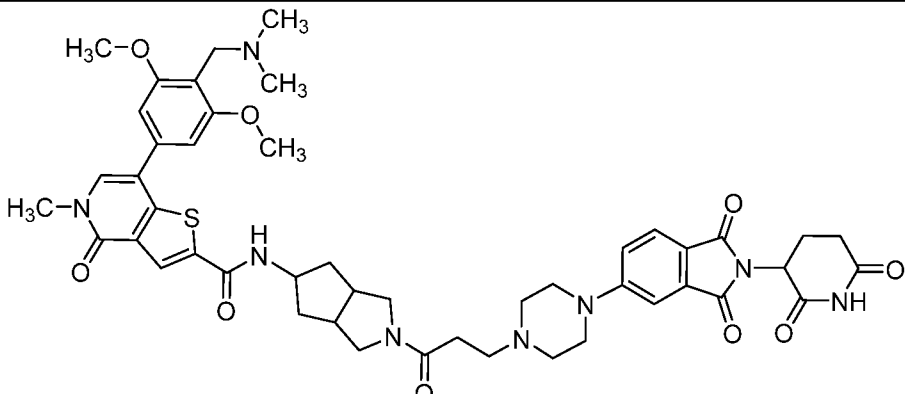
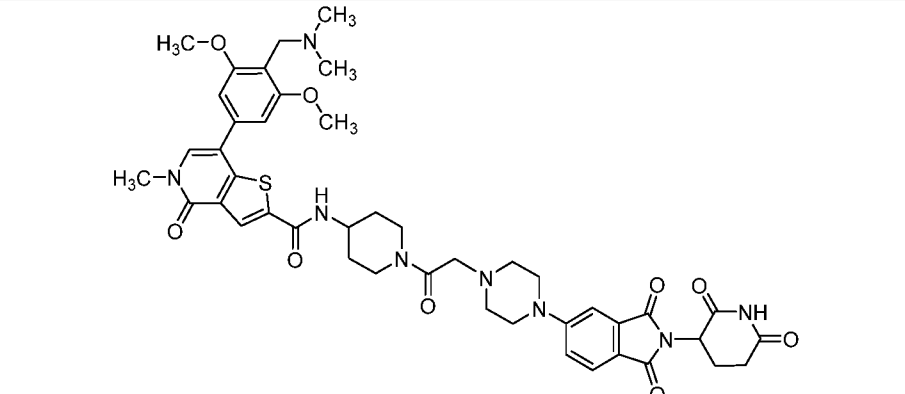
Compound No.	Structure
D54	
D55	
D56	
D57	

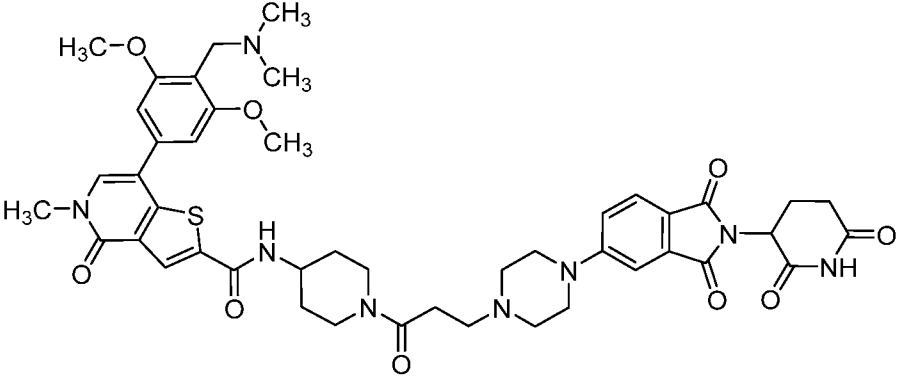
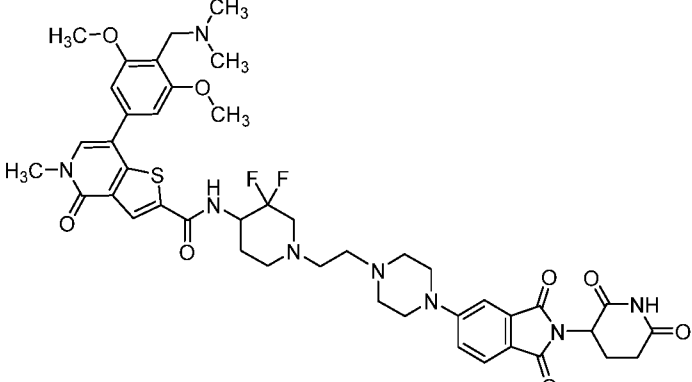
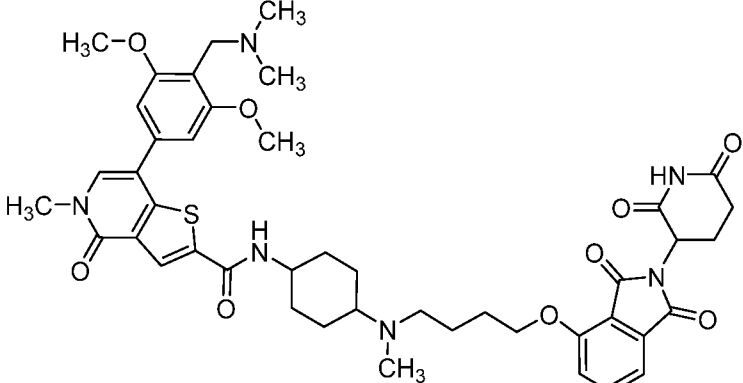
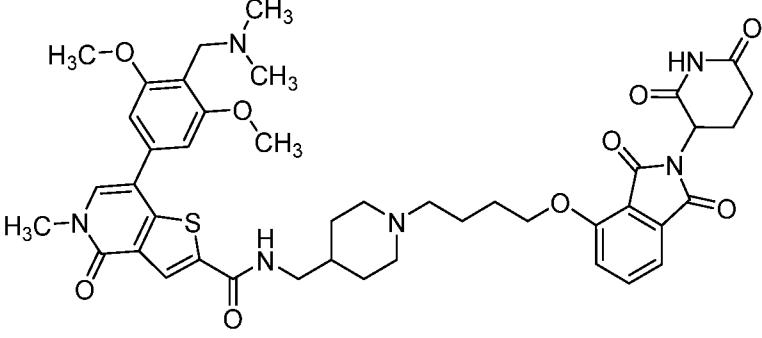
Compound No.	Structure
D58	 Chemical structure of compound D58. It features a 4-methoxy-2-(dimethylamino)phenyl group attached to a 6-methoxy-3-methyl-1,2,4-thiazine-5-carboxamide moiety. This thiazine is linked via its 4-position to a 1,2,3,4-tetrahydro-1H-pyridine-5-carboxamide group. The pyridine ring is further connected to a 1,2,3,4-tetrahydro-1H-pyridine-5-carboxamide group, which is then linked to a 1,2,3,4-tetrahydro-1H-pyridine-5-carboxamide group. The final group is a 1,2,3,4-tetrahydro-1H-pyridine-5-carboxamide group.
D59	 Chemical structure of compound D59. It features a 4-methoxy-2-(dimethylamino)phenyl group attached to a 6-methoxy-3-methyl-1,2,4-thiazine-5-carboxamide moiety. This thiazine is linked via its 4-position to a 1,2,3,4-tetrahydro-1H-pyridine-5-carboxamide group. The pyridine ring is further connected to a 1,2,3,4-tetrahydro-1H-pyridine-5-carboxamide group, which is then linked to a 1,2,3,4-tetrahydro-1H-pyridine-5-carboxamide group. The final group is a 1,2,3,4-tetrahydro-1H-pyridine-5-carboxamide group.
D60	 Chemical structure of compound D60. It features a 4-methoxy-2-(dimethylamino)phenyl group attached to a 6-methoxy-3-methyl-1,2,4-thiazine-5-carboxamide moiety. This thiazine is linked via its 4-position to a 1,2,3,4-tetrahydro-1H-pyridine-5-carboxamide group. The pyridine ring is further connected to a 1,2,3,4-tetrahydro-1H-pyridine-5-carboxamide group, which is then linked to a 1,2,3,4-tetrahydro-1H-pyridine-5-carboxamide group. The final group is a 1,2,3,4-tetrahydro-1H-pyridine-5-carboxamide group.
D61	 Chemical structure of compound D61. It features a 4-methoxy-2-(dimethylamino)phenyl group attached to a 6-methoxy-3-methyl-1,2,4-thiazine-5-carboxamide moiety. This thiazine is linked via its 4-position to a 1,2,3,4-tetrahydro-1H-pyridine-5-carboxamide group. The pyridine ring is further connected to a 1,2,3,4-tetrahydro-1H-pyridine-5-carboxamide group, which is then linked to a 1,2,3,4-tetrahydro-1H-pyridine-5-carboxamide group. The final group is a 1,2,3,4-tetrahydro-1H-pyridine-5-carboxamide group.

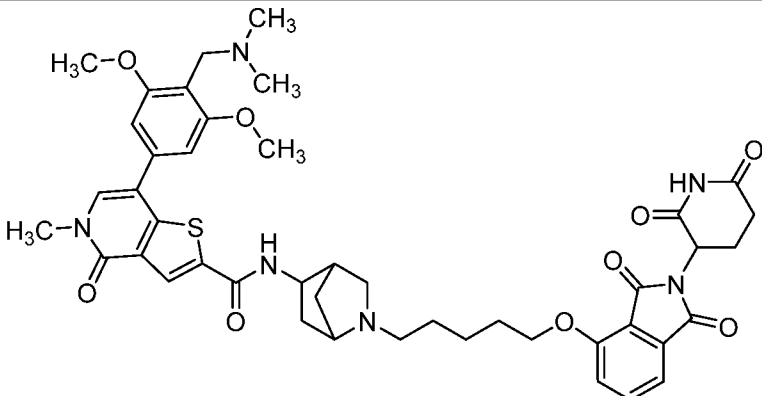
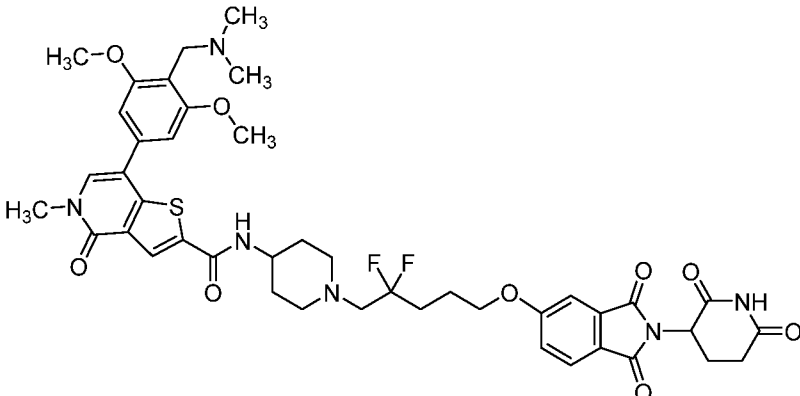
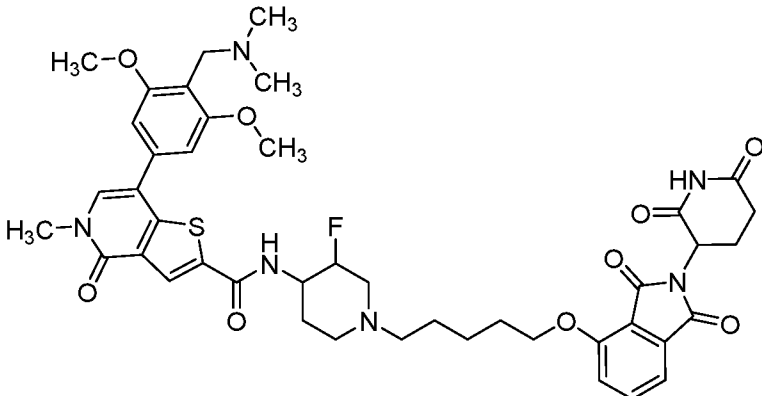
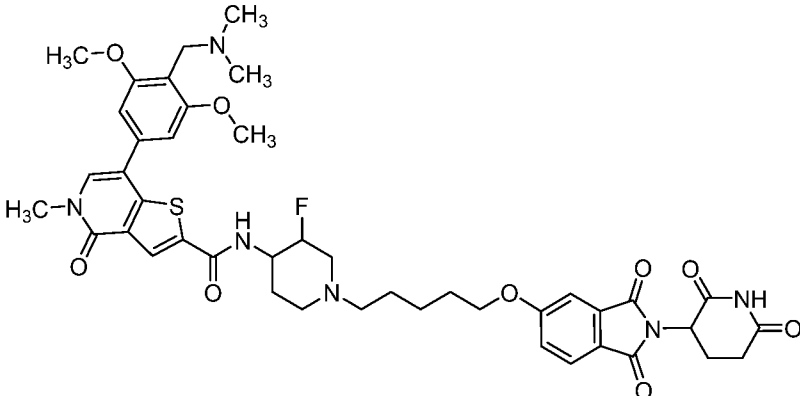
Compound No.	Structure
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D63	
D64	
D65	

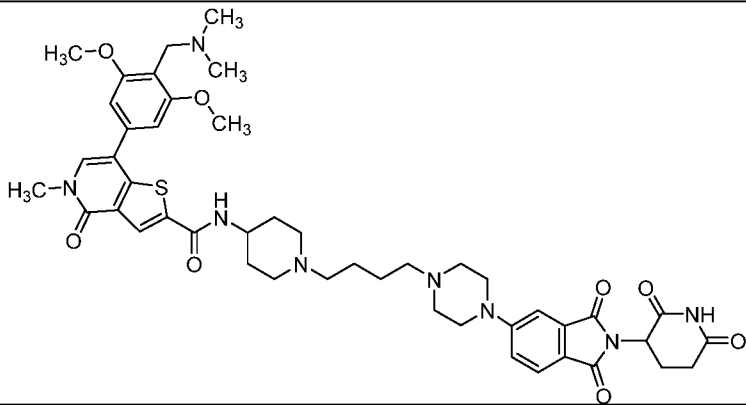
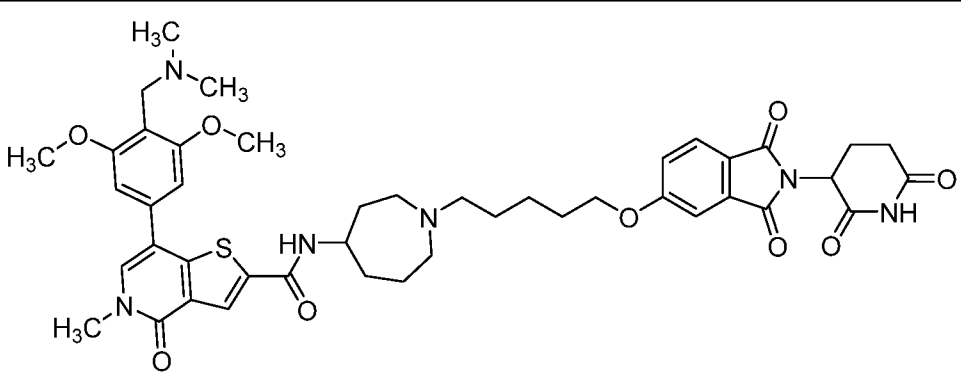
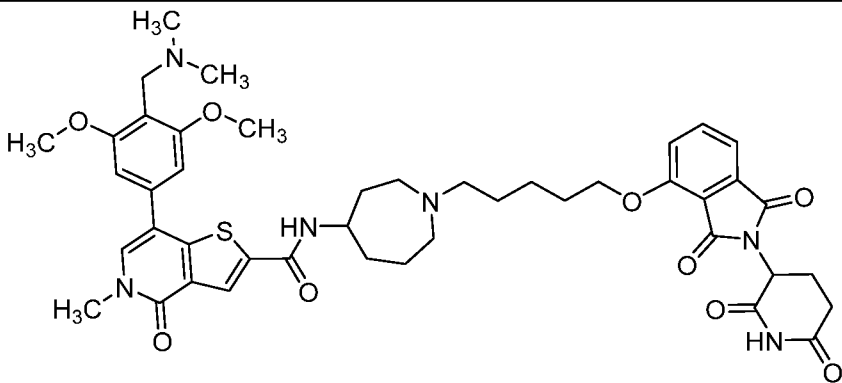
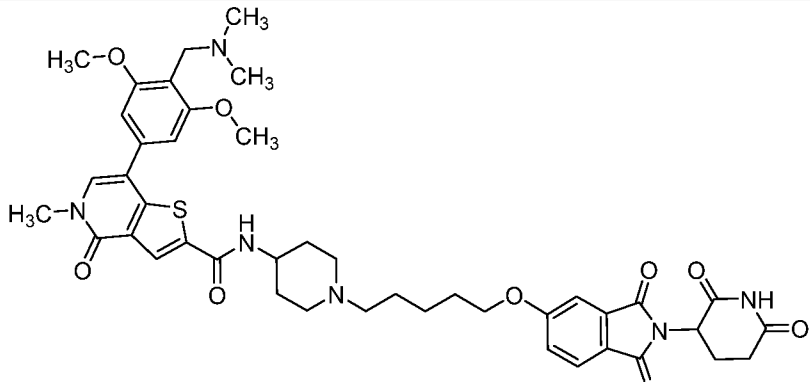
Compound No.	Structure
D66	 Chemical structure of compound D66: A thienopyridine core substituted with a 3,5-bis(methoxy)-4-(dimethylamino)phenyl group at position 6, a methyl group at position 4, and a carbonyl group at position 3. The carbonyl group is linked via an amide bond to a bicyclic amine (8-azabicyclo[3.2.1]octane), which is further connected via a piperazine ring to a phthalimide moiety, which is finally linked to a 2,6-pyridinedione derivative.
D67	 Chemical structure of compound D67: A thienopyridine core substituted with a 3,5-bis(methoxy)-4-(dimethylamino)phenyl group at position 6, a methyl group at position 4, and a carbonyl group at position 3. The carbonyl group is linked via an amide bond to a bicyclic amine (8-azabicyclo[3.2.1]octane), which is further connected via a piperazine ring to a phthalimide moiety, which is finally linked to a 2,6-pyridinedione derivative.
D68	 Chemical structure of compound D68: A thienopyridine core substituted with a 3,5-bis(methoxy)-4-(dimethylamino)phenyl group at position 6, a methyl group at position 4, and a carbonyl group at position 3. The carbonyl group is linked via an amide bond to a bicyclic amine (8-azabicyclo[3.2.1]octane), which is further connected via a piperazine ring to a phthalimide moiety, which is finally linked to a 2,6-pyridinedione derivative.
D69	 Chemical structure of compound D69: A thienopyridine core substituted with a 3,5-bis(methoxy)-4-(dimethylamino)phenyl group at position 6, a methyl group at position 4, and a carbonyl group at position 3. The carbonyl group is linked via an amide bond to a bicyclic amine (8-azabicyclo[3.2.1]octane), which is further connected via a piperazine ring to a phthalimide moiety, which is finally linked to a 2,6-pyridinedione derivative.

Compound No.	Structure
D70	 Chemical structure of compound D70: A thienopyridine core substituted with a 3,4-dimethoxybenzyl-dimethylamino group at position 6, a methyl group at position 4, and a carbonyl group at position 3. The carbonyl group is linked via an amide bond to a bicyclic amine, which is further connected via a methylene chain to a piperazine ring. The piperazine ring is substituted with a 1,2,3,4-tetrahydroquinolin-5(1H)-one moiety.
D71	 Chemical structure of compound D71: A thienopyridine core substituted with a 3,4-dimethoxybenzyl-dimethylamino group at position 6, a methyl group at position 4, and a carbonyl group at position 3. The carbonyl group is linked via an amide bond to a piperidine ring, which is further connected via a carbonyl group to a 4-(4-oxo-1,2,3,4-tetrahydroquinolin-5-yl)butyl ether moiety.
D72	 Chemical structure of compound D72: A thienopyridine core substituted with a 3,4-dimethoxybenzyl-dimethylamino group at position 6, a methyl group at position 4, and a carbonyl group at position 3. The carbonyl group is linked via an amide bond to a bicyclic amine, which is further connected via a carbonyl group to a piperazine ring. The piperazine ring is substituted with a 1,2,3,4-tetrahydroquinolin-5(1H)-one moiety.
D73	 Chemical structure of compound D73: A thienopyridine core substituted with a 3,4-dimethoxybenzyl-dimethylamino group at position 6, a methyl group at position 4, and a carbonyl group at position 3. The carbonyl group is linked via an amide bond to a bicyclic amine, which is further connected via a propyl chain to a piperazine ring. The piperazine ring is substituted with a 1,2,3,4-tetrahydroquinolin-5(1H)-one moiety.

Compound No.	Structure
D74	 Chemical structure of D74: A complex molecule featuring a 4-methoxy-2-(dimethylamino)phenyl group attached to a thienopyridine core. The thienopyridine core is substituted with a methyl group and a carbonyl group. The carbonyl group is linked via an amide bond to a bicyclic amine system (a cyclobutane ring fused to a pyrrolidine ring). This bicyclic system is further linked via an amide bond to a piperazine ring, which is connected to a benzimidazole system. The benzimidazole system is substituted with a methyl group and a carbonyl group, and is linked via an amide bond to a piperidine ring.
D75	 Chemical structure of D75: A complex molecule featuring a 4-methoxy-2-(dimethylamino)phenyl group attached to a thienopyridine core. The thienopyridine core is substituted with a methyl group and a carbonyl group. The carbonyl group is linked via an amide bond to a bicyclic amine system (a cyclobutane ring fused to a pyrrolidine ring). This bicyclic system is further linked via an amide bond to a piperazine ring, which is connected to a benzimidazole system. The benzimidazole system is substituted with a methyl group and a carbonyl group, and is linked via an amide bond to a piperidine ring.
D76	 Chemical structure of D76: A complex molecule featuring a 4-methoxy-2-(dimethylamino)phenyl group attached to a thienopyridine core. The thienopyridine core is substituted with a methyl group and a carbonyl group. The carbonyl group is linked via an amide bond to a bicyclic amine system (a cyclobutane ring fused to a pyrrolidine ring). This bicyclic system is further linked via an amide bond to a piperazine ring, which is connected to a benzimidazole system. The benzimidazole system is substituted with a methyl group and a carbonyl group, and is linked via an amide bond to a piperidine ring.
D77	 Chemical structure of D77: A complex molecule featuring a 4-methoxy-2-(dimethylamino)phenyl group attached to a thienopyridine core. The thienopyridine core is substituted with a methyl group and a carbonyl group. The carbonyl group is linked via an amide bond to a bicyclic amine system (a cyclobutane ring fused to a pyrrolidine ring). This bicyclic system is further linked via an amide bond to a piperazine ring, which is connected to a benzimidazole system. The benzimidazole system is substituted with a methyl group and a carbonyl group, and is linked via an amide bond to a piperidine ring.

Compound No.	Structure
D78	 Chemical structure of D78: A complex molecule featuring a 4-methoxy-2-(dimethylamino)phenyl group attached to a 6-methyl-2-thienylpyridine-3-carboxamide moiety. This is linked via a piperidine ring to a 2-(2-(2-oxo-2,3,4,5-tetrahydropyridin-1(2H)-yl)phenyl)propan-1-one moiety.
D79	 Chemical structure of D79: Similar to D78, but the piperidine ring is substituted with two fluorine atoms at the 4-position.
D80	 Chemical structure of D80: Similar to D78, but the piperidine ring is substituted with a methyl group at the 4-position, and the linker is a 4-methoxyphenyl group.
D81	 Chemical structure of D81: Similar to D80, but the piperidine ring is substituted with a methyl group at the 4-position, and the linker is a 4-methoxyphenyl group.

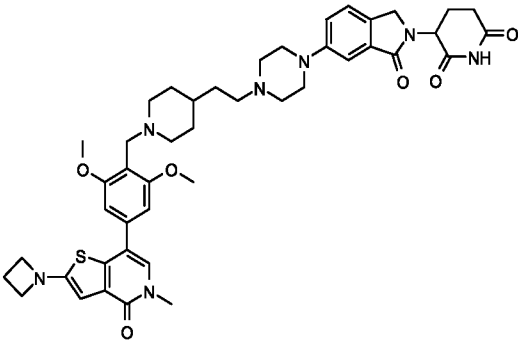
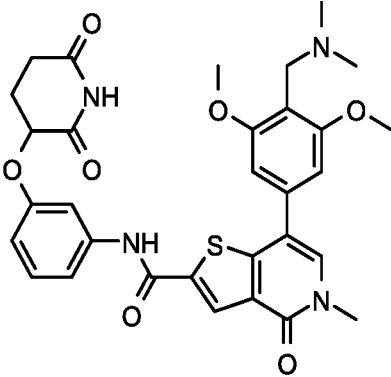
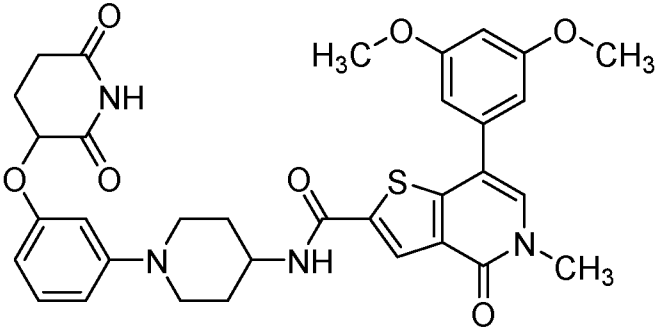
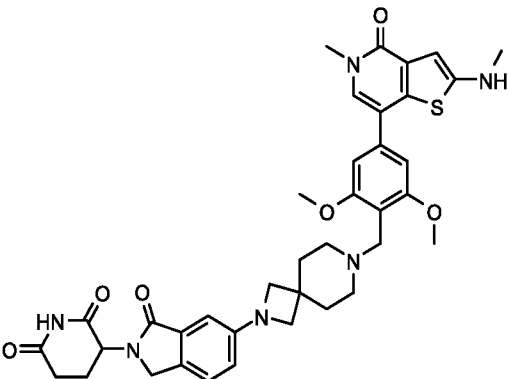
Compound No.	Structure
D82	 Chemical structure of compound D82. It features a central thiophene ring substituted with a 4-(dimethylamino)-3,5-dimethoxyphenyl group, a methyl N-methylpyridine-2-carboxamide group, and a (6-((6-oxo-1,2,3,4-tetrahydropyridin-1(2H)-ylidene)-1H-indolizin-5-yl)oxy)carbamoyl group.
D83	 Chemical structure of compound D83. It features a central thiophene ring substituted with a 4-(dimethylamino)-3,5-dimethoxyphenyl group, a methyl N-methylpyridine-2-carboxamide group, and a (2-(2,2-difluoroethyl)carbamoyl) group.
D84	 Chemical structure of compound D84. It features a central thiophene ring substituted with a 4-(dimethylamino)-3,5-dimethoxyphenyl group, a methyl N-methylpyridine-2-carboxamide group, and a (2-(2-fluoroethyl)carbamoyl) group.
D85	 Chemical structure of compound D85. It features a central thiophene ring substituted with a 4-(dimethylamino)-3,5-dimethoxyphenyl group, a methyl N-methylpyridine-2-carboxamide group, and a (2-(2-fluoroethyl)carbamoyl) group.

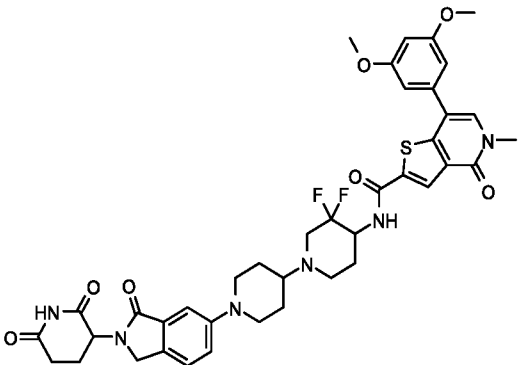
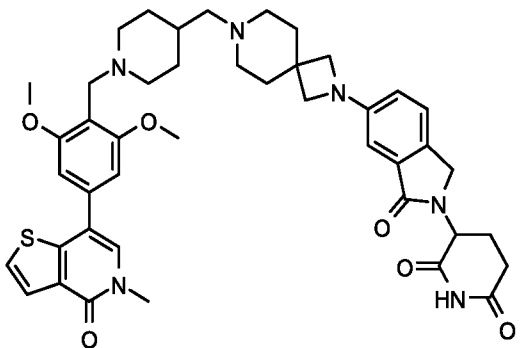
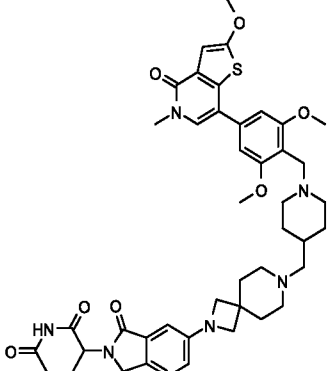
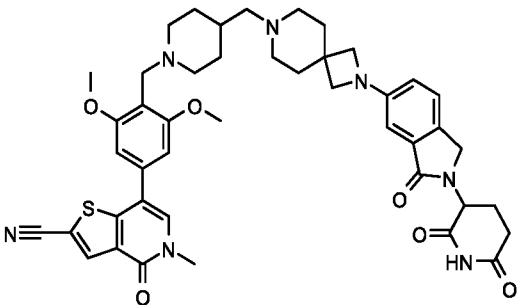
Compound No.	Structure
D86	 Chemical structure of compound D86: A thienopyridine core substituted with a 3,4-dimethoxybenzyl(methyl)amino group at position 6, a methyl group on the pyridine nitrogen, and a (4-((4-methyl-2-oxo-1,2,3,4-tetrahydropyridin-1(2H)-yl)-1H-benzimidazol-5-yl)oxy)butyl)carbamoyl group at position 3.
D87	 Chemical structure of compound D87: A thienopyridine core substituted with a 3,4-dimethoxybenzyl(methyl)amino group at position 6, a methyl group on the pyridine nitrogen, and a (4-((4-methyl-2-oxo-1,2,3,4-tetrahydropyridin-1(2H)-yl)-1H-benzimidazol-5-yl)oxy)octyl)carbamoyl group at position 3.
D88	 Chemical structure of compound D88: A thienopyridine core substituted with a 3,4-dimethoxybenzyl(methyl)amino group at position 6, a methyl group on the pyridine nitrogen, and a (4-((4-methyl-2-oxo-1,2,3,4-tetrahydropyridin-1(2H)-yl)-1H-benzimidazol-5-yl)oxy)octyl)carbamoyl group at position 3.
D89	 Chemical structure of compound D89: A thienopyridine core substituted with a 3,4-dimethoxybenzyl(methyl)amino group at position 6, a methyl group on the pyridine nitrogen, and a (4-((4-methyl-2-oxo-1,2,3,4-tetrahydropyridin-1(2H)-yl)-1H-benzimidazol-5-yl)oxy)butyl)carbamoyl group at position 3.

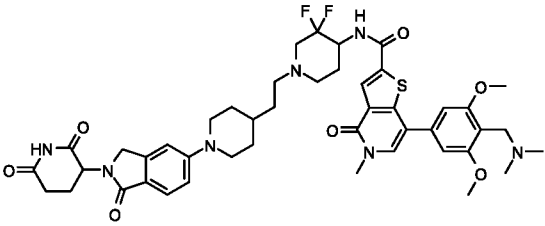
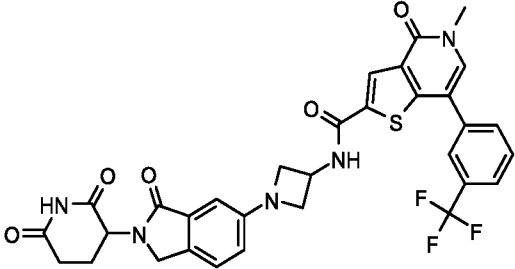
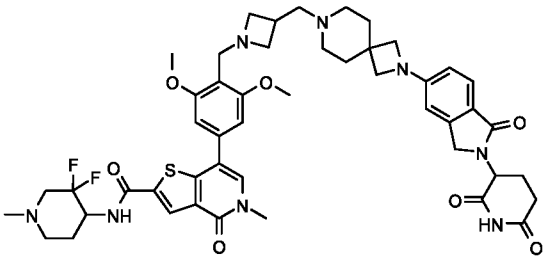
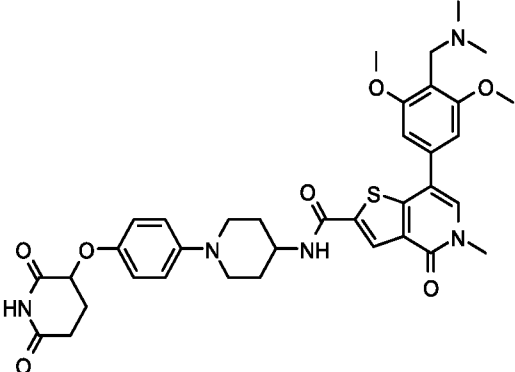
Compound No.	Structure
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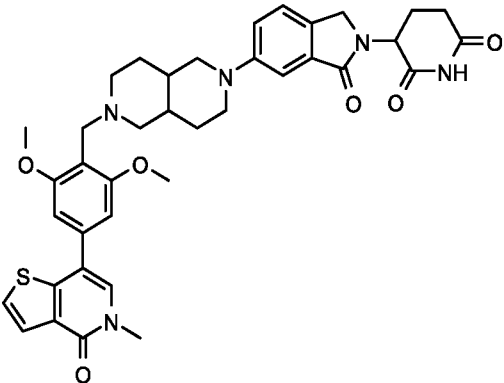
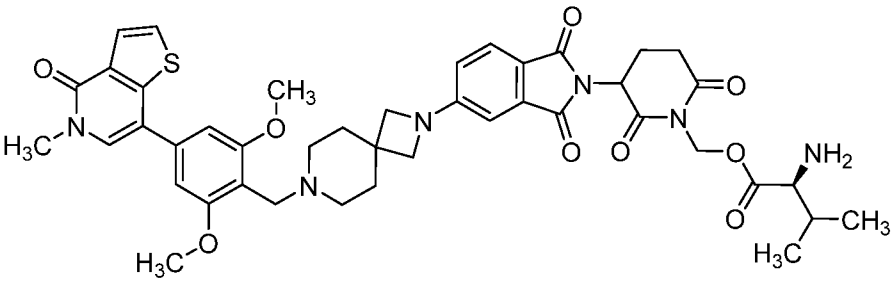
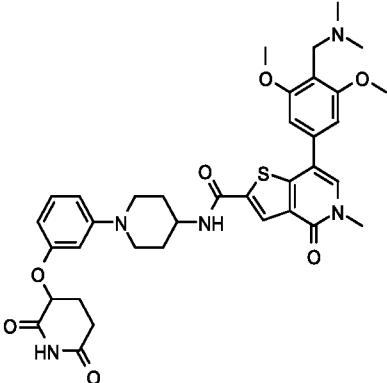
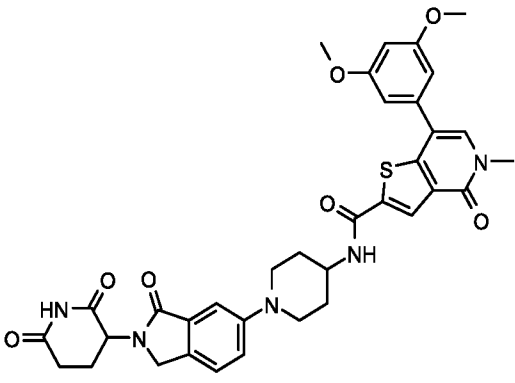
Table 2C. Compounds D91-D220 of the Disclosure

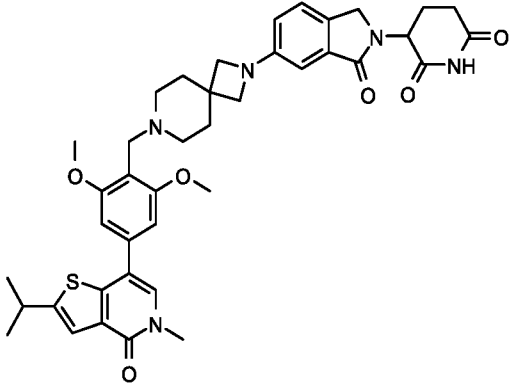
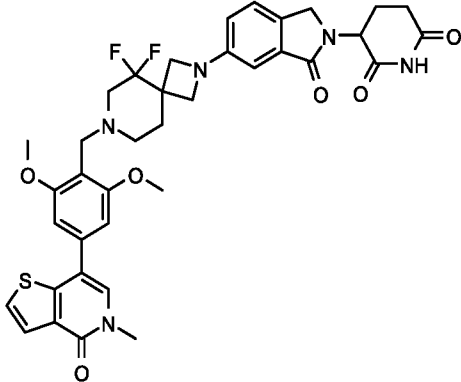
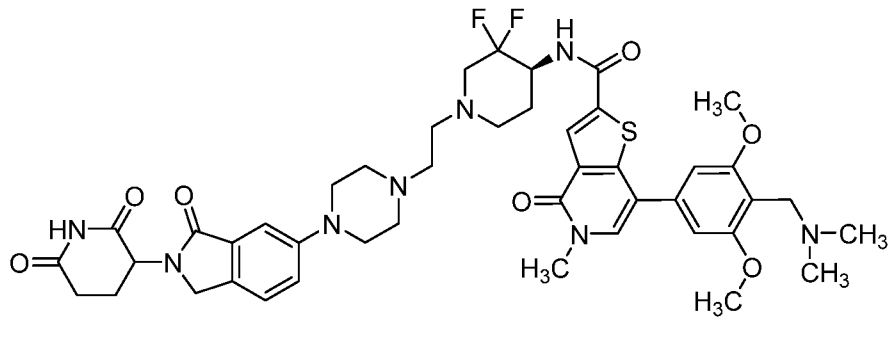
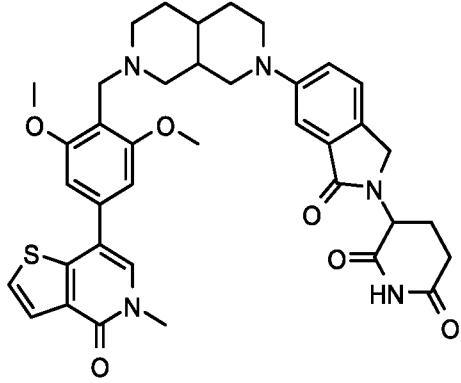
Compound No.	Structure
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D92	
D93	

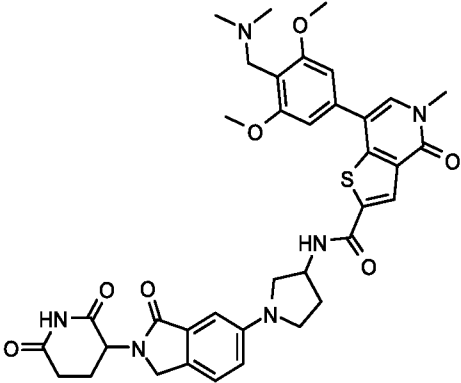
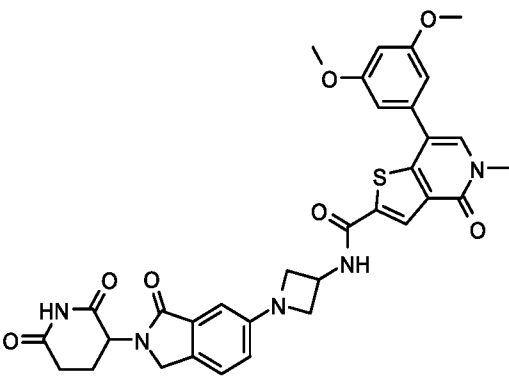
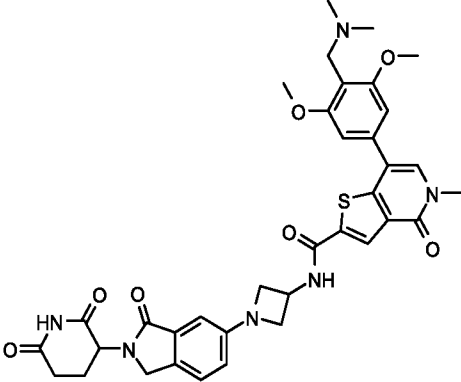
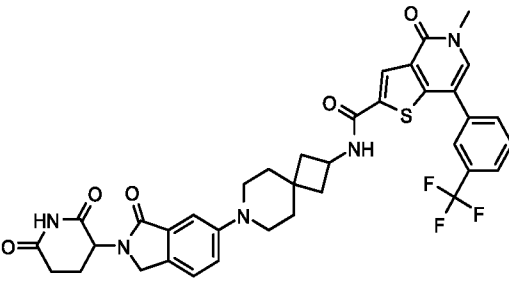
Compound No.	Structure
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D95	
D96	
D97	

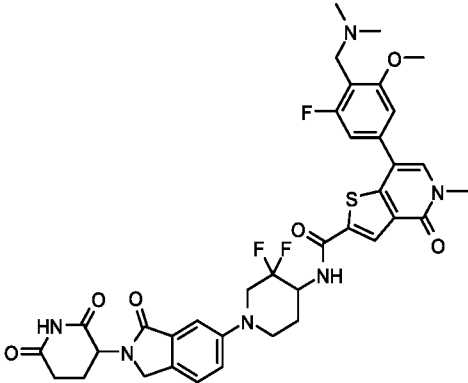
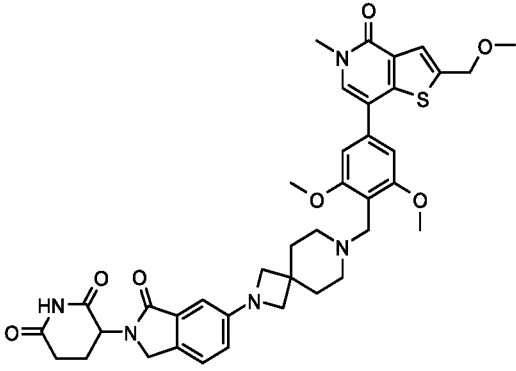
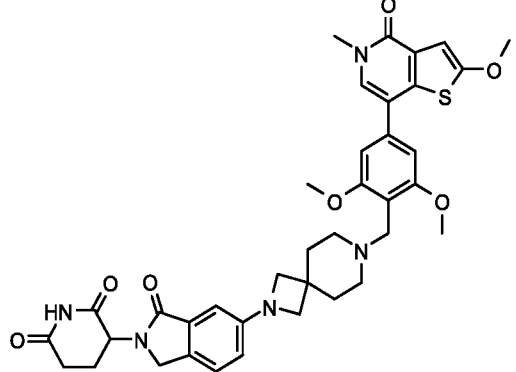
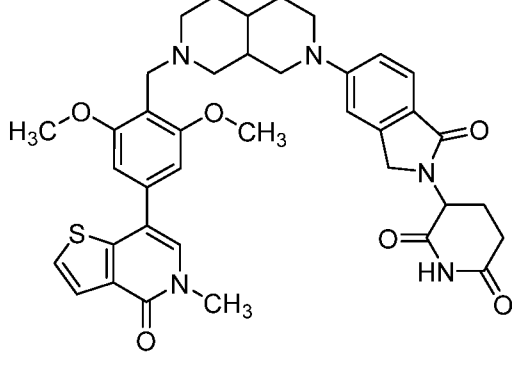
Compound No.	Structure
D98	 Chemical structure of compound D98. It features a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. The benzene ring is substituted at the 2-position with a piperidine ring, which is further substituted at the 4-position with a 1,1-difluoroethyl group. The piperidine ring is also substituted at the 2-position with a 4-methoxyphenyl group.
D99	 Chemical structure of compound D99. It features a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. The benzene ring is substituted at the 2-position with a piperidine ring, which is further substituted at the 4-position with a 1,1-difluoroethyl group. The piperidine ring is also substituted at the 2-position with a 4-methoxyphenyl group.
D100	 Chemical structure of compound D100. It features a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. The benzene ring is substituted at the 2-position with a piperidine ring, which is further substituted at the 4-position with a 1,1-difluoroethyl group. The piperidine ring is also substituted at the 2-position with a 4-methoxyphenyl group.
D101	 Chemical structure of compound D101. It features a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. The benzene ring is substituted at the 2-position with a piperidine ring, which is further substituted at the 4-position with a 1,1-difluoroethyl group. The piperidine ring is also substituted at the 2-position with a 4-methoxyphenyl group.

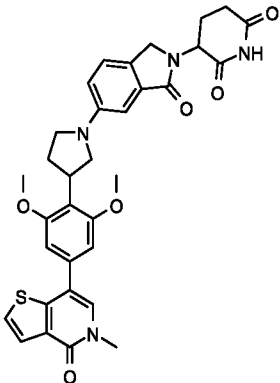
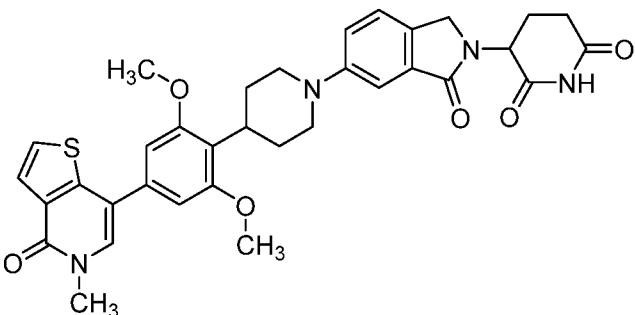
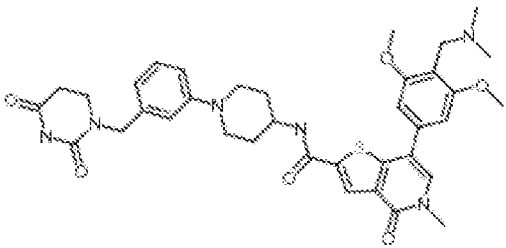
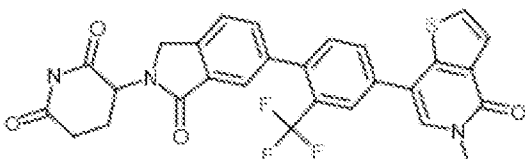
Compound No.	Structure
D102	 Chemical structure of D102: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. The benzene ring is substituted with a piperidine ring at the 2-position and a 4-(2,6-dimethoxyphenyl)-2,6-dimethyl-1,2,4-triazine-3-carboxamide group at the 3-position. The piperidine ring is further substituted with a 4-(2,6-difluoro-4-oxo-4,5,6,7-tetrahydro-1H-benzothiazol-3-yl)-2,6-dimethyl-1,2,4-triazine-3-carboxamide group at the 4-position.
D103	 Chemical structure of D103: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. The benzene ring is substituted with a piperidine ring at the 2-position and a 4-(2,6-difluoro-4-oxo-4,5,6,7-tetrahydro-1H-benzothiazol-3-yl)-2,6-dimethyl-1,2,4-triazine-3-carboxamide group at the 3-position. The piperidine ring is further substituted with a 4-(2,6-difluoro-4-oxo-4,5,6,7-tetrahydro-1H-benzothiazol-3-yl)-2,6-dimethyl-1,2,4-triazine-3-carboxamide group at the 4-position.
D104	 Chemical structure of D104: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. The benzene ring is substituted with a piperidine ring at the 2-position and a 4-(2,6-difluoro-4-oxo-4,5,6,7-tetrahydro-1H-benzothiazol-3-yl)-2,6-dimethyl-1,2,4-triazine-3-carboxamide group at the 3-position. The piperidine ring is further substituted with a 4-(2,6-difluoro-4-oxo-4,5,6,7-tetrahydro-1H-benzothiazol-3-yl)-2,6-dimethyl-1,2,4-triazine-3-carboxamide group at the 4-position.
D105	 Chemical structure of D105: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. The benzene ring is substituted with a piperidine ring at the 2-position and a 4-(2,6-difluoro-4-oxo-4,5,6,7-tetrahydro-1H-benzothiazol-3-yl)-2,6-dimethyl-1,2,4-triazine-3-carboxamide group at the 3-position. The piperidine ring is further substituted with a 4-(2,6-difluoro-4-oxo-4,5,6,7-tetrahydro-1H-benzothiazol-3-yl)-2,6-dimethyl-1,2,4-triazine-3-carboxamide group at the 4-position.

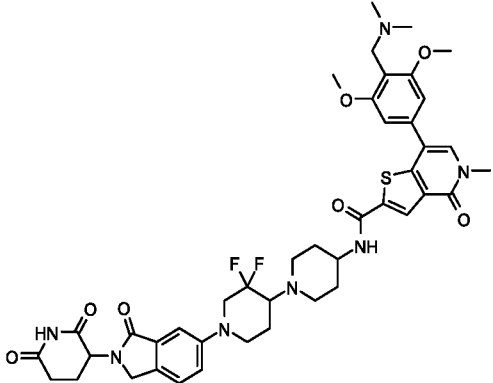
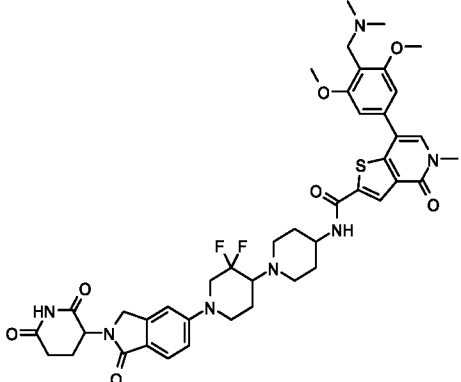
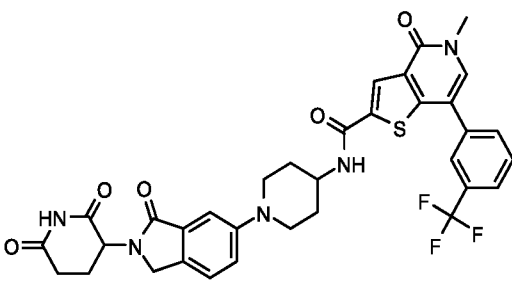
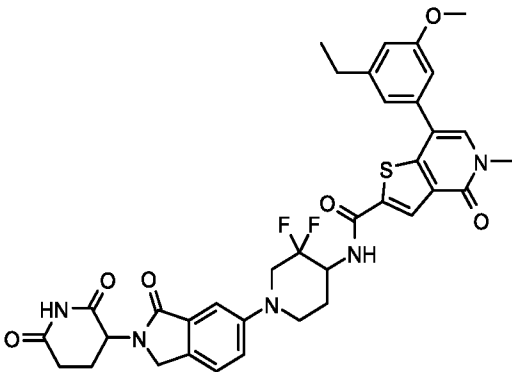
Compound No.	Structure
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D107	
D108	
D109	

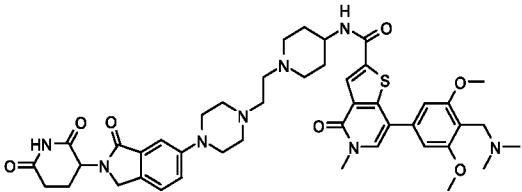
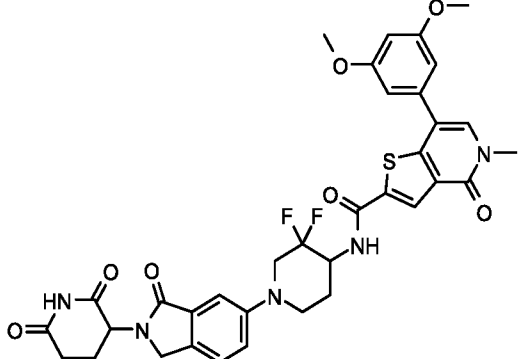
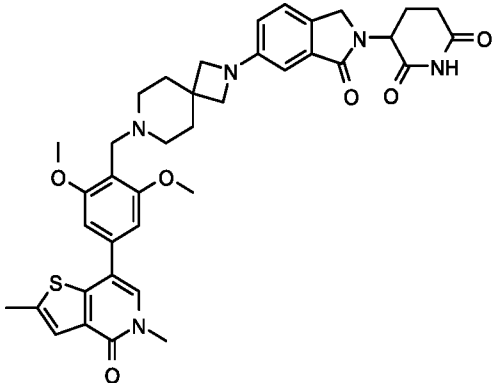
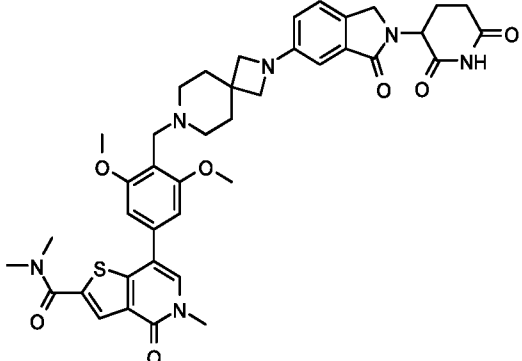
Compound No.	Structure
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D111	
D112	
D113	

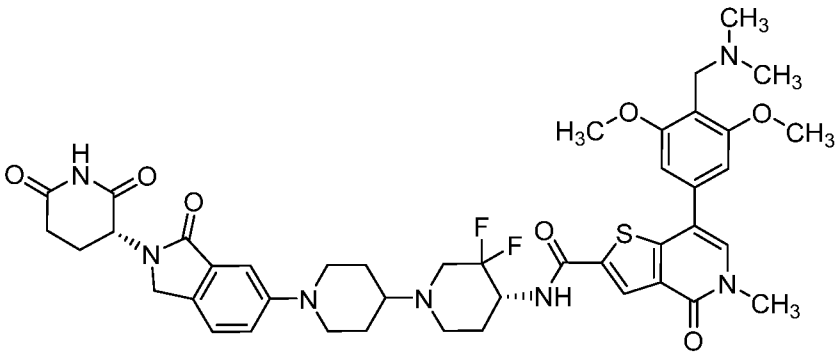
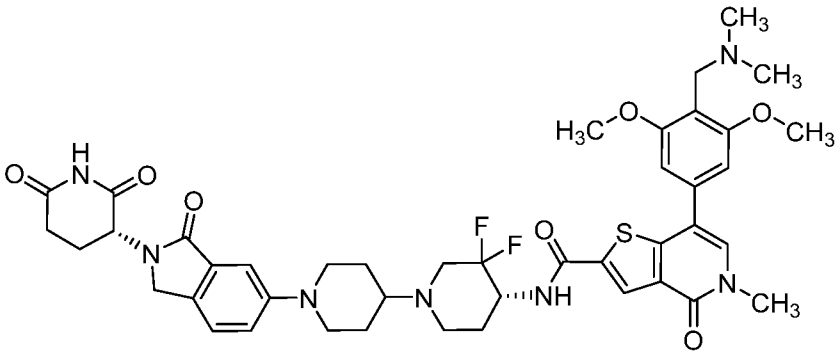
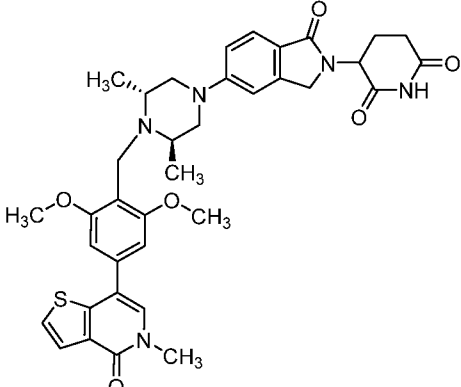
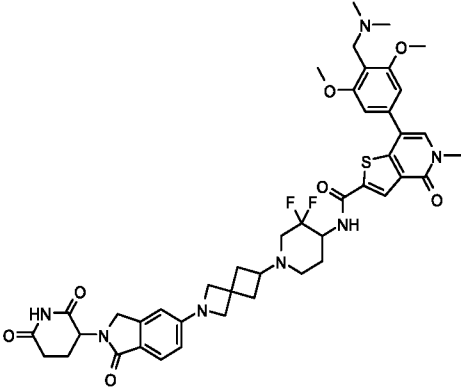
Compound No.	Structure
D114	 Chemical structure of D114: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. The core is substituted at the 2-position with a 4-methoxy-2-(dimethylamino)phenyl group and at the 3-position with a 4-methoxy-2-(dimethylamino)phenyl group. The 4-position of the phenyl ring is substituted with a 4-methoxy-2-(dimethylamino)phenyl group. The 5-position of the phenyl ring is substituted with a 4-methoxy-2-(dimethylamino)phenyl group.
D115	 Chemical structure of D115: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. The core is substituted at the 2-position with a 4-methoxy-2-(dimethylamino)phenyl group and at the 3-position with a 4-methoxy-2-(dimethylamino)phenyl group. The 4-position of the phenyl ring is substituted with a 4-methoxy-2-(dimethylamino)phenyl group. The 5-position of the phenyl ring is substituted with a 4-methoxy-2-(dimethylamino)phenyl group.
D116	 Chemical structure of D116: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. The core is substituted at the 2-position with a 4-methoxy-2-(dimethylamino)phenyl group and at the 3-position with a 4-methoxy-2-(dimethylamino)phenyl group. The 4-position of the phenyl ring is substituted with a 4-methoxy-2-(dimethylamino)phenyl group. The 5-position of the phenyl ring is substituted with a 4-methoxy-2-(dimethylamino)phenyl group.
D117	 Chemical structure of D117: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. The core is substituted at the 2-position with a 4-methoxy-2-(dimethylamino)phenyl group and at the 3-position with a 4-methoxy-2-(dimethylamino)phenyl group. The 4-position of the phenyl ring is substituted with a 4-methoxy-2-(dimethylamino)phenyl group. The 5-position of the phenyl ring is substituted with a 4-methoxy-2-(dimethylamino)phenyl group.

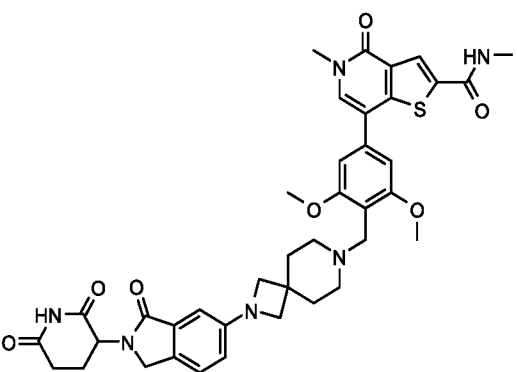
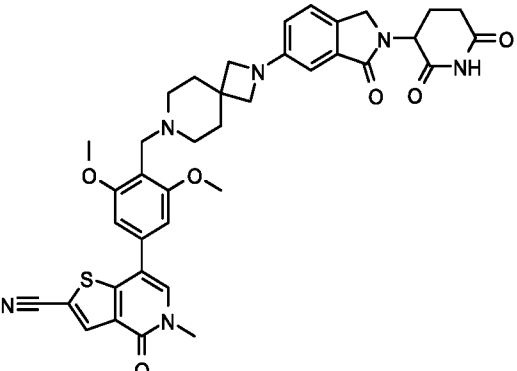
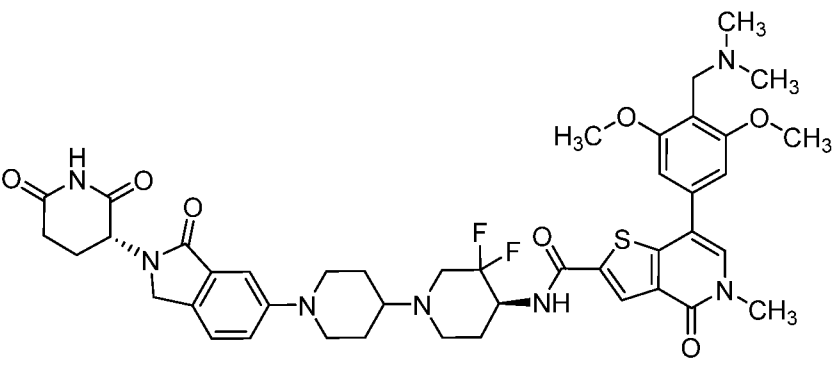
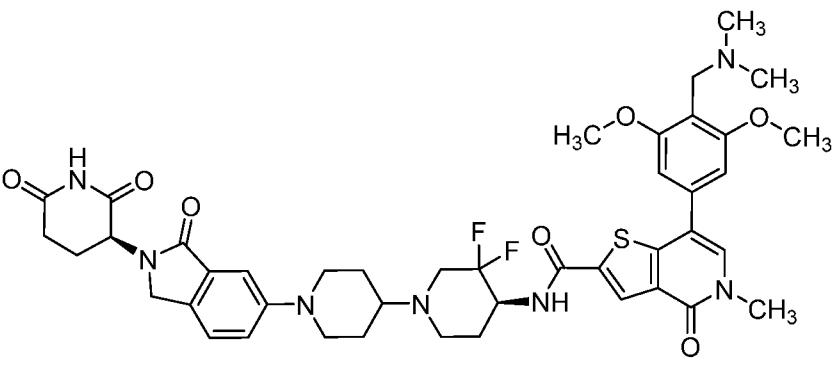
Compound No.	Structure
D118	 Chemical structure of D118: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. This core is linked via a piperidine ring to a 2,2-difluoroethylamine moiety. The amine is further connected to a thiazole ring, which is substituted with a 4-(dimethylamino)-2-fluorophenyl group and a methyl group.
D119	 Chemical structure of D119: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. This core is linked via a piperidine ring to a 2,2-difluoroethylamine moiety. The amine is further connected to a thiazole ring, which is substituted with a 4-(dimethylamino)-2-fluorophenyl group and a methyl group.
D120	 Chemical structure of D120: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. This core is linked via a piperidine ring to a 2,2-difluoroethylamine moiety. The amine is further connected to a thiazole ring, which is substituted with a 4-(dimethylamino)-2-fluorophenyl group and a methyl group.
D121	 Chemical structure of D121: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. This core is linked via a piperidine ring to a 2,2-difluoroethylamine moiety. The amine is further connected to a thiazole ring, which is substituted with a 4-(dimethylamino)-2-fluorophenyl group and a methyl group.

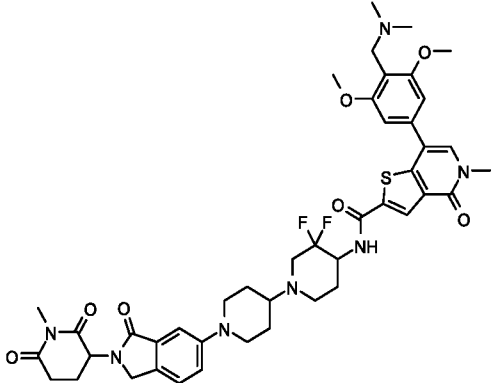
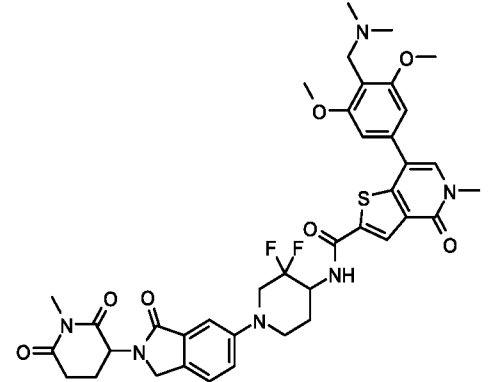
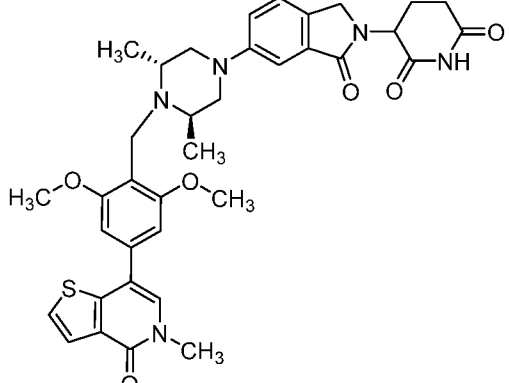
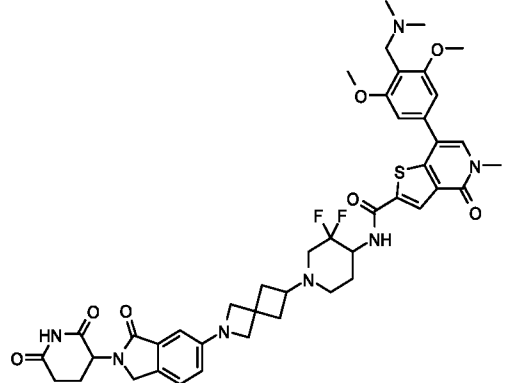
Compound No.	Structure
D122	 Chemical structure of D122: A 6-methyl-2-thienylpyridine-3-carboxamide derivative. The pyridine ring is substituted with a methyl group at position 6 and a thienyl group at position 3. The amide group is attached to the pyridine ring via a methylene linker. The thienyl group is substituted with a methoxy group at position 5 and a methoxymethyl group at position 4. The amide group is further substituted with a methylene linker, which is connected to a benzimidazole ring system. The benzimidazole ring is substituted with a methoxy group at position 2 and a methoxymethyl group at position 4. The amide group is further substituted with a methylene linker, which is connected to a benzimidazole ring system. The benzimidazole ring is substituted with a methoxy group at position 2 and a methoxymethyl group at position 4.
D123	 Chemical structure of D123: A 6-methoxy-2-thienylpyridine-3-carboxamide derivative. The pyridine ring is substituted with a methoxy group at position 6 and a thienyl group at position 3. The amide group is attached to the pyridine ring via a methylene linker. The thienyl group is substituted with a methoxy group at position 5 and a methoxymethyl group at position 4. The amide group is further substituted with a methylene linker, which is connected to a benzimidazole ring system. The benzimidazole ring is substituted with a methoxy group at position 2 and a methoxymethyl group at position 4. The amide group is further substituted with a methylene linker, which is connected to a benzimidazole ring system. The benzimidazole ring is substituted with a methoxy group at position 2 and a methoxymethyl group at position 4.
D124	 Chemical structure of D124: A 6-methoxy-2-thienylpyridine-3-carboxamide derivative. The pyridine ring is substituted with a methoxy group at position 6 and a thienyl group at position 3. The amide group is attached to the pyridine ring via a methylene linker. The thienyl group is substituted with a methoxy group at position 5 and a methoxymethyl group at position 4. The amide group is further substituted with a methylene linker, which is connected to a benzimidazole ring system. The benzimidazole ring is substituted with a methoxy group at position 2 and a methoxymethyl group at position 4. The amide group is further substituted with a methylene linker, which is connected to a benzimidazole ring system. The benzimidazole ring is substituted with a methoxy group at position 2 and a methoxymethyl group at position 4.
D125	 Chemical structure of D125: A 6-methoxy-2-thienylpyridine-3-carboxamide derivative. The pyridine ring is substituted with a methoxy group at position 6 and a thienyl group at position 3. The amide group is attached to the pyridine ring via a methylene linker. The thienyl group is substituted with a methoxy group at position 5 and a methoxymethyl group at position 4. The amide group is further substituted with a methylene linker, which is connected to a benzimidazole ring system. The benzimidazole ring is substituted with a methoxy group at position 2 and a methoxymethyl group at position 4. The amide group is further substituted with a methylene linker, which is connected to a benzimidazole ring system. The benzimidazole ring is substituted with a methoxy group at position 2 and a methoxymethyl group at position 4.

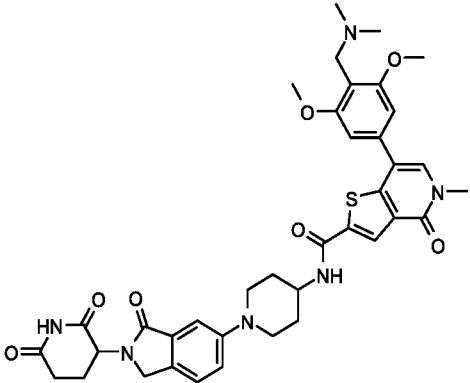
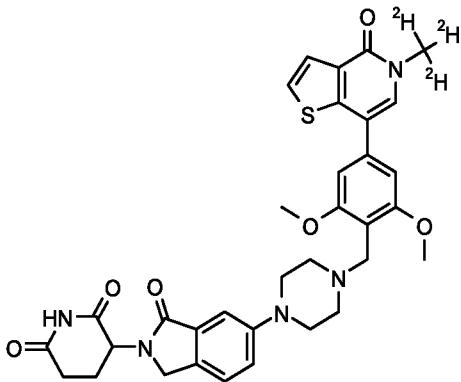
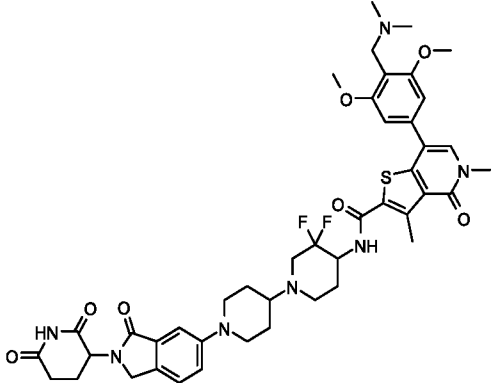
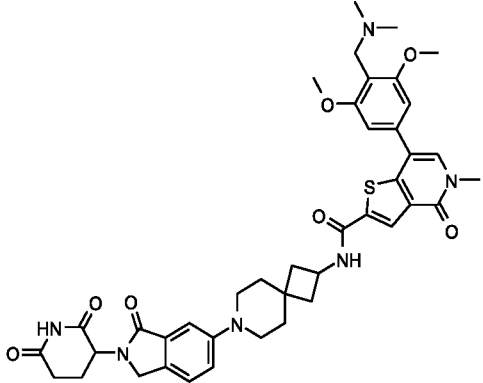
Compound No.	Structure
D126	 Chemical structure of D126: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. The core is substituted with a 4-(2,6-dimethoxy-4-(2-methoxy-2-methyl-4-(2-methyl-4-methoxyphenyl)-5-methylthiazol-4-yl)-5-methylthiazol-2-yl)-2-methylthiazol-4-yl group. The core is also substituted with a 4-(2,6-dimethoxy-4-(2-methoxy-2-methyl-4-(2-methyl-4-methoxyphenyl)-5-methylthiazol-4-yl)-5-methylthiazol-2-yl)-2-methylthiazol-4-yl group.
D127	 Chemical structure of D127: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. The core is substituted with a 4-(2,6-dimethoxy-4-(2-methoxy-2-methyl-4-(2-methyl-4-methoxyphenyl)-5-methylthiazol-4-yl)-5-methylthiazol-2-yl)-2-methylthiazol-4-yl group. The core is also substituted with a 4-(2,6-dimethoxy-4-(2-methoxy-2-methyl-4-(2-methyl-4-methoxyphenyl)-5-methylthiazol-4-yl)-5-methylthiazol-2-yl)-2-methylthiazol-4-yl group.
D128	 Chemical structure of D128: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. The core is substituted with a 4-(2,6-dimethoxy-4-(2-methoxy-2-methyl-4-(2-methyl-4-methoxyphenyl)-5-methylthiazol-4-yl)-5-methylthiazol-2-yl)-2-methylthiazol-4-yl group. The core is also substituted with a 4-(2,6-dimethoxy-4-(2-methoxy-2-methyl-4-(2-methyl-4-methoxyphenyl)-5-methylthiazol-4-yl)-5-methylthiazol-2-yl)-2-methylthiazol-4-yl group.
D129	 Chemical structure of D129: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. The core is substituted with a 4-(2,6-dimethoxy-4-(2-methoxy-2-methyl-4-(2-methyl-4-methoxyphenyl)-5-methylthiazol-4-yl)-5-methylthiazol-2-yl)-2-methylthiazol-4-yl group. The core is also substituted with a 4-(2,6-dimethoxy-4-(2-methoxy-2-methyl-4-(2-methyl-4-methoxyphenyl)-5-methylthiazol-4-yl)-5-methylthiazol-2-yl)-2-methylthiazol-4-yl group.

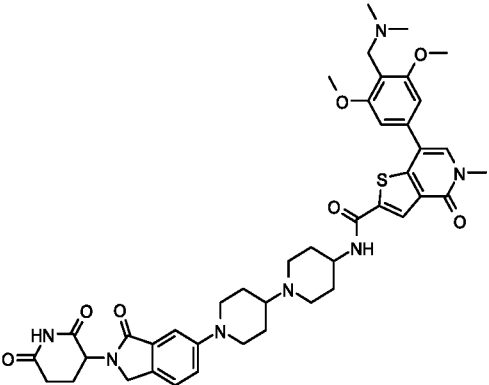
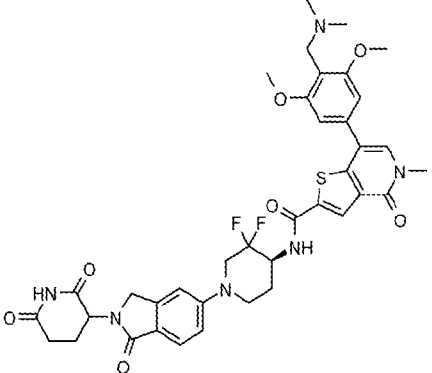
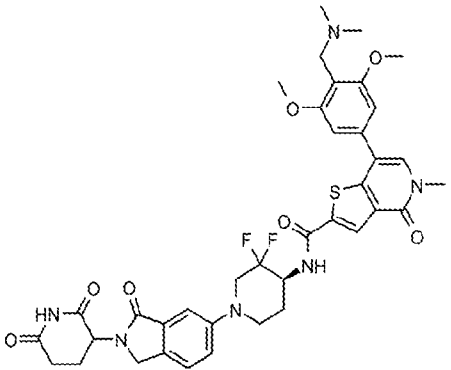
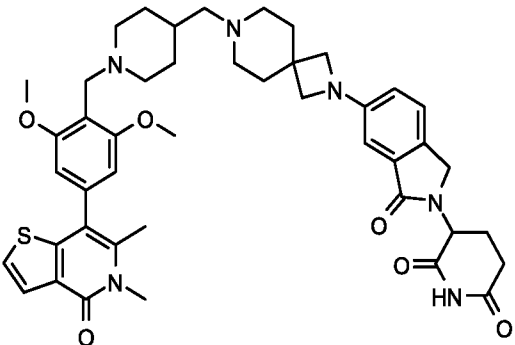
Compound No.	Structure
D130	 Chemical structure of D130: A complex molecule featuring a 1,2,3,4-tetrahydroquinolin-5(1H)-one core. The quinoline ring is substituted at the 6-position with a piperazine ring, which is further substituted with a 4-methoxyphenyl group and a 4-methoxy-2-methyl-5-(dimethylamino)phenyl group. The quinoline ring is also substituted at the 8-position with a 4-methoxyphenyl group.
D131	 Chemical structure of D131: A complex molecule featuring a 1,2,3,4-tetrahydroquinolin-5(1H)-one core. The quinoline ring is substituted at the 6-position with a piperazine ring, which is further substituted with a 4-methoxyphenyl group and a 4-methoxy-2-methyl-5-(dimethylamino)phenyl group. The quinoline ring is also substituted at the 8-position with a 4-methoxyphenyl group.
D132	 Chemical structure of D132: A complex molecule featuring a 1,2,3,4-tetrahydroquinolin-5(1H)-one core. The quinoline ring is substituted at the 6-position with a piperazine ring, which is further substituted with a 4-methoxyphenyl group and a 4-methoxy-2-methyl-5-(dimethylamino)phenyl group. The quinoline ring is also substituted at the 8-position with a 4-methoxyphenyl group.
D133	 Chemical structure of D133: A complex molecule featuring a 1,2,3,4-tetrahydroquinolin-5(1H)-one core. The quinoline ring is substituted at the 6-position with a piperazine ring, which is further substituted with a 4-methoxyphenyl group and a 4-methoxy-2-methyl-5-(dimethylamino)phenyl group. The quinoline ring is also substituted at the 8-position with a 4-methoxyphenyl group.

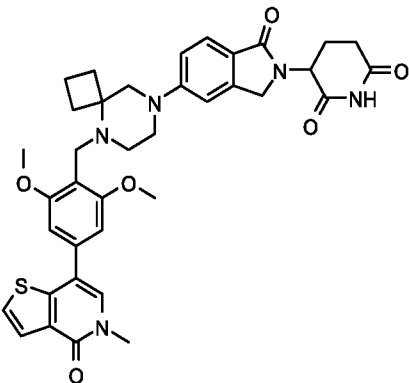
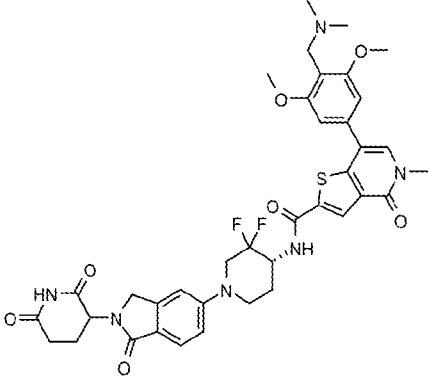
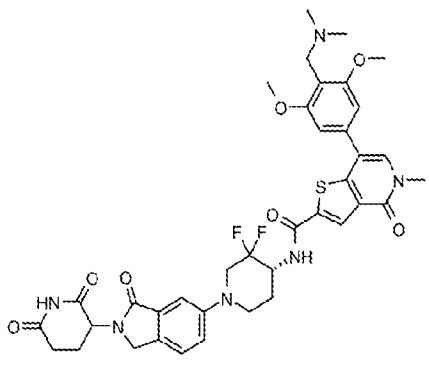
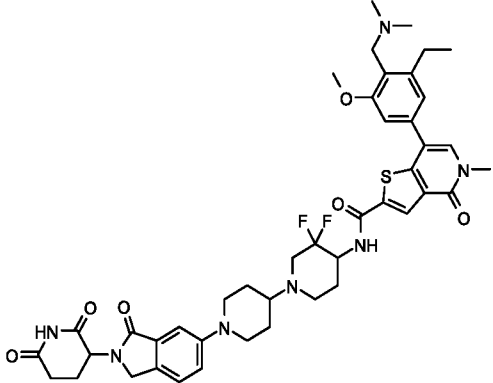
Compound No.	Structure
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D135	
D136	
D137	

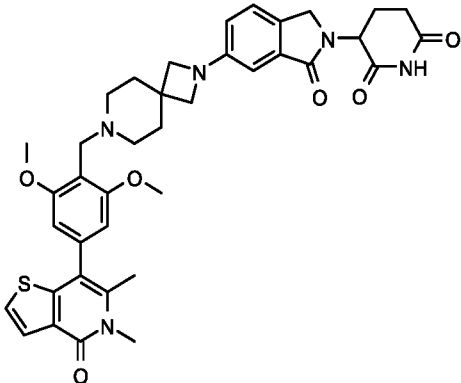
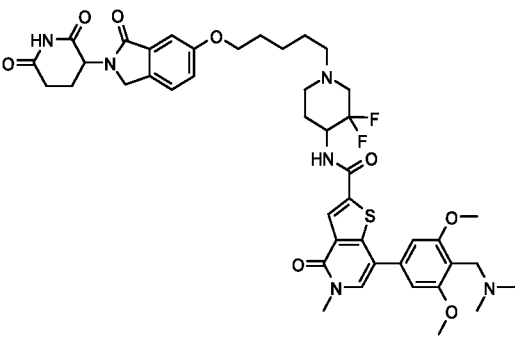
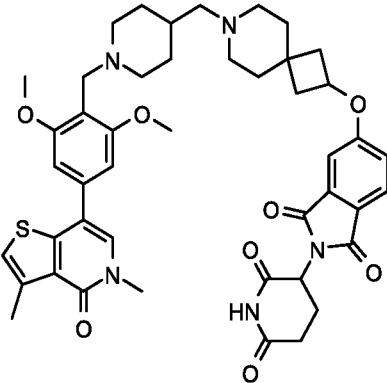
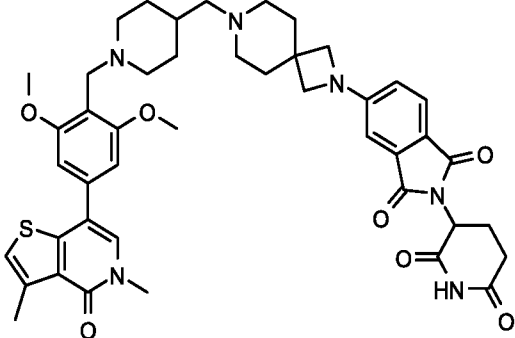
Compound No.	Structure
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D139	
D140	
D141	

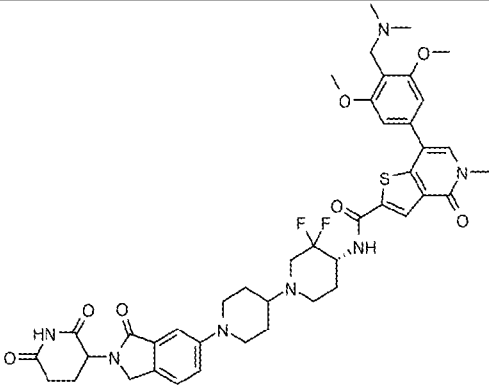
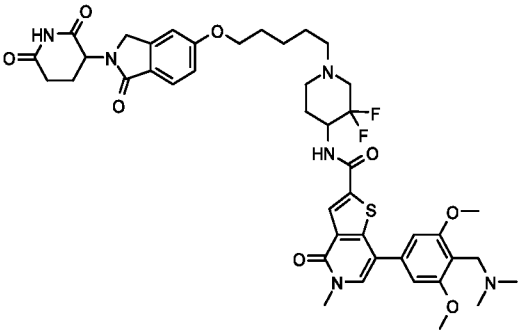
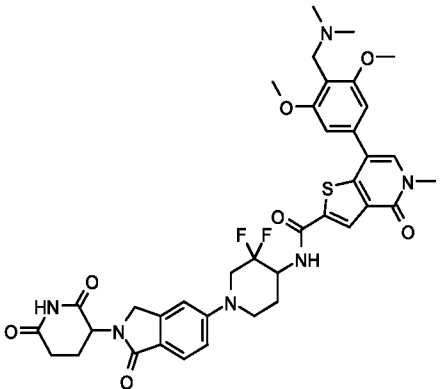
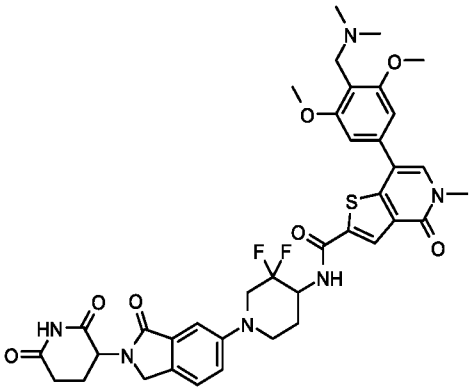
Compound No.	Structure
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D143	
D144	
D145	

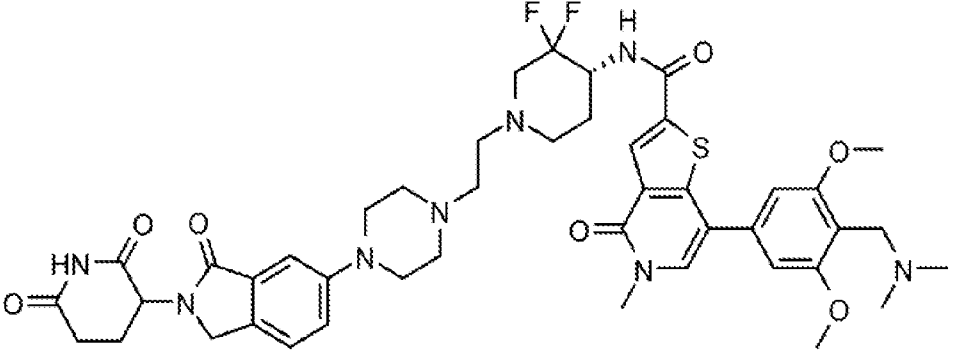
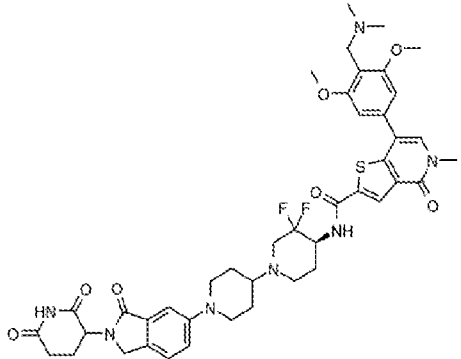
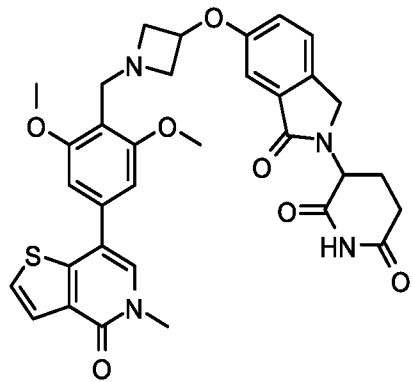
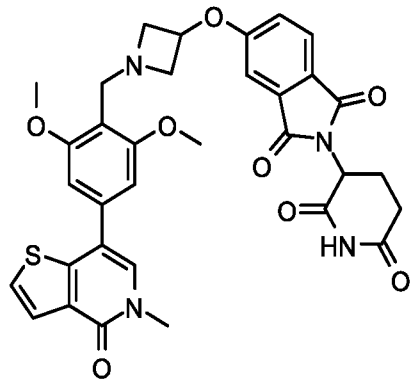
Compound No.	Structure
D146	 Chemical structure of D146: A complex molecule featuring a 6,7-bis(methylene)indole-1,3-dione core. The indole ring is substituted with a piperidine ring at the 2-position. The piperidine ring is further substituted with a 4-(dimethylamino)-2-methoxyphenyl group at the 4-position and a 4-(dimethylamino)-2-methoxyphenyl group at the 6-position. The 4-(dimethylamino)-2-methoxyphenyl group is also substituted with a 4-(dimethylamino)-2-methoxyphenyl group at the 4-position.
D147	 Chemical structure of D147: A complex molecule featuring a 6,7-bis(methylene)indole-1,3-dione core. The indole ring is substituted with a piperidine ring at the 2-position. The piperidine ring is further substituted with a 4-(dimethylamino)-2-methoxyphenyl group at the 4-position and a 4-(dimethylamino)-2-methoxyphenyl group at the 6-position. The 4-(dimethylamino)-2-methoxyphenyl group is also substituted with a 4-(dimethylamino)-2-methoxyphenyl group at the 4-position.
D148	 Chemical structure of D148: A complex molecule featuring a 6,7-bis(methylene)indole-1,3-dione core. The indole ring is substituted with a piperidine ring at the 2-position. The piperidine ring is further substituted with a 4-(dimethylamino)-2-methoxyphenyl group at the 4-position and a 4-(dimethylamino)-2-methoxyphenyl group at the 6-position. The 4-(dimethylamino)-2-methoxyphenyl group is also substituted with a 4-(dimethylamino)-2-methoxyphenyl group at the 4-position.
D149	 Chemical structure of D149: A complex molecule featuring a 6,7-bis(methylene)indole-1,3-dione core. The indole ring is substituted with a piperidine ring at the 2-position. The piperidine ring is further substituted with a 4-(dimethylamino)-2-methoxyphenyl group at the 4-position and a 4-(dimethylamino)-2-methoxyphenyl group at the 6-position. The 4-(dimethylamino)-2-methoxyphenyl group is also substituted with a 4-(dimethylamino)-2-methoxyphenyl group at the 4-position.

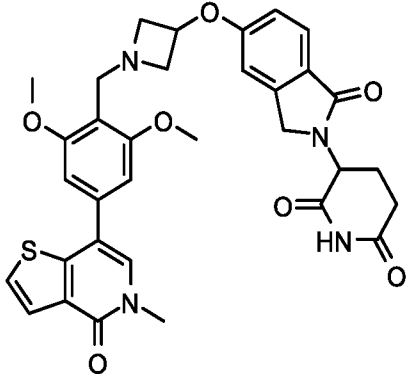
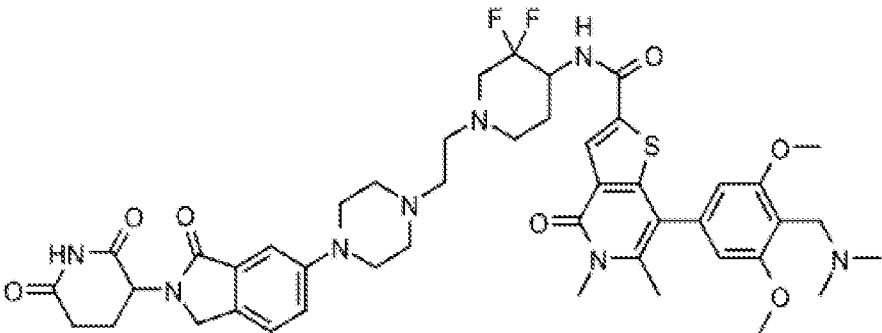
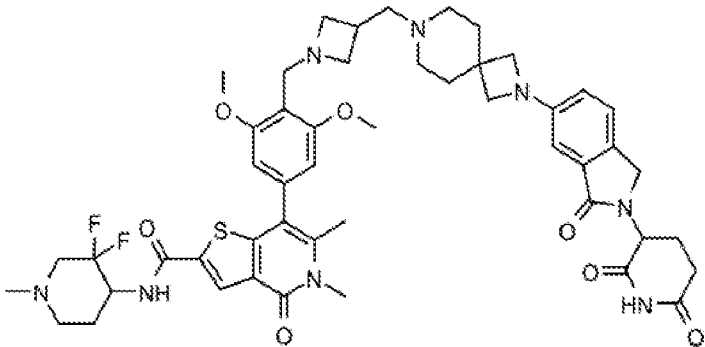
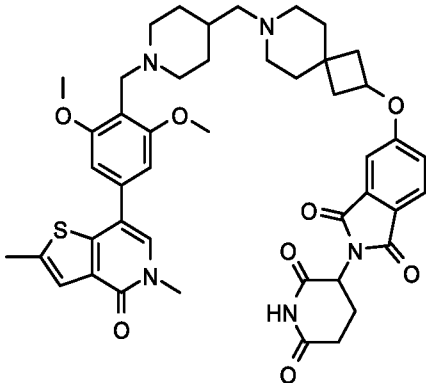
Compound No.	Structure
D150	 Chemical structure of D150: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. This core is linked via a piperidine ring to another piperidine ring, which is further connected to a thiazole ring. The thiazole ring is substituted with a 4-methoxy-2-(dimethylamino)phenyl group and a carbonyl group. The carbonyl group is linked to a piperidine ring, which is also connected to a thiazole ring. The thiazole ring is substituted with a 4-methoxy-2-(dimethylamino)phenyl group and a carbonyl group.
D151	 Chemical structure of D151: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. This core is linked via a piperidine ring to another piperidine ring, which is further connected to a thiazole ring. The thiazole ring is substituted with a 4-methoxy-2-(dimethylamino)phenyl group and a carbonyl group. The carbonyl group is linked to a piperidine ring, which is also connected to a thiazole ring. The thiazole ring is substituted with a 4-methoxy-2-(dimethylamino)phenyl group and a carbonyl group.
D152	 Chemical structure of D152: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. This core is linked via a piperidine ring to another piperidine ring, which is further connected to a thiazole ring. The thiazole ring is substituted with a 4-methoxy-2-(dimethylamino)phenyl group and a carbonyl group. The carbonyl group is linked to a piperidine ring, which is also connected to a thiazole ring. The thiazole ring is substituted with a 4-methoxy-2-(dimethylamino)phenyl group and a carbonyl group.
D153	 Chemical structure of D153: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. This core is linked via a piperidine ring to another piperidine ring, which is further connected to a thiazole ring. The thiazole ring is substituted with a 4-methoxy-2-(dimethylamino)phenyl group and a carbonyl group. The carbonyl group is linked to a piperidine ring, which is also connected to a thiazole ring. The thiazole ring is substituted with a 4-methoxy-2-(dimethylamino)phenyl group and a carbonyl group.

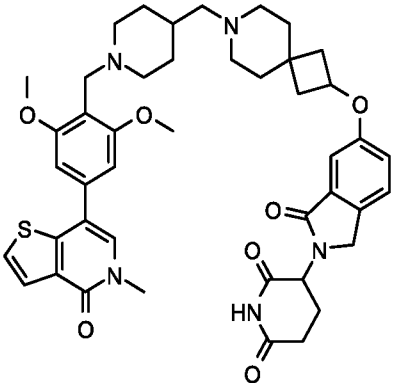
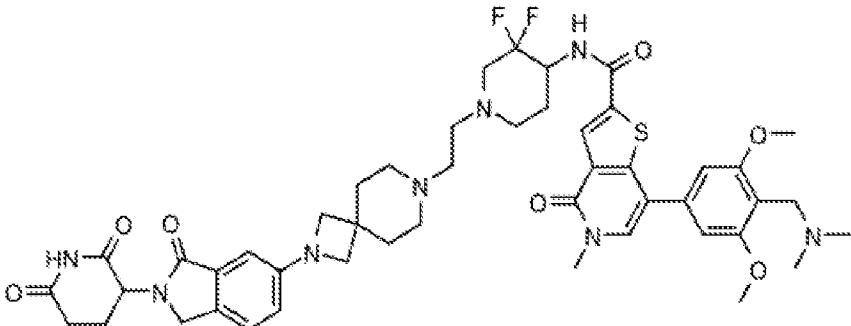
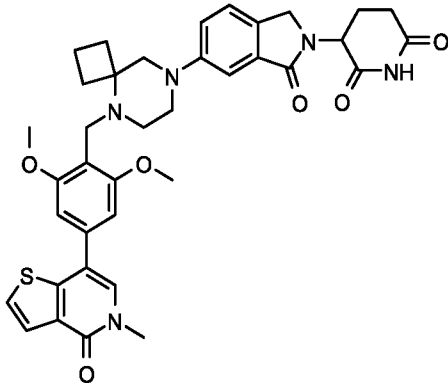
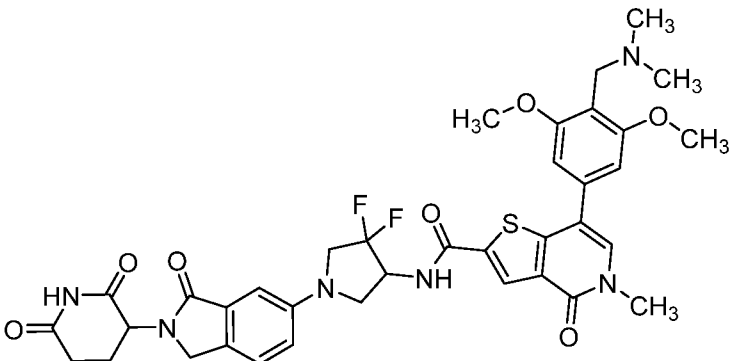
Compound No.	Structure
D154	 Chemical structure of D154: A complex molecule featuring a 4-methoxy-2-(methylthio)phenyl group connected via a methylene bridge to a piperazine ring. The piperazine ring is further substituted with a cyclobutyl group and a 1-(2-oxo-2,3-dihydro-1H-benz[e][1,2,4]oxadiazol-5-yl) group. The benz[e][1,2,4]oxadiazole moiety is linked to a 2-oxo-2,3-dihydro-1H-benz[e][1,2,4]oxadiazole-5-yl group.
D155	 Chemical structure of D155: A complex molecule featuring a 4-methoxy-2-(methylthio)phenyl group connected via a methylene bridge to a piperazine ring. The piperazine ring is further substituted with a 2-oxo-2,3-dihydro-1H-benz[e][1,2,4]oxadiazol-5-yl group and a 2-oxo-2,3-dihydro-1H-benz[e][1,2,4]oxadiazol-5-yl group. The benz[e][1,2,4]oxadiazole moiety is linked to a 2-oxo-2,3-dihydro-1H-benz[e][1,2,4]oxadiazole-5-yl group.
D156	 Chemical structure of D156: A complex molecule featuring a 4-methoxy-2-(methylthio)phenyl group connected via a methylene bridge to a piperazine ring. The piperazine ring is further substituted with a 2-oxo-2,3-dihydro-1H-benz[e][1,2,4]oxadiazol-5-yl group and a 2-oxo-2,3-dihydro-1H-benz[e][1,2,4]oxadiazol-5-yl group. The benz[e][1,2,4]oxadiazole moiety is linked to a 2-oxo-2,3-dihydro-1H-benz[e][1,2,4]oxadiazole-5-yl group.
D157	 Chemical structure of D157: A complex molecule featuring a 4-methoxy-2-(methylthio)phenyl group connected via a methylene bridge to a piperazine ring. The piperazine ring is further substituted with a 2-oxo-2,3-dihydro-1H-benz[e][1,2,4]oxadiazol-5-yl group and a 2-oxo-2,3-dihydro-1H-benz[e][1,2,4]oxadiazol-5-yl group. The benz[e][1,2,4]oxadiazole moiety is linked to a 2-oxo-2,3-dihydro-1H-benz[e][1,2,4]oxadiazole-5-yl group.

Compound No.	Structure
D158	 Chemical structure of D158: A complex molecule featuring a 2,6-dimethoxyphenyl group connected via a methylene bridge to a piperidine ring. This piperidine is further connected to a spirocyclic system consisting of a cyclobutane ring fused to a piperidine ring. The piperidine ring of the spiro system is connected to a benzimidazole moiety, which is in turn linked to a 2,6-pyridinedione (phthalimide) derivative.
D159	 Chemical structure of D159: A molecule featuring a 2,6-dimethoxyphenyl group connected via a methylene bridge to a piperidine ring. This piperidine is further connected to a spirocyclic system consisting of a cyclobutane ring fused to a piperidine ring. The piperidine ring of the spiro system is connected to a benzimidazole moiety, which is in turn linked to a 2,6-pyridinedione (phthalimide) derivative.
D160	 Chemical structure of D160: A molecule featuring a 2,6-dimethoxyphenyl group connected via a methylene bridge to a piperidine ring. This piperidine is further connected to a spirocyclic system consisting of a cyclobutane ring fused to a piperidine ring. The piperidine ring of the spiro system is connected to a benzimidazole moiety, which is in turn linked to a 2,6-pyridinedione (phthalimide) derivative.
D161	 Chemical structure of D161: A molecule featuring a 2,6-dimethoxyphenyl group connected via a methylene bridge to a piperidine ring. This piperidine is further connected to a spirocyclic system consisting of a cyclobutane ring fused to a piperidine ring. The piperidine ring of the spiro system is connected to a benzimidazole moiety, which is in turn linked to a 2,6-pyridinedione (phthalimide) derivative.

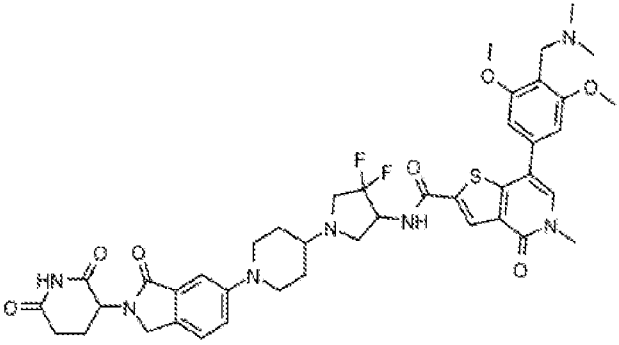
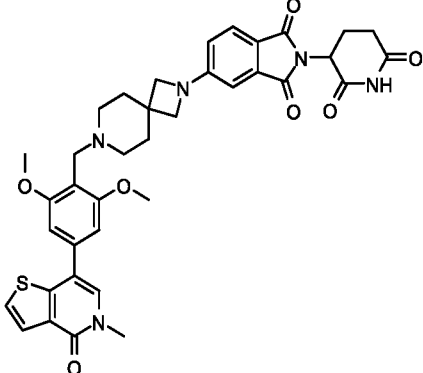
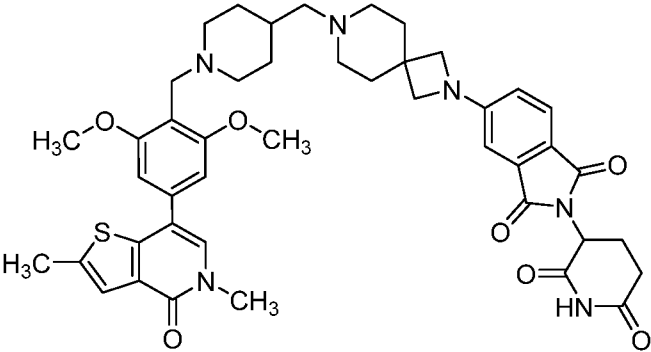
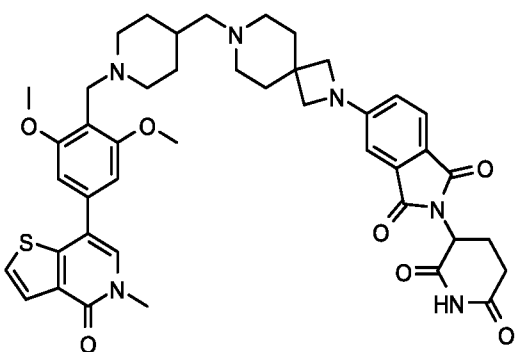
Compound No.	Structure
D162	 Chemical structure of D162: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. This core is linked via a piperidine ring to a 4,4-difluoro-1,2,3,4-tetrahydropyrimidin-2-amine moiety. The latter is further connected to a 2-methyl-4-methoxyphenyl group, which is in turn linked to a 2-methyl-4-methoxyphenyl group via a pyrazole ring.
D163	 Chemical structure of D163: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. This core is linked via a piperidine ring to a 4,4-difluoro-1,2,3,4-tetrahydropyrimidin-2-amine moiety. The latter is further connected to a 2-methyl-4-methoxyphenyl group, which is in turn linked to a 2-methyl-4-methoxyphenyl group via a pyrazole ring.
D164	 Chemical structure of D164: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. This core is linked via a piperidine ring to a 4,4-difluoro-1,2,3,4-tetrahydropyrimidin-2-amine moiety. The latter is further connected to a 2-methyl-4-methoxyphenyl group, which is in turn linked to a 2-methyl-4-methoxyphenyl group via a pyrazole ring.
D165	 Chemical structure of D165: A complex molecule featuring a 6,7-dihydro-5H-benzocyclohepta[b]pyridine-5-carboxamide core. This core is linked via a piperidine ring to a 4,4-difluoro-1,2,3,4-tetrahydropyrimidin-2-amine moiety. The latter is further connected to a 2-methyl-4-methoxyphenyl group, which is in turn linked to a 2-methyl-4-methoxyphenyl group via a pyrazole ring.

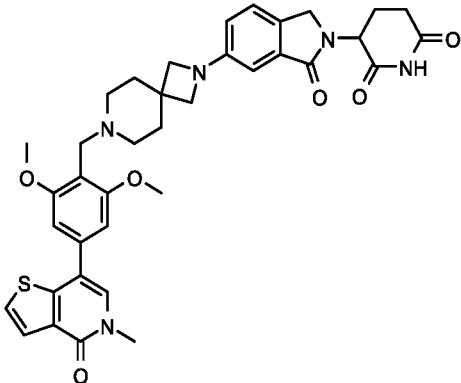
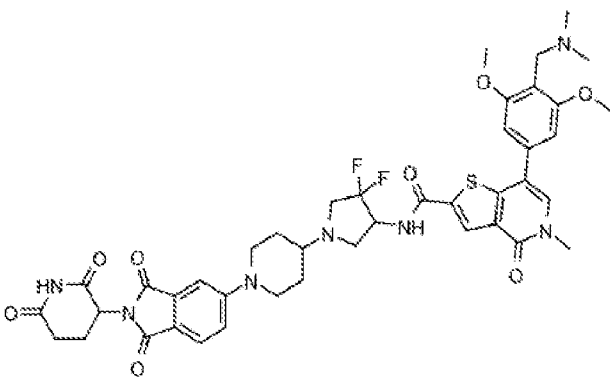
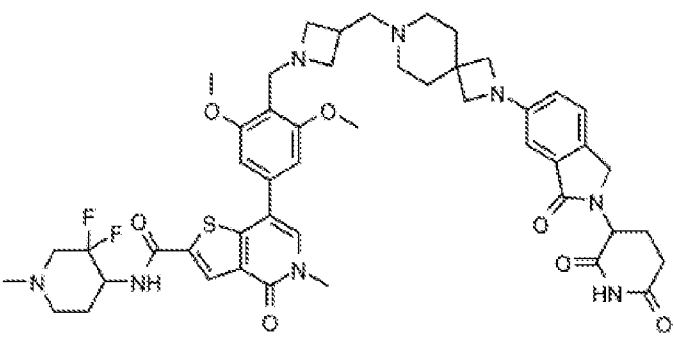
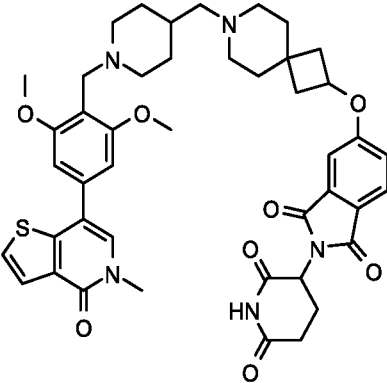
Compound No.	Structure
D166	 Chemical structure of D166: A complex molecule featuring a 6,7-bis(methylene)isoindolin-1-one moiety linked via a piperazine ring to a 4-(dimethylamino)-2-methoxyphenyl group. This phenyl group is further connected to a thienopyridine system, which is substituted with a 2,2-difluoroethyl group and a 2-oxo-2-(dimethylamino)ethyl group.
D167	 Chemical structure of D167: A complex molecule featuring a 6,7-bis(methylene)isoindolin-1-one moiety linked via a piperazine ring to a 4-(dimethylamino)-2-methoxyphenyl group. This phenyl group is further connected to a thienopyridine system, which is substituted with a 2,2-difluoroethyl group and a 2-oxo-2-(dimethylamino)ethyl group.
D168	 Chemical structure of D168: A complex molecule featuring a 6,7-bis(methylene)isoindolin-1-one moiety linked via a piperazine ring to a 4-(dimethylamino)-2-methoxyphenyl group. This phenyl group is further connected to a thienopyridine system, which is substituted with a 2,2-difluoroethyl group and a 2-oxo-2-(dimethylamino)ethyl group.
D169	 Chemical structure of D169: A complex molecule featuring a 6,7-bis(methylene)isoindolin-1-one moiety linked via a piperazine ring to a 4-(dimethylamino)-2-methoxyphenyl group. This phenyl group is further connected to a thienopyridine system, which is substituted with a 2,2-difluoroethyl group and a 2-oxo-2-(dimethylamino)ethyl group.

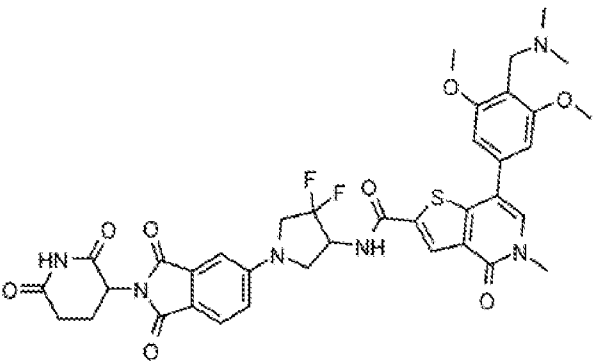
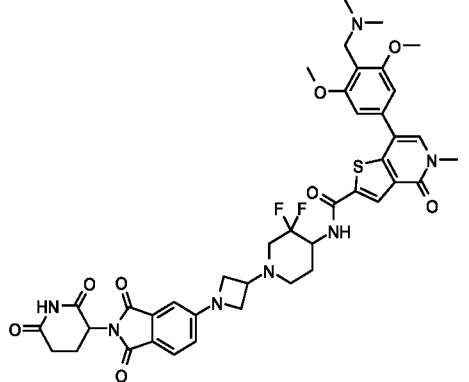
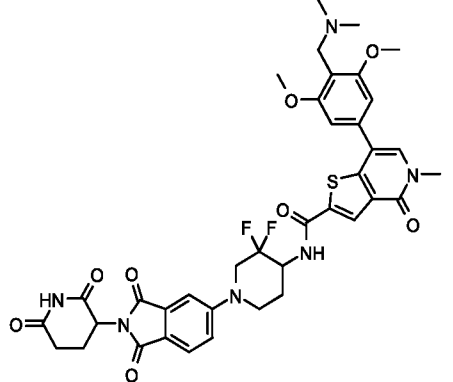
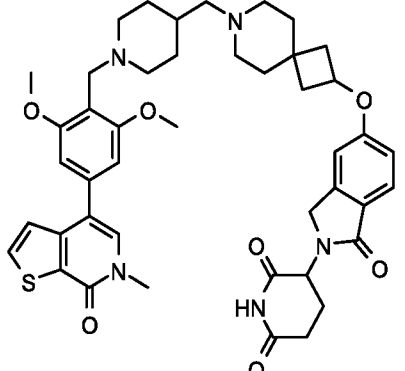
Compound No.	Structure
D170	 Chemical structure of D170: A complex molecule featuring a central benzene ring substituted with a 3,4-dimethoxyphenyl group, a 2-methyl-4-thienyl group, and a 2-methyl-4-thienyl group. The 2-methyl-4-thienyl group is further substituted with a 2-methyl-4-thienyl group. The 2-methyl-4-thienyl group is further substituted with a 2-methyl-4-thienyl group. The 2-methyl-4-thienyl group is further substituted with a 2-methyl-4-thienyl group.
D171	 Chemical structure of D171: A complex molecule featuring a central benzene ring substituted with a 3,4-dimethoxyphenyl group, a 2-methyl-4-thienyl group, and a 2-methyl-4-thienyl group. The 2-methyl-4-thienyl group is further substituted with a 2-methyl-4-thienyl group. The 2-methyl-4-thienyl group is further substituted with a 2-methyl-4-thienyl group. The 2-methyl-4-thienyl group is further substituted with a 2-methyl-4-thienyl group.
D172	 Chemical structure of D172: A complex molecule featuring a central benzene ring substituted with a 3,4-dimethoxyphenyl group, a 2-methyl-4-thienyl group, and a 2-methyl-4-thienyl group. The 2-methyl-4-thienyl group is further substituted with a 2-methyl-4-thienyl group. The 2-methyl-4-thienyl group is further substituted with a 2-methyl-4-thienyl group. The 2-methyl-4-thienyl group is further substituted with a 2-methyl-4-thienyl group.
D173	 Chemical structure of D173: A complex molecule featuring a central benzene ring substituted with a 3,4-dimethoxyphenyl group, a 2-methyl-4-thienyl group, and a 2-methyl-4-thienyl group. The 2-methyl-4-thienyl group is further substituted with a 2-methyl-4-thienyl group. The 2-methyl-4-thienyl group is further substituted with a 2-methyl-4-thienyl group. The 2-methyl-4-thienyl group is further substituted with a 2-methyl-4-thienyl group.

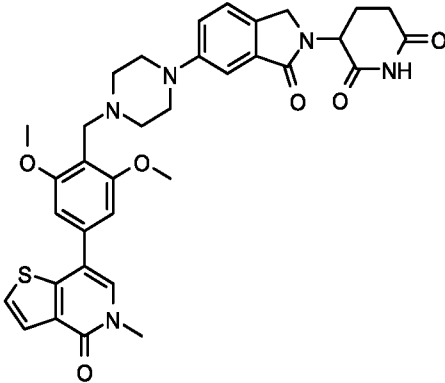
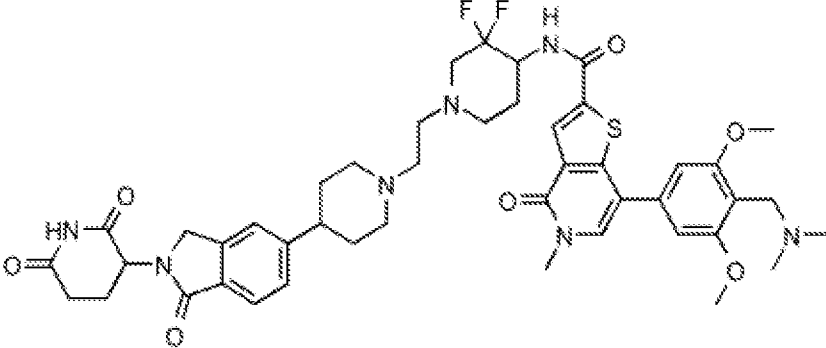
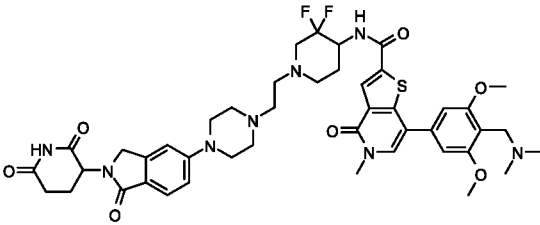
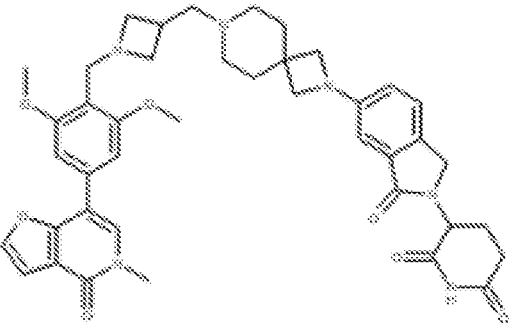
Compound No.	Structure
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D175	
D176	
D177	

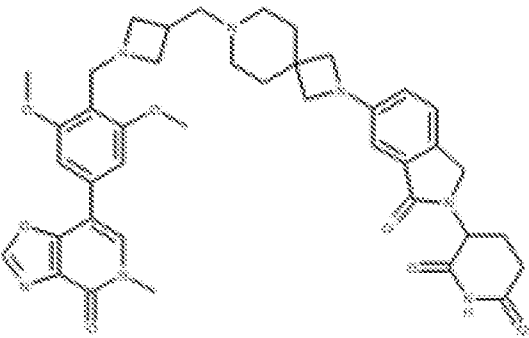
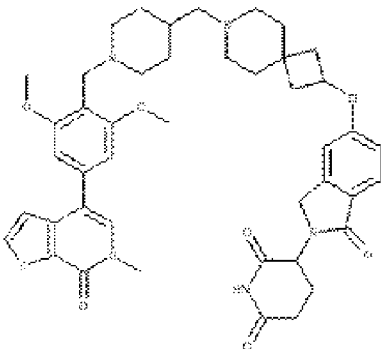
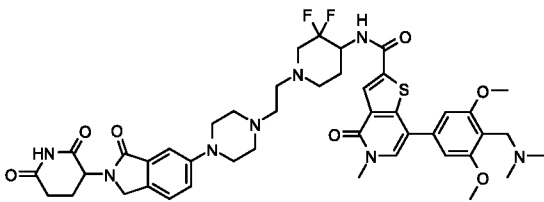
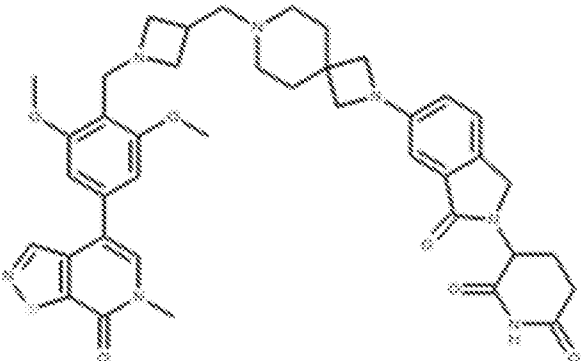
Compound No.	Structure
D178	
D179	
D180	
D181	

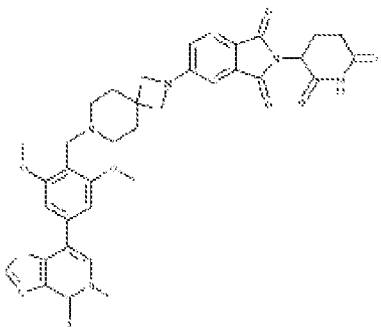
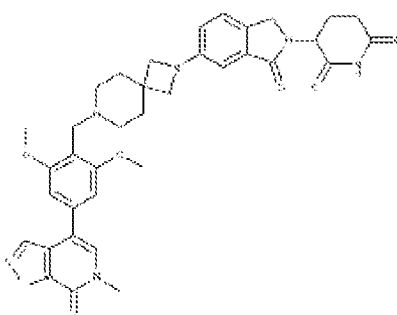
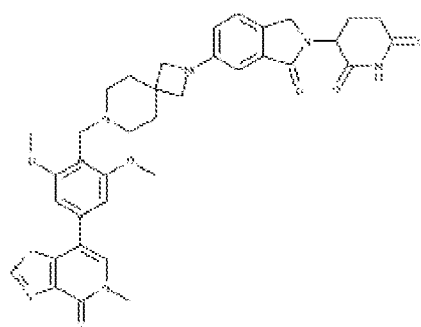
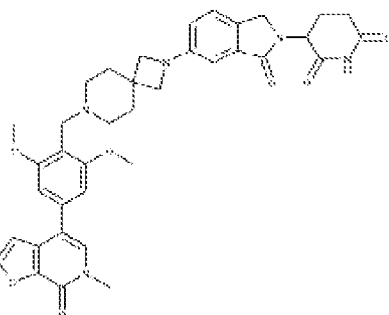
Compound No.	Structure
D182	 Chemical structure of D182: A complex molecule featuring a 1,2,3,4-tetrahydroquinolin-5(1H)-one core. The nitrogen at position 1 is substituted with a 2-oxo-2,3,4,5-tetrahydro-1H-benzothiazol-5-yl group. The benzene ring of the quinolinone is substituted at position 6 with a 4-(2-(2,6-dimethyl-4-iodo-3-methoxyphenyl)-1,3-dioxol-5-yl)butyl group. The 1,3-dioxolane ring is further substituted with a 2,2-difluoro-1,3-dioxol-5-yl group.
D183	 Chemical structure of D183: A molecule consisting of a 1,2,3,4-tetrahydroquinolin-5(1H)-one core. The nitrogen at position 1 is substituted with a 2-(2,6-dimethoxyphenyl)ethyl group. The benzene ring of the quinolinone is substituted at position 6 with a 2-(2,6-dimethoxyphenyl)ethyl group. The 1,3-dioxolane ring is further substituted with a 2,2-difluoro-1,3-dioxol-5-yl group.
D184	 Chemical structure of D184: A molecule consisting of a 1,2,3,4-tetrahydroquinolin-5(1H)-one core. The nitrogen at position 1 is substituted with a 2-(2,6-dimethoxyphenyl)ethyl group. The benzene ring of the quinolinone is substituted at position 6 with a 2-(2,6-dimethoxyphenyl)ethyl group. The 1,3-dioxolane ring is further substituted with a 2,2-difluoro-1,3-dioxol-5-yl group.
D185	 Chemical structure of D185: A molecule consisting of a 1,2,3,4-tetrahydroquinolin-5(1H)-one core. The nitrogen at position 1 is substituted with a 2-(2,6-dimethoxyphenyl)ethyl group. The benzene ring of the quinolinone is substituted at position 6 with a 2-(2,6-dimethoxyphenyl)ethyl group. The 1,3-dioxolane ring is further substituted with a 2,2-difluoro-1,3-dioxol-5-yl group.

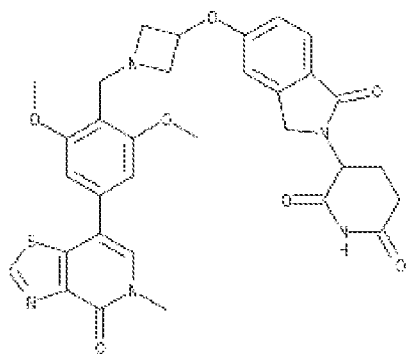
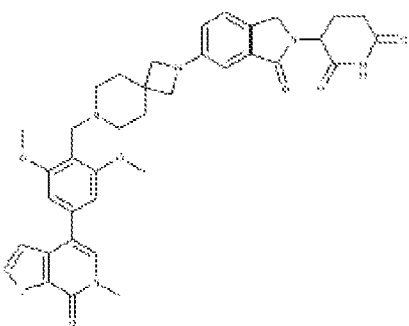
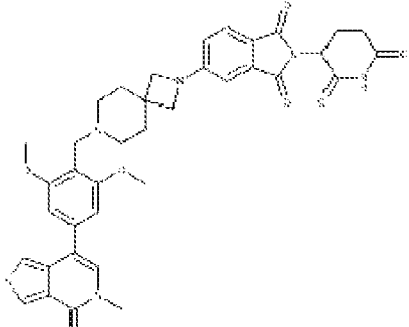
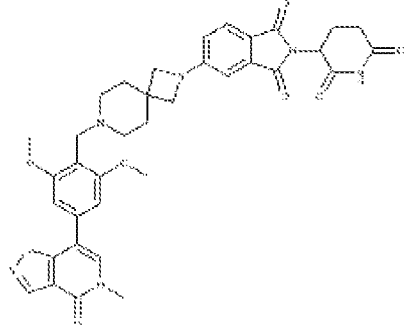
Compound No.	Structure
D186	 Chemical structure of D186: A complex molecule featuring a 6-methoxy-2-(methylthio)pyridine-3-carboxamide moiety linked via a methylene group to a 2,6-dimethoxyphenyl ring. This phenyl ring is further connected through a methylene group to a 1,4-diazepane ring, which is linked to a 1,2,3,4-tetrahydroquinoline-5-carboxamide moiety.
D187	 Chemical structure of D187: A complex molecule featuring a 6-methoxy-2-(methylthio)pyridine-3-carboxamide moiety linked via a methylene group to a 2,6-dimethoxyphenyl ring. This phenyl ring is further connected through a methylene group to a 1,4-diazepane ring, which is linked to a 1,2,3,4-tetrahydroquinoline-5-carboxamide moiety.
D188	 Chemical structure of D188: A complex molecule featuring a 6-methoxy-2-(methylthio)pyridine-3-carboxamide moiety linked via a methylene group to a 2,6-dimethoxyphenyl ring. This phenyl ring is further connected through a methylene group to a 1,4-diazepane ring, which is linked to a 1,2,3,4-tetrahydroquinoline-5-carboxamide moiety.
D189	 Chemical structure of D189: A complex molecule featuring a 6-methoxy-2-(methylthio)pyridine-3-carboxamide moiety linked via a methylene group to a 2,6-dimethoxyphenyl ring. This phenyl ring is further connected through a methylene group to a 1,4-diazepane ring, which is linked to a 1,2,3,4-tetrahydroquinoline-5-carboxamide moiety.

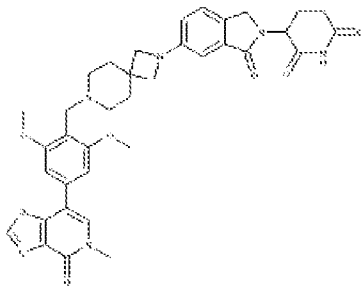
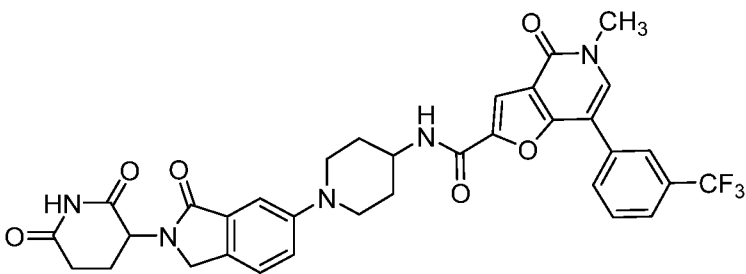
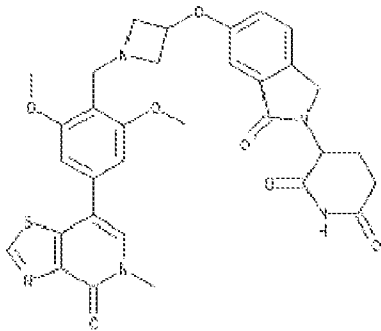
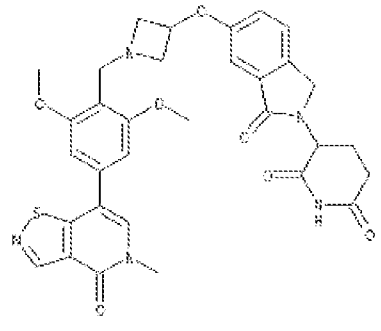
Compound No.	Structure
D190	 Chemical structure of D190: A complex molecule featuring a 6,7-dihydro-5H-benzodicyclopenta[b]pyridine-5-one core. This core is substituted at the 2-position with a 1,1-difluoro-2-((2-methoxy-4-(dimethylamino)phenyl)-5-methylthiazol-4-yl)ethanone group. The 4-position of the thiazole ring is further substituted with a 2-methoxy-4-(dimethylamino)phenyl group.
D191	 Chemical structure of D191: A complex molecule featuring a 6,7-dihydro-5H-benzodicyclopenta[b]pyridine-5-one core. This core is substituted at the 2-position with a 1,1-difluoro-2-((2-methoxy-4-(dimethylamino)phenyl)-5-methylthiazol-4-yl)ethanone group. The 4-position of the thiazole ring is further substituted with a 2-methoxy-4-(dimethylamino)phenyl group.
D192	 Chemical structure of D192: A complex molecule featuring a 6,7-dihydro-5H-benzodicyclopenta[b]pyridine-5-one core. This core is substituted at the 2-position with a 1,1-difluoro-2-((2-methoxy-4-(dimethylamino)phenyl)-5-methylthiazol-4-yl)ethanone group. The 4-position of the thiazole ring is further substituted with a 2-methoxy-4-(dimethylamino)phenyl group.
D193	 Chemical structure of D193: A complex molecule featuring a 6,7-dihydro-5H-benzodicyclopenta[b]pyridine-5-one core. This core is substituted at the 2-position with a 1,1-difluoro-2-((2-methoxy-4-(dimethylamino)phenyl)-5-methylthiazol-4-yl)ethanone group. The 4-position of the thiazole ring is further substituted with a 2-methoxy-4-(dimethylamino)phenyl group.

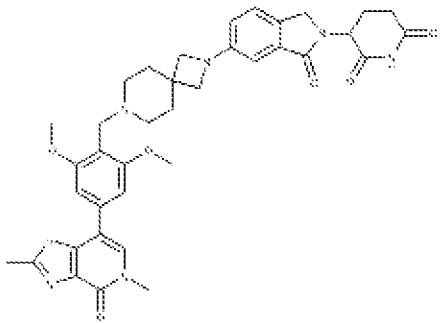
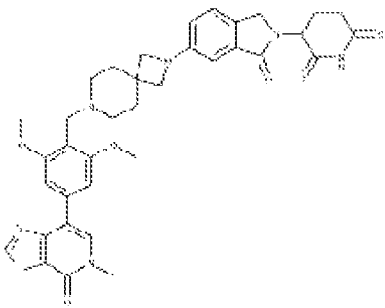
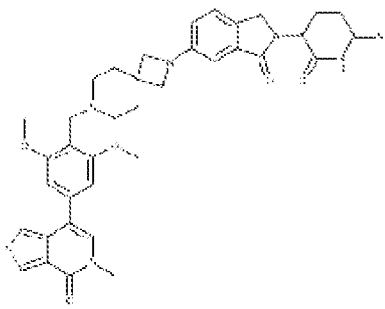
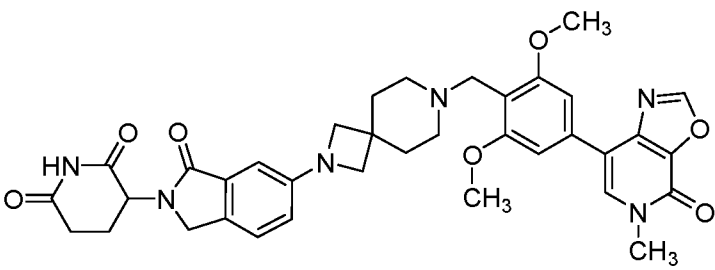
Compound No.	Structure
D194	 Chemical structure of D194: A complex molecule featuring a central benzene ring substituted with a 3,5-dimethoxybenzyl group, a 4-methoxyphenyl group, and a 2-methyl-4-thienyl-1H-pyridin-1-one group. This central benzene ring is connected via a piperazine ring to a 2,3-difluoro-4-(2-oxo-2,3,4,5-tetrahydro-1H-pyridin-1-yl)phenyl group.
D195	 Chemical structure of D195: A complex molecule featuring a central benzene ring substituted with a 2-oxo-2,3,4,5-tetrahydro-1H-pyridin-1-yl group, a 2-methyl-4-thienyl-1H-pyridin-1-one group, and a 4-methoxyphenyl group. This central benzene ring is connected via a piperazine ring to a 2,3-difluoro-4-(2-oxo-2,3,4,5-tetrahydro-1H-pyridin-1-yl)phenyl group.
D196	 Chemical structure of D196: A complex molecule featuring a central benzene ring substituted with a 2-oxo-2,3,4,5-tetrahydro-1H-pyridin-1-yl group, a 2-methyl-4-thienyl-1H-pyridin-1-one group, and a 4-methoxyphenyl group. This central benzene ring is connected via a piperazine ring to a 2,3-difluoro-4-(2-oxo-2,3,4,5-tetrahydro-1H-pyridin-1-yl)phenyl group.
D197	 Chemical structure of D197: A complex molecule featuring a central benzene ring substituted with a 2-oxo-2,3,4,5-tetrahydro-1H-pyridin-1-yl group, a 2-methyl-4-thienyl-1H-pyridin-1-one group, and a 4-methoxyphenyl group. This central benzene ring is connected via a piperazine ring to a 2,3-difluoro-4-(2-oxo-2,3,4,5-tetrahydro-1H-pyridin-1-yl)phenyl group.

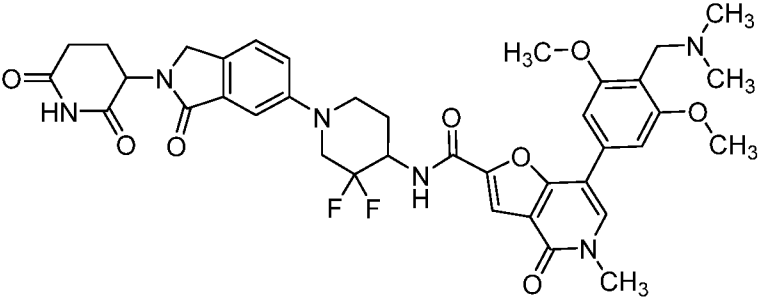
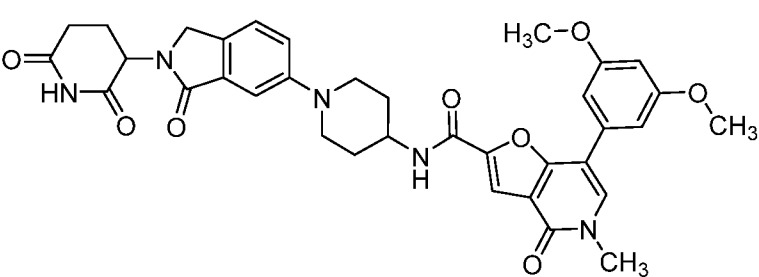
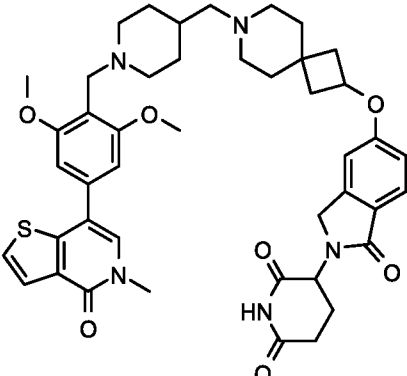
Compound No.	Structure
D198	
D199	
D200	
D201	

Compound No.	Structure
D202	 Chemical structure of compound D202. It features a 1,4-dimethyl-5-(cyclopent-1-en-1-yl)phenyl group connected via a methylene bridge to a 1,4-dimethyl-2-(cyclohexylmethyl)phenyl group. This is further connected via a methylene bridge to a cyclohexane ring, which is linked through a cyclobutane ring to a fluorene derivative system.
D203	 Chemical structure of compound D203. It features a 1,4-dimethyl-5-(cyclopent-1-en-1-yl)phenyl group connected via a methylene bridge to a 1,4-dimethyl-2-(cyclohexylmethyl)phenyl group. This is further connected via a methylene bridge to a cyclohexane ring, which is linked through a cyclobutane ring to a fluorene derivative system, with a different substitution pattern compared to D202.
D204	 Chemical structure of compound D204. It features a 1,4-dimethyl-5-(cyclopent-1-en-1-yl)phenyl group connected via a methylene bridge to a 1,4-dimethyl-2-(cyclohexylmethyl)phenyl group. This is further connected via a methylene bridge to a cyclohexane ring, which is linked through a cyclobutane ring to a fluorene derivative system.
D205	 Chemical structure of compound D205. It features a 1,4-dimethyl-5-(cyclopent-1-en-1-yl)phenyl group connected via a methylene bridge to a 1,4-dimethyl-2-(cyclohexylmethyl)phenyl group. This is further connected via a methylene bridge to a cyclohexane ring, which is linked through a cyclobutane ring to a fluorene derivative system.

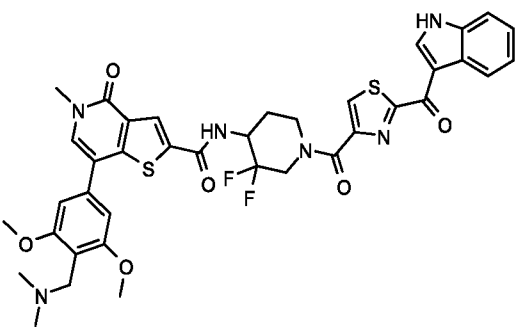
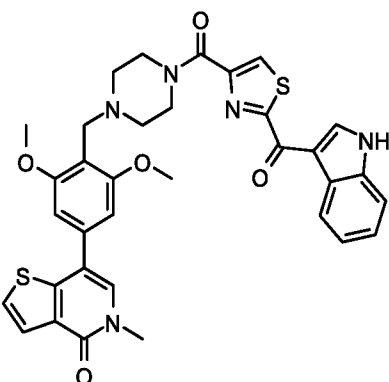
Compound No.	Structure
D206	 Chemical structure of D206: A complex molecule featuring a central benzene ring substituted with a methoxy group, a methyl group, and a 4-methyl-5-oxo-1H-benzimidazol-2-yl group. This central ring is connected via a methylene group to a 1,3-dioxolane ring, which is further linked to a 4-methoxyphenyl group. The 4-methoxyphenyl group is connected via an ester linkage to a 2-methyl-6-oxo-1,2,3,4-tetrahydropyridine-5-carboxamide group.
D207	 Chemical structure of D207: A complex molecule featuring a central benzene ring substituted with a methoxy group, a methyl group, and a 4-methyl-5-oxo-1H-benzimidazol-2-yl group. This central ring is connected via a methylene group to a 1,3-dioxolane ring, which is further linked to a 4-methoxyphenyl group. The 4-methoxyphenyl group is connected via an ester linkage to a 2-methyl-6-oxo-1,2,3,4-tetrahydropyridine-5-carboxamide group.
D208	 Chemical structure of D208: A complex molecule featuring a central benzene ring substituted with a methoxy group, a methyl group, and a 4-methyl-5-oxo-1H-benzimidazol-2-yl group. This central ring is connected via a methylene group to a 1,3-dioxolane ring, which is further linked to a 4-methoxyphenyl group. The 4-methoxyphenyl group is connected via an ester linkage to a 2-methyl-6-oxo-1,2,3,4-tetrahydropyridine-5-carboxamide group.
D209	 Chemical structure of D209: A complex molecule featuring a central benzene ring substituted with a methoxy group, a methyl group, and a 4-methyl-5-oxo-1H-benzimidazol-2-yl group. This central ring is connected via a methylene group to a 1,3-dioxolane ring, which is further linked to a 4-methoxyphenyl group. The 4-methoxyphenyl group is connected via an ester linkage to a 2-methyl-6-oxo-1,2,3,4-tetrahydropyridine-5-carboxamide group.

Compound No.	Structure
D210	 Chemical structure of compound D210: A complex molecule featuring a central benzene ring substituted with a 1,3-dimethyl-5-(4-methyl-5-(2-methyl-1H-imidazol-2-yl)phenyl)phenyl group and a 1,3-dimethyl-5-(4-methyl-5-(2-methyl-1H-imidazol-2-yl)phenyl)phenyl group.
D211	 Chemical structure of compound D211: A complex molecule featuring a central benzene ring substituted with a 1,3-dimethyl-5-(4-methyl-5-(2-methyl-1H-imidazol-2-yl)phenyl)phenyl group and a 1,3-dimethyl-5-(4-methyl-5-(2-methyl-1H-imidazol-2-yl)phenyl)phenyl group.
D212	 Chemical structure of compound D212: A complex molecule featuring a central benzene ring substituted with a 1,3-dimethyl-5-(4-methyl-5-(2-methyl-1H-imidazol-2-yl)phenyl)phenyl group and a 1,3-dimethyl-5-(4-methyl-5-(2-methyl-1H-imidazol-2-yl)phenyl)phenyl group.
D213	 Chemical structure of compound D213: A complex molecule featuring a central benzene ring substituted with a 1,3-dimethyl-5-(4-methyl-5-(2-methyl-1H-imidazol-2-yl)phenyl)phenyl group and a 1,3-dimethyl-5-(4-methyl-5-(2-methyl-1H-imidazol-2-yl)phenyl)phenyl group.

Compound No.	Structure
D214	 Chemical structure of compound D214: A complex molecule featuring a central benzene ring substituted with a 4-ethyl-2-methylphenyl group, a 4-ethyl-2-methylphenyl group, and a 4-ethyl-2-methylphenyl group. The central benzene ring is also substituted with a 4-ethyl-2-methylphenyl group. The molecule includes a 4-ethyl-2-methylphenyl group and a 4-ethyl-2-methylphenyl group.
D215	 Chemical structure of compound D215: A complex molecule featuring a central benzene ring substituted with a 4-ethyl-2-methylphenyl group, a 4-ethyl-2-methylphenyl group, and a 4-ethyl-2-methylphenyl group. The central benzene ring is also substituted with a 4-ethyl-2-methylphenyl group. The molecule includes a 4-ethyl-2-methylphenyl group and a 4-ethyl-2-methylphenyl group.
D216	 Chemical structure of compound D216: A complex molecule featuring a central benzene ring substituted with a 4-ethyl-2-methylphenyl group, a 4-ethyl-2-methylphenyl group, and a 4-ethyl-2-methylphenyl group. The central benzene ring is also substituted with a 4-ethyl-2-methylphenyl group. The molecule includes a 4-ethyl-2-methylphenyl group and a 4-ethyl-2-methylphenyl group.
D217	 Chemical structure of compound D217: A complex molecule featuring a central benzene ring substituted with a 4-ethyl-2-methylphenyl group, a 4-ethyl-2-methylphenyl group, and a 4-ethyl-2-methylphenyl group. The central benzene ring is also substituted with a 4-ethyl-2-methylphenyl group. The molecule includes a 4-ethyl-2-methylphenyl group and a 4-ethyl-2-methylphenyl group.

Compound No.	Structure
D218	 Chemical structure of compound D218. It features a 6,7-dihydro-5H-benzodisole-5-carboxamide group connected via a piperidine ring (with a difluoromethyl group) to a 4-methoxy-2-methyl-5-(dimethylaminomethyl)phenyl group. The piperidine ring is also connected to a 4-methoxy-2-methyl-5-(dimethylaminomethyl)phenyl group.
D219	 Chemical structure of compound D219. It features a 6,7-dihydro-5H-benzodisole-5-carboxamide group connected via a piperidine ring to a 4-methoxy-2-methyl-5-(dimethylaminomethyl)phenyl group. The piperidine ring is also connected to a 4-methoxy-2-methyl-5-(dimethylaminomethyl)phenyl group.
D220	 Chemical structure of compound D220. It features a 6,7-dihydro-5H-benzodisole-5-carboxamide group connected via a piperidine ring to a 4-methoxy-2-methyl-5-(dimethylaminomethyl)phenyl group. The piperidine ring is also connected to a 4-methoxy-2-methyl-5-(dimethylaminomethyl)phenyl group.

In an aspect, the disclosure features a compound having the structure of any one of DD1 and DD2, or a pharmaceutically acceptable salt thereof.

DD1	
DD2	

In another aspect, the disclosure features a pharmaceutical composition including any of the foregoing compounds, or pharmaceutically acceptable salts thereof, and a pharmaceutically acceptable excipient.

In an aspect, the disclosure features a method of inhibiting the level and/or activity of BRD9 in a cell, the method involving contacting the cell with an effective amount of any of the foregoing compounds, or pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof.

In another aspect, the disclosure features a method of reducing the level and/or activity of BRD9 in a cell, the method involving contacting the cell with an effective amount of any of the foregoing compounds, or pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof.

In some embodiments, the cell is a cancer cell.

In some embodiments, the cancer is a malignant, rhabdoid tumor, a CD8+ T-cell lymphoma, endometrial carcinoma, ovarian carcinoma, bladder cancer, stomach cancer, pancreatic cancer, esophageal cancer, prostate cancer, renal cell carcinoma, melanoma, colorectal cancer, a sarcoma (e.g., a soft tissue sarcoma, synovial sarcoma, Ewing's sarcoma, osteosarcoma, rhabdomyosarcoma, adult fibrosarcoma, alveolar soft-part sarcoma, angiosarcoma, clear cell sarcoma, desmoplastic small round cell tumor, epithelioid sarcoma, fibromyxoid sarcoma, gastrointestinal stromal tumor, Kaposi sarcoma, liposarcoma, leiomyosarcoma, malignant mesenchymoma malignant peripheral nerve sheath tumors, myxofibrosarcoma, low-grade rhabdomyosarcoma), non-small cell lung cancer (e.g., squamous or adenocarcinoma), stomach cancer, or breast cancer. In some embodiments, the cancer is a malignant, rhabdoid tumor, a CD8+ T-cell lymphoma, endometrial carcinoma, ovarian carcinoma, bladder cancer,

stomach cancer, pancreatic cancer, esophageal cancer, prostate cancer, renal cell carcinoma, melanoma, or colorectal cancer. In some embodiments, the cancer is a sarcoma (e.g., synovial sarcoma or Ewing's sarcoma), non-small cell lung cancer (e.g., squamous or adenocarcinoma), stomach cancer, or breast cancer. In some embodiments, the cancer is sarcoma (e.g., synovial sarcoma or Ewing's sarcoma). In some embodiments, the sarcoma is synovial sarcoma.

In an aspect, the disclosure features a method of treating a BAF complex-related disorder in a subject in need thereof, the method involving administering to the subject an effective amount of any of the foregoing compounds, or pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof. In some embodiments, the BAF complex-related disorder is cancer. In some embodiments, the BAF complex-related disorder is infection.

In another aspect, the disclosure features a method of treating an SS18-SSX fusion protein-related disorder in a subject in need thereof, the method involving administering to the subject an effective amount of any of the foregoing compounds, or pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof. In some embodiments, the SS18-SSX fusion protein-related disorder is cancer. In some embodiments, the SS18-SSX fusion protein-related disorder is infection. In some embodiments of any of the foregoing methods, the SS18-SSX fusion protein is a SS18-SSX1 fusion protein, a SS18-SSX2 fusion protein, or a SS18-SSX4 fusion protein.

In yet another aspect, the disclosure features a method of treating a BRD9-related disorder in a subject in need thereof, the method involving administering to the subject an effective amount of any of the foregoing compounds, or pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof. In some embodiments, the BRD9-related disorder is cancer. In some embodiments, the BRD9-related disorder is infection.

In some embodiments, the cancer is squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, hepatocellular carcinomas, and renal cell carcinomas, cancer of the bladder, bowel, breast, cervix, colon, esophagus, head, kidney, liver, lung, neck, ovary, pancreas, prostate, and stomach; leukemias; benign and malignant lymphomas, particularly Burkitt's lymphoma and Non-Hodgkin's lymphoma; benign and malignant melanomas; myeloproliferative diseases; sarcomas, including Ewing's sarcoma, hemangiosarcoma, Kaposi's sarcoma, liposarcoma, myosarcomas, peripheral neuroepithelioma, synovial sarcoma, gliomas, astrocytomas, oligodendrogliomas, ependymomas, glioblastomas, neuroblastomas, ganglioneuromas, gangliogliomas, medulloblastomas, pineal cell tumors, meningiomas, meningeal sarcomas, neurofibromas, and Schwannomas; bowel cancer, breast cancer, prostate cancer, cervical cancer, uterine cancer, lung cancer, ovarian cancer, testicular cancer, thyroid cancer, astrocytoma, esophageal cancer, pancreatic cancer, stomach cancer, liver cancer, colon cancer, melanoma; carcinosarcoma, Hodgkin's disease, Wilms' tumor and teratocarcinomas. Additional cancers which may be treated using the disclosed compounds according to the present invention include, for example, acute granulocytic leukemia, acute lymphocytic leukemia (ALL), acute myelogenous leukemia (AML), adenocarcinoma, adenosarcoma, adrenal cancer, adrenocortical carcinoma, anal cancer, anaplastic astrocytoma, angiosarcoma, appendix cancer, astrocytoma, Basal cell carcinoma, B-Cell lymphoma, bile duct cancer, bladder cancer, bone cancer, bone marrow cancer, bowel cancer, brain cancer, brain stem glioma, breast cancer, triple (estrogen, progesterone and HER-2) negative breast cancer, double negative breast cancer (two of estrogen, progesterone and HER-2 are negative), single

negative (one of estrogen, progesterone and HER-2 is negative), estrogen-receptor positive, HER2-negative breast cancer, estrogen receptor-negative breast cancer, estrogen receptor positive breast cancer, metastatic breast cancer, luminal A breast cancer, luminal B breast cancer, Her2-negative breast cancer, HER2-positive or negative breast cancer, progesterone receptor-negative breast cancer,

5 progesterone receptor-positive breast cancer, recurrent breast cancer, carcinoid tumors, cervical cancer, cholangiocarcinoma, chondrosarcoma, chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), colon cancer, colorectal cancer, craniopharyngioma, cutaneous lymphoma, cutaneous melanoma, diffuse astrocytoma, ductal carcinoma in situ (DCIS), endometrial cancer, ependymoma, epithelioid sarcoma, esophageal cancer, ewing sarcoma, extrahepatic bile duct cancer, eye cancer,

10 fallopian tube cancer, fibrosarcoma, gallbladder cancer, gastric cancer, gastrointestinal cancer, gastrointestinal carcinoid cancer, gastrointestinal stromal tumors (GIST), germ cell tumor glioblastoma multiforme (GBM), glioma, hairy cell leukemia, head and neck cancer, hemangioendothelioma, Hodgkin lymphoma, hypopharyngeal cancer, infiltrating ductal carcinoma (IDC), infiltrating lobular carcinoma (ILC), inflammatory breast cancer (IBC), intestinal Cancer, intrahepatic bile duct cancer, invasive/infiltrating

15 breast cancer, Islet cell cancer, jaw cancer, Kaposi sarcoma, kidney cancer, laryngeal cancer, leiomyosarcoma, leptomeningeal metastases, leukemia, lip cancer, liposarcoma, liver cancer, lobular carcinoma in situ, low-grade astrocytoma, lung cancer, lymph node cancer, lymphoma, male breast cancer, medullary carcinoma, medulloblastoma, melanoma, meningioma, Merkel cell carcinoma, mesenchymal chondrosarcoma, mesenchymous, mesothelioma metastatic breast cancer, metastatic

20 melanoma metastatic squamous neck cancer, mixed gliomas, monodermal teratoma, mouth cancer mucinous carcinoma, mucosal melanoma, multiple myeloma, Mycosis Fungoides, myelodysplastic syndrome, nasal cavity cancer, nasopharyngeal cancer, neck cancer, neuroblastoma, neuroendocrine tumors (NETs), non-Hodgkin's lymphoma, non-small cell lung cancer (NSCLC), oat cell cancer, ocular cancer, ocular melanoma, oligodendroglioma, oral cancer, oral cavity cancer, oropharyngeal cancer,

25 osteogenic sarcoma, osteosarcoma, ovarian cancer, ovarian epithelial cancer ovarian germ cell tumor, ovarian primary peritoneal carcinoma, ovarian sex cord stromal tumor, Paget's disease, pancreatic cancer, papillary carcinoma, paranasal sinus cancer, parathyroid cancer, pelvic cancer, penile cancer, peripheral nerve cancer, peritoneal cancer, pharyngeal cancer, pheochromocytoma, pilocytic astrocytoma, pineal region tumor, pineoblastoma, pituitary gland cancer, primary central nervous system

30 (CNS) lymphoma, prostate cancer, rectal cancer, renal cell carcinoma, renal pelvis cancer, rhabdomyosarcoma, salivary gland cancer, soft tissue sarcoma, bone sarcoma, sarcoma, sinus cancer, skin cancer, small cell lung cancer (SCLC), small intestine cancer, spinal cancer, spinal column cancer, spinal cord cancer, squamous cell carcinoma, stomach cancer, synovial sarcoma, T-cell lymphoma, testicular cancer, throat cancer, thymoma/thymic carcinoma, thyroid cancer, tongue cancer, tonsil cancer,

35 transitional cell cancer, tubal cancer, tubular carcinoma, undiagnosed cancer, ureteral cancer, urethral cancer, uterine adenocarcinoma, uterine cancer, uterine sarcoma, vaginal cancer, vulvar cancer, T-cell lineage acute lymphoblastic leukemia (T-ALL), T-cell lineage lymphoblastic lymphoma (T-LL), peripheral T-cell lymphoma, Adult T-cell leukemia, Pre-B ALL, Pre-B lymphomas, large B-cell lymphoma, Burkitts lymphoma, B-cell ALL, Philadelphia chromosome positive ALL, Philadelphia chromosome positive CML,

40 juvenile myelomonocytic leukemia (JMML), acute promyelocytic leukemia (a subtype of AML), large granular lymphocytic leukemia, Adult T-cell chronic leukemia, diffuse large B cell lymphoma, follicular

lymphoma; Mucosa-Associated Lymphatic Tissue lymphoma (MALT), small cell lymphocytic lymphoma, mediastinal large B cell lymphoma, nodal marginal zone B cell lymphoma (NMZL); splenic marginal zone lymphoma (SMZL); intravascular large B-cell lymphoma; primary effusion lymphoma; or lymphomatoid granulomatosis;; B-cell prolymphocytic leukemia; splenic lymphoma/leukemia, unclassifiable, splenic diffuse red pulp small B-cell lymphoma; lymphoplasmacytic lymphoma; heavy chain diseases, for example, Alpha heavy chain disease, Gamma heavy chain disease, Mu heavy chain disease, plasma cell myeloma, solitary plasmacytoma of bone; extraosseous plasmacytoma; primary cutaneous follicle center lymphoma, T cell/histocyte rich large B-cell lymphoma, DLBCL associated with chronic inflammation; Epstein-Barr virus (EBV)+ DLBCL of the elderly; primary mediastinal (thymic) large B-cell lymphoma, primary cutaneous DLBCL, leg type, ALK+ large B-cell lymphoma, plasmablastic lymphoma; large B-cell lymphoma arising in HHV8-associated multicentric, Castleman disease; B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma, or B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and classical Hodgkin lymphoma.

In some embodiments, the cancer is a malignant, rhabdoid tumor, a CD8+ T-cell lymphoma, endometrial carcinoma, ovarian carcinoma, bladder cancer, stomach cancer, pancreatic cancer, esophageal cancer, prostate cancer, renal cell carcinoma, melanoma, colorectal cancer, a sarcoma (e.g., a soft tissue sarcoma, synovial sarcoma, Ewing's sarcoma, osteosarcoma, rhabdomyosarcoma, adult fibrosarcoma, alveolar soft-part sarcoma, angiosarcoma, clear cell sarcoma, desmoplastic small round cell tumor, epithelioid sarcoma, fibromyxoid sarcoma, gastrointestinal stromal tumor, Kaposi sarcoma, liposarcoma, leiomyosarcoma, malignant mesenchymoma malignant peripheral nerve sheath tumors, myxofibrosarcoma, low-grade rhabdomyosarcoma), non-small cell lung cancer (e.g., squamous or adenocarcinoma), stomach cancer, or breast cancer. In some embodiments, the cancer is a malignant, rhabdoid tumor, a CD8+ T-cell lymphoma, endometrial carcinoma, ovarian carcinoma, bladder cancer, stomach cancer, pancreatic cancer, esophageal cancer, prostate cancer, renal cell carcinoma, melanoma, or colorectal cancer. In some embodiments, the cancer is a sarcoma (e.g., synovial sarcoma or Ewing's sarcoma), non-small cell lung cancer (e.g., squamous or adenocarcinoma), stomach cancer, or breast cancer. In some embodiments, the cancer is sarcoma (e.g., synovial sarcoma or Ewing's sarcoma). In some embodiments, the sarcoma is synovial sarcoma.

In some embodiments, the infection is viral infection (e.g., an infection with a virus of the Retroviridae family such as the lentiviruses (e.g. Human immunodeficiency virus (HIV) and deltaretroviruses (e.g., human T cell leukemia virus I (HTLV-I), human T cell leukemia virus II (HTLV-II)); Hepadnaviridae family (e.g. hepatitis B virus (HBV)); Flaviviridae family (e.g. hepatitis C virus (HCV)); Adenoviridae family (e.g. Human Adenovirus); Herpesviridae family (e.g. Human cytomegalovirus (HCMV), Epstein-Barr virus, herpes simplex virus 1 (HSV-1), herpes simplex virus 2 (HSV-2), human herpesvirus 6 (HHV-6), Herpesvirus K*, CMV, varicella-zoster virus); Papillomaviridae family (e.g. Human Papillomavirus (HPV, HPV E1)); Parvoviridae family (e.g. Parvovirus B19); Polyomaviridae family (e.g. JC virus and BK virus); Paramyxoviridae family (e.g. Measles virus); or Togaviridae family (e.g. Rubella virus)). In some embodiments, the disorder is Coffin Siris, Neurofibromatosis (e.g., NF-1, NF-2, or Schwannomatosis), or Multiple Meningioma. In an aspect, the disclosure features a method of treating a cancer in a subject in need thereof, the method including administering to the subject an effective amount

of any of the foregoing compounds, or pharmaceutically acceptable salts thereof, or any of the foregoing pharmaceutical compositions.

In some embodiments, the cancer is squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, hepatocellular carcinomas, and renal cell carcinomas, cancer of the bladder, bowel, breast, cervix, colon, esophagus, head, kidney, liver, lung, neck, ovary, pancreas, prostate, and stomach; leukemias; benign and malignant lymphomas, particularly Burkitt's lymphoma and Non-Hodgkin's lymphoma; benign and malignant melanomas; myeloproliferative diseases; sarcomas, including Ewing's sarcoma, hemangiosarcoma, Kaposi's sarcoma, liposarcoma, myosarcomas, peripheral neuroepithelioma, synovial sarcoma, gliomas, astrocytomas, oligodendrogliomas, ependymomas, glioblastomas, neuroblastomas, ganglioneuromas, gangliogliomas, medulloblastomas, pineal cell tumors, meningiomas, meningeal sarcomas, neurofibromas, and Schwannomas; bowel cancer, breast cancer, prostate cancer, cervical cancer, uterine cancer, lung cancer, ovarian cancer, testicular cancer, thyroid cancer, astrocytoma, esophageal cancer, pancreatic cancer, stomach cancer, liver cancer, colon cancer, melanoma; carcinosarcoma, Hodgkin's disease, Wilms' tumor and teratocarcinomas. Additional cancers which may be treated using the disclosed compounds according to the present invention include, for example, acute granulocytic leukemia, acute lymphocytic leukemia (ALL), acute myelogenous leukemia (AML), adenocarcinoma, adenosarcoma, adrenal cancer, adrenocortical carcinoma, anal cancer, anaplastic astrocytoma, angiosarcoma, appendix cancer, astrocytoma, Basal cell carcinoma, B-Cell lymphoma, bile duct cancer, bladder cancer, bone cancer, bone marrow cancer, bowel cancer, brain cancer, brain stem glioma, breast cancer, triple (estrogen, progesterone and HER-2) negative breast cancer, double negative breast cancer (two of estrogen, progesterone and HER-2 are negative), single negative (one of estrogen, progesterone and HER-2 is negative), estrogen-receptor positive, HER2-negative breast cancer, estrogen receptor-negative breast cancer, estrogen receptor positive breast cancer, metastatic breast cancer, luminal A breast cancer, luminal B breast cancer, Her2-negative breast cancer, HER2-positive or negative breast cancer, progesterone receptor-negative breast cancer, progesterone receptor-positive breast cancer, recurrent breast cancer, carcinoid tumors, cervical cancer, cholangiocarcinoma, chondrosarcoma, chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), colon cancer, colorectal cancer, craniopharyngioma, cutaneous lymphoma, cutaneous melanoma, diffuse astrocytoma, ductal carcinoma in situ (DCIS), endometrial cancer, ependymoma, epithelioid sarcoma, esophageal cancer, ewing sarcoma, extrahepatic bile duct cancer, eye cancer, fallopian tube cancer, fibrosarcoma, gallbladder cancer, gastric cancer, gastrointestinal cancer, gastrointestinal carcinoid cancer, gastrointestinal stromal tumors (GIST), germ cell tumor glioblastoma multiforme (GBM), glioma, hairy cell leukemia, head and neck cancer, hemangioendothelioma, Hodgkin lymphoma, hypopharyngeal cancer, infiltrating ductal carcinoma (IDC), infiltrating lobular carcinoma (ILC), inflammatory breast cancer (IBC), intestinal Cancer, intrahepatic bile duct cancer, invasive/infiltrating breast cancer, Islet cell cancer, jaw cancer, Kaposi sarcoma, kidney cancer, laryngeal cancer, leiomyosarcoma, leptomeningeal metastases, leukemia, lip cancer, liposarcoma, liver cancer, lobular carcinoma in situ, low-grade astrocytoma, lung cancer, lymph node cancer, lymphoma, male breast cancer, medullary carcinoma, medulloblastoma, melanoma, meningioma, Merkel cell carcinoma, mesenchymal chondrosarcoma, mesenchymous, mesothelioma metastatic breast cancer, metastatic melanoma metastatic squamous neck cancer, mixed gliomas, monodermal teratoma, mouth cancer

mucinous carcinoma, mucosal melanoma, multiple myeloma, Mycosis Fungoides, myelodysplastic syndrome, nasal cavity cancer, nasopharyngeal cancer, neck cancer, neuroblastoma, neuroendocrine tumors (NETs), non-Hodgkin's lymphoma, non-small cell lung cancer (NSCLC), oat cell cancer, ocular cancer, ocular melanoma, oligodendroglioma, oral cancer, oral cavity cancer, oropharyngeal cancer, osteogenic sarcoma, osteosarcoma, ovarian cancer, ovarian epithelial cancer ovarian germ cell tumor, ovarian primary peritoneal carcinoma, ovarian sex cord stromal tumor, Paget's disease, pancreatic cancer, papillary carcinoma, paranasal sinus cancer, parathyroid cancer, pelvic cancer, penile cancer, peripheral nerve cancer, peritoneal cancer, pharyngeal cancer, pheochromocytoma, pilocytic astrocytoma, pineal region tumor, pineoblastoma, pituitary gland cancer, primary central nervous system (CNS) lymphoma, prostate cancer, rectal cancer, renal cell carcinoma, renal pelvis cancer, rhabdomyosarcoma, salivary gland cancer, soft tissue sarcoma, bone sarcoma, sarcoma, sinus cancer, skin cancer, small cell lung cancer (SCLC), small intestine cancer, spinal cancer, spinal column cancer, spinal cord cancer, squamous cell carcinoma, stomach cancer, synovial sarcoma, T-cell lymphoma, testicular cancer, throat cancer, thymoma/thymic carcinoma, thyroid cancer, tongue cancer, tonsil cancer, transitional cell cancer, tubal cancer, tubular carcinoma, undiagnosed cancer, ureteral cancer, urethral cancer, uterine adenocarcinoma, uterine cancer, uterine sarcoma, vaginal cancer, vulvar cancer, T-cell lineage acute lymphoblastic leukemia (T-ALL), T-cell lineage lymphoblastic lymphoma (T-LL), peripheral T-cell lymphoma, Adult T-cell leukemia, Pre-B ALL, Pre-B lymphomas, large B-cell lymphoma, Burkitts lymphoma, B-cell ALL, Philadelphia chromosome positive ALL, Philadelphia chromosome positive CML, juvenile myelomonocytic leukemia (JMML), acute promyelocytic leukemia (a subtype of AML), large granular lymphocytic leukemia, Adult T-cell chronic leukemia, diffuse large B cell lymphoma, follicular lymphoma; Mucosa-Associated Lymphatic Tissue lymphoma (MALT), small cell lymphocytic lymphoma, mediastinal large B cell lymphoma, nodal marginal zone B cell lymphoma (NMZL); splenic marginal zone lymphoma (SMZL); intravascular large B-cell lymphoma; primary effusion lymphoma; or lymphomatoid granulomatosis;; B-cell prolymphocytic leukemia; splenic lymphoma/leukemia, unclassifiable, splenic diffuse red pulp small B-cell lymphoma; lymphoplasmacytic lymphoma; heavy chain diseases, for example, Alpha heavy chain disease, Gamma heavy chain disease, Mu heavy chain disease, plasma cell myeloma, solitary plasmacytoma of bone; extraosseous plasmacytoma; primary cutaneous follicle center lymphoma, T cell/histocyte rich large B-cell lymphoma, DLBCL associated with chronic inflammation; Epstein-Barr virus (EBV)+ DLBCL of the elderly; primary mediastinal (thymic) large B-cell lymphoma, primary cutaneous DLBCL, leg type, ALK+ large B-cell lymphoma, plasmablastic lymphoma; large B-cell lymphoma arising in HHV8-associated multicentric, Castleman disease; B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma, or B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and classical Hodgkin lymphoma.

In some embodiments, the cancer is a malignant, rhabdoid tumor, a CD8+ T-cell lymphoma, endometrial carcinoma, ovarian carcinoma, bladder cancer, stomach cancer, pancreatic cancer, esophageal cancer, prostate cancer, renal cell carcinoma, melanoma, colorectal cancer, a sarcoma (e.g., a soft tissue sarcoma, synovial sarcoma, Ewing's sarcoma, osteosarcoma, rhabdomyosarcoma, adult fibrosarcoma, alveolar soft-part sarcoma, angiosarcoma, clear cell sarcoma, desmoplastic small round cell tumor, epithelioid sarcoma, fibromyxoid sarcoma, gastrointestinal stromal tumor, Kaposi sarcoma, liposarcoma, leiomyosarcoma, malignant mesenchymoma malignant peripheral nerve sheath tumors,

myxofibrosarcoma, low-grade rhabdomyosarcoma), non-small cell lung cancer (e.g., squamous or adenocarcinoma), stomach cancer, or breast cancer. In some embodiments, the cancer is a malignant, rhabdoid tumor, a CD8+ T-cell lymphoma, endometrial carcinoma, ovarian carcinoma, bladder cancer, stomach cancer, pancreatic cancer, esophageal cancer, prostate cancer, renal cell carcinoma, melanoma, or colorectal cancer. In some embodiments, the cancer is a sarcoma (e.g., synovial sarcoma or Ewing's sarcoma), non-small cell lung cancer (e.g., squamous or adenocarcinoma), stomach cancer, or breast cancer. In some embodiments, the cancer is sarcoma (e.g., synovial sarcoma or Ewing's sarcoma). In some embodiments, the sarcoma is synovial sarcoma.

In another aspect, the disclosure features a method for treating a viral infection in a subject in need thereof. This method includes administering to the subject an effective amount of any of the foregoing compounds, or pharmaceutically acceptable salts thereof, or any of the foregoing pharmaceutical compositions. In some embodiments, the viral infection is an infection with a virus of the Retroviridae family such as the lentiviruses (e.g. Human immunodeficiency virus (HIV) and deltaretroviruses (e.g., human T cell leukemia virus I (HTLV-I), human T cell leukemia virus II (HTLV-II)); Hepadnaviridae family (e.g. hepatitis B virus (HBV)), Flaviviridae family (e.g. hepatitis C virus (HCV)), Adenoviridae family (e.g. Human Adenovirus), Herpesviridae family (e.g. Human cytomegalovirus (HCMV), Epstein-Barr virus, herpes simplex virus 1 (HSV-1), herpes simplex virus 2 (HSV-2), human herpesvirus 6 (HHV-6), Herpesvirus K*, CMV, varicella-zoster virus), Papillomaviridae family (e.g. Human Papillomavirus (HPV, HPV E1)), Parvoviridae family (e.g. Parvovirus B19), Polyomaviridae family (e.g. JC virus and BK virus), Paramyxoviridae family (e.g. Measles virus), Togaviridae family (e.g. Rubella virus).

In another embodiment of any of the foregoing methods, the method further includes administering to the subject an additional anticancer therapy (e.g., chemotherapeutic or cytotoxic agent or radiotherapy).

In particular embodiments, the additional anticancer therapy is: a chemotherapeutic or cytotoxic agent (e.g., doxorubicin or ifosfamide), a differentiation-inducing agent (e.g., retinoic acid, vitamin D, cytokines), a hormonal agent, an immunological agent, or an anti-angiogenic agent. Chemotherapeutic and cytotoxic agents include, but are not limited to, alkylating agents, cytotoxic antibiotics, antimetabolites, vinca alkaloids, etoposides, and others (e.g., paclitaxel, taxol, docetaxel, taxotere, cis-platinum). A list of additional compounds having anticancer activity can be found in L. Brunton, B. Chabner and B. Knollman (eds). Goodman and Gilman's The Pharmacological Basis of Therapeutics, Twelfth Edition, 2011, McGraw Hill Companies, New York, NY.

In particular embodiments, the compound of the invention and the additional anticancer therapy and any of the foregoing compounds or pharmaceutical compositions are administered within 28 days of each other (e.g., within 21, 14, 10, 7, 5, 4, 3, 2, or 1 days) or within 24 hours (e.g., 12, 6, 3, 2, or 1 hours; or concomitantly) each in an amount that together are effective to treat the subject.

Chemical Terms

The terminology employed herein is for the purpose of describing particular embodiments and is not intended to be limiting.

For any of the following chemical definitions, a number following an atomic symbol indicates that total number of atoms of that element that are present in a particular chemical moiety. As will be

understood, other atoms, such as hydrogen atoms, or substituent groups, as described herein, may be present, as necessary, to satisfy the valences of the atoms. For example, an unsubstituted C₂ alkyl group has the formula –CH₂CH₃. When used with the groups defined herein, a reference to the number of carbon atoms includes the divalent carbon in acetal and ketal groups but does not include the carbonyl carbon in acyl, ester, carbonate, or carbamate groups. A reference to the number of oxygen, nitrogen, or sulfur atoms in a heteroaryl group only includes those atoms that form a part of a heterocyclic ring.

Herein a phrase of the form “optionally substituted X” (e.g., optionally substituted alkyl) is intended to be equivalent to “X, wherein X is optionally substituted” (e.g., “alkyl, wherein said alkyl is optionally substituted”). It is not intended to mean that the feature “X” (e.g., alkyl) *per se* is optional. As described herein, certain compounds of interest may contain one or more “optionally substituted” moieties. In general, the term “substituted”, whether preceded by the term “optionally” or not, means that one or more hydrogens of the designated moiety are replaced with a suitable substituent, e.g., any of the substituents or groups described herein. Unless otherwise indicated, an “optionally substituted” group may have a suitable substituent at each substitutable position of the group, and when more than one position in any given structure may be substituted with more than one substituent selected from a specified group, the substituent may be either the same or different at every position. Combinations of substituents envisioned by the present disclosure are preferably those that result in the formation of stable or chemically feasible compounds. The term “stable”, as used herein, refers to compounds that are not substantially altered when subjected to conditions to allow for their production, detection, and, in certain embodiments, their recovery, purification, and use for one or more of the purposes disclosed herein.

The term “aliphatic,” as used herein, refers to a saturated or unsaturated, straight, branched, or cyclic hydrocarbon. “Aliphatic” is intended herein to include, but is not limited to, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, and cycloalkynyl moieties, and thus incorporates each of these definitions. In one embodiment, “aliphatic” is used to indicate those aliphatic groups having 1-20 carbon atoms. The aliphatic chain can be, for example, mono-unsaturated, di-unsaturated, tri-unsaturated, or polyunsaturated, or alkynyl. Unsaturated aliphatic groups can be in a cis or trans configuration. In one embodiment, the aliphatic group contains from 1 to about 12 carbon atoms, more generally from 1 to about 6 carbon atoms or from 1 to about 4 carbon atoms. In one embodiment, the aliphatic group contains from 1 to about 8 carbon atoms. In certain embodiments, the aliphatic group is C₁-C₂, C₁-C₃, C₁-C₄, C₁-C₅, or C₁-C₆. The specified ranges as used herein indicate an aliphatic group having each member of the range described as an independent species. For example, the term C₁-C₆ aliphatic as used herein indicates a straight or branched alkyl, alkenyl, or alkynyl group having from 1, 2, 3, 4, 5, or 6 carbon atoms and is intended to mean that each of these is described as an independent species. For example, the term C₁-C₄ aliphatic as used herein indicates a straight or branched alkyl, alkenyl, or alkynyl group having from 1, 2, 3, or 4 carbon atoms and is intended to mean that each of these is described as an independent species. In one embodiment, the aliphatic group is substituted with one or more functional groups that results in the formation of a stable moiety.

The term “heteroaliphatic,” as used herein, refers to an aliphatic moiety that contains at least one heteroatom in the chain, for example, an amine, carbonyl, carboxy, oxo, thio, phosphate, phosphonate, nitrogen, phosphorus, silicon, or boron atoms in place of a carbon atom. In one embodiment, the only

heteroatom is nitrogen. In one embodiment, the only heteroatom is oxygen. In one embodiment, the only heteroatom is sulfur. "Heteroaliphatic" is intended herein to include, but is not limited to, heteroalkyl, heteroalkenyl, heteroalkynyl, heterocycloalkyl, heterocycloalkenyl, and heterocycloalkynyl moieties. In one embodiment, "heteroaliphatic" is used to indicate a heteroaliphatic group (cyclic, acyclic, substituted, unsubstituted, branched or unbranched) having 1-20 carbon atoms. In one embodiment, the heteroaliphatic group is optionally substituted in a manner that results in the formation of a stable moiety. Nonlimiting examples of heteroaliphatic moieties are polyethylene glycol, polyalkylene glycol, amide, polyamide, polylactide, polyglycolide, thioether, ether, alkyl-heterocycle-alkyl, —O-alkyl-O-alkyl, and alkyl-O-haloalkyl.

The term "acyl," as used herein, represents a hydrogen or an alkyl group that is attached to a parent molecular group through a carbonyl group, as defined herein, and is exemplified by formyl (i.e., a carboxyaldehyde group), acetyl, trifluoroacetyl, propionyl, and butanoyl. Exemplary unsubstituted acyl groups include from 1 to 6, from 1 to 11, or from 1 to 21 carbons.

The term "alkyl," as used herein, refers to a branched or straight-chain monovalent saturated aliphatic hydrocarbon radical of 1 to 20 carbon atoms (e.g., 1 to 16 carbon atoms, 1 to 10 carbon atoms, 1 to 6 carbon atoms, or 1 to 3 carbon atoms). An "alkylene" is a divalent alkyl group.

The term "alkenyl," as used herein, alone or in combination with other groups, refers to a straight chain or branched hydrocarbon residue having a carbon-carbon double bond and having 2 to 20 carbon atoms (e.g., 2 to 16 carbon atoms, 2 to 10 carbon atoms, 2 to 6, or 2 carbon atoms). An "alkenylene" is a divalent alkenyl group.

The term "alkynyl," as used herein, alone or in combination with other groups, refers to a straight chain or branched hydrocarbon residue having a carbon-carbon triple bond and having 2 to 20 carbon atoms (e.g., 2 to 16 carbon atoms, 2 to 10 carbon atoms, 2 to 6, or 2 carbon atoms). An "alkynylene" is a divalent alkynyl group.

The term "amino," as used herein, represents $-N(R^{N1})_2$, wherein each R^{N1} is, independently, H, OH, NO_2 , $N(R^{N2})_2$, SO_2OR^{N2} , SO_2R^{N2} , SOR^{N2} , an *N*-protecting group, alkyl, alkoxy, aryl, arylalkyl, cycloalkyl, acyl (e.g., acetyl, trifluoroacetyl, or others described herein), wherein each of these recited R^{N1} groups can be optionally substituted; or two R^{N1} combine to form an alkylene or heteroalkylene, and wherein each R^{N2} is, independently, H, alkyl, or aryl. The amino groups of the compounds described herein can be an unsubstituted amino (i.e., $-NH_2$) or a substituted amino (i.e., $-N(R^{N1})_2$).

The term "aryl," as used herein, refers to an aromatic mono- or polycarbocyclic radical of, e.g., 6 to 12, carbon atoms having at least one aromatic ring. Examples of such groups include, but are not limited to, phenyl, naphthyl, 1,2,3,4-tetrahydronaphthyl, 1,2-dihydronaphthyl, indanyl, and 1H-indenyl.

The term "arylalkyl," as used herein, represents an alkyl group substituted with an aryl group. Exemplary unsubstituted arylalkyl groups are from 7 to 30 carbons (e.g., from 7 to 16 or from 7 to 20 carbons, such as C_1 - C_6 alkyl C_6 - C_{10} aryl, C_1 - C_{10} alkyl C_6 - C_{10} aryl, or C_1 - C_{20} alkyl C_6 - C_{10} aryl), such as, benzyl and phenethyl. In some embodiments, the alkyl and the aryl each can be further substituted with 1, 2, 3, or 4 substituent groups as defined herein for the respective groups.

The term "azido," as used herein, represents a $-N_3$ group.

The term “bridged cyclyl,” as used herein, refers to a bridged polycyclic group of 5 to 20 atoms, containing from 1 to 3 bridges. Bridged cyclyl includes bridged carbocyclyl (e.g., norbornyl) and bridged heterocyclyl (e.g., 1,4-diazabicyclo[2.2.2]octane).

The term “cyano,” as used herein, represents a –CN group.

5 The term “carbocyclyl,” as used herein, refers to a non-aromatic C₃-C₁₂, monocyclic or polycyclic (e.g., bicyclic or tricyclic) structure in which the rings are formed by carbon atoms. Carbocyclyl structures include cycloalkyl groups (e.g., cyclohexyl) and unsaturated carbocyclyl radicals (e.g., cyclohexenyl). Polycyclic carbocyclyl includes spirocyclic carbocyclyl, bridged carbocyclyl, and fused carbocyclyl. A “carbocyclylene” is a divalent carbocyclyl group.

10 The term “cycloalkyl,” as used herein, refers to a saturated, non-aromatic, monovalent mono- or polycarbocyclic radical of 3 to 10, preferably 3 to 6 carbon atoms. This term is further exemplified by radicals such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, norbornyl, and adamantyl.

The terms “halo” or “halogen,” as used herein, mean a fluorine (fluoro), chlorine (chloro), bromine (bromo), or iodine (iodo) radical.

15 The term “heteroalkyl,” as used herein, refers to an alkyl group, as defined herein, in which one or more of the constituent carbon atoms have been replaced by nitrogen, oxygen, or sulfur. In some embodiments, the heteroalkyl group can be further substituted with 1, 2, 3, or 4 substituent groups as described herein for alkyl groups. Examples of heteroalkyl groups are an “alkoxy” which, as used herein, refers to alkyl–O– (e.g., methoxy and ethoxy), and an “alkylamino” which, as used herein, refers to
20 –N(alkyl)R^{Na}, where R^{Na} is H or alkyl (e.g., methylamino). A “heteroalkylene” is a divalent heteroalkyl group.

The term “heteroalkenyl,” as used herein, refers to an alkenyl group, as defined herein, in which one or more of the constituent carbon atoms have been replaced by nitrogen, oxygen, or sulfur. In some embodiments, the heteroalkenyl group can be further substituted with 1, 2, 3, or 4 substituent groups as
25 described herein for alkenyl groups. Examples of heteroalkenyl groups are an “alkenoxy” which, as used herein, refers to alkenyl–O–. A “heteroalkenylene” is a divalent heteroalkenyl group.

The term “heteroalkynyl,” as used herein, refers to an alkynyl group, as defined herein, in which one or more of the constituent carbon atoms have been replaced by nitrogen, oxygen, or sulfur. In some embodiments, the heteroalkynyl group can be further substituted with 1, 2, 3, or 4 substituent groups as
30 described herein for alkynyl groups. Examples of heteroalkynyl groups are an “alkynoxy” which, as used herein, refers to alkynyl–O–. A “heteroalkynylene” is a divalent heteroalkynyl group.

The term “heteroaryl,” as used herein, refers to an aromatic monocyclic or polycyclic structure of 5 to 12 atoms having at least one aromatic ring containing 1, 2, or 3 ring atoms selected from nitrogen, oxygen, and sulfur, with the remaining ring atoms being carbon. One or two ring carbon atoms of the
35 heteroaryl group may be replaced with a carbonyl group. Examples of heteroaryl groups are pyridyl, pyrazoyl, benzooxazolyl, benzoimidazolyl, benzothiazolyl, imidazolyl, oxazolyl, and thiazolyl. A “heteroarylene” is a divalent heteroaryl group.

The term “heteroarylalkyl,” as used herein, represents an alkyl group substituted with a heteroaryl group. Exemplary unsubstituted heteroarylalkyl groups are from 7 to 30 carbons (e.g., from 7 to 16 or
40 from 7 to 20 carbons, such as C₁-C₆ alkyl C₂-C₉ heteroaryl, C₁-C₁₀ alkyl C₂-C₉ heteroaryl, or C₁-C₂₀ alkyl

C₂-C₉ heteroaryl). In some embodiments, the alkyl and the heteroaryl each can be further substituted with 1, 2, 3, or 4 substituent groups as defined herein for the respective groups.

The term "heterocyclyl," as used herein, refers a monocyclic or polycyclic radical (e.g., bicyclic or tricyclic) having 3 to 12 atoms having at least one non-aromatic ring containing 1, 2, 3, or 4 ring atoms selected from N, O, or S, and no aromatic ring containing any N, O, or S atoms. Polycyclic heterocyclyl includes spirocyclic heterocyclyl, bridged heterocyclyl, and fused heterocyclyl. Examples of heterocyclyl groups include, but are not limited to, morpholinyl, thiomorpholinyl, furyl, piperazinyl, piperidinyl, pyranyl, pyrrolidinyl, tetrahydropyranyl, tetrahydrofuranlyl, and 1,3-dioxanyl. A "heterocyclylene" is a divalent heterocyclyl group.

The term "heterocyclylalkyl," as used herein, represents an alkyl group substituted with a heterocyclyl group. Exemplary unsubstituted heterocyclylalkyl groups are from 7 to 30 carbons (e.g., from 7 to 16 or from 7 to 20 carbons, such as C₁-C₆ alkyl C₂-C₉ heterocyclyl, C₁-C₁₀ alkyl C₂-C₉ heterocyclyl, or C₁-C₂₀ alkyl C₂-C₉ heterocyclyl). In some embodiments, the alkyl and the heterocyclyl each can be further substituted with 1, 2, 3, or 4 substituent groups as defined herein for the respective groups.

The term "hydroxyalkyl," as used herein, represents alkyl group substituted with an -OH group.

The term "hydroxyl," as used herein, represents an -OH group.

The term "imine," as used herein, represents =NR^N group, where R^N is, e.g., H or alkyl.

The term "*N*-protecting group," as used herein, represents those groups intended to protect an amino group against undesirable reactions during synthetic procedures. Commonly used *N*-protecting groups are disclosed in Greene, "Protective Groups in Organic Synthesis," 3rd Edition (John Wiley & Sons, New York, 1999). *N*-protecting groups include, but are not limited to, acyl, aryloyl, or carbamyl groups such as formyl, acetyl, propionyl, pivaloyl, t-butylacetyl, 2-chloroacetyl, 2-bromoacetyl, trifluoroacetyl, trichloroacetyl, phthalyl, o-nitrophenoxyacetyl, α-chlorobutyryl, benzoyl, 4-chlorobenzoyl, 4-bromobenzoyl, 4-nitrobenzoyl, and chiral auxiliaries such as protected or unprotected D, L, or D, L-amino acids such as alanine, leucine, and phenylalanine; sulfonyl-containing groups such as benzenesulfonyl, and p-toluenesulfonyl; carbamate forming groups such as benzyloxycarbonyl, p-chlorobenzyloxycarbonyl, p-methoxybenzyloxycarbonyl, p-nitrobenzyloxycarbonyl, 2-nitrobenzyloxycarbonyl, p-bromobenzyloxycarbonyl, 3,4-dimethoxybenzyloxycarbonyl, 3,5-dimethoxybenzyloxycarbonyl, 2,4-dimethoxybenzyloxycarbonyl, 4-methoxybenzyloxycarbonyl, 2-nitro-4,5-dimethoxybenzyloxycarbonyl, 3,4,5-trimethoxybenzyloxycarbonyl, 1-(p-biphenyl)-1-methylethoxycarbonyl, α,α-dimethyl-3,5-dimethoxybenzyloxycarbonyl, benzhydryloxy carbonyl, t-butyloxycarbonyl, diisopropylmethoxycarbonyl, isopropylloxycarbonyl, ethoxycarbonyl, methoxycarbonyl, allyloxycarbonyl, 2,2,2-trichloroethoxycarbonyl, phenoxycarbonyl, 4-nitrophenoxy carbonyl, fluorenyl-9-methoxycarbonyl, cyclopentylloxycarbonyl, adamantylloxycarbonyl, cyclohexylloxycarbonyl, and phenylthiocarbonyl, arylalkyl groups such as benzyl, triphenylmethyl, and benzyloxymethyl, and silyl groups, such as trimethylsilyl. Preferred *N*-protecting groups are alloc, formyl, acetyl, benzoyl, pivaloyl, t-butylacetyl, alanyl, phenylsulfonyl, benzyl, t-butyloxycarbonyl (Boc), and benzyloxycarbonyl (Cbz).

The term "nitro," as used herein, represents an -NO₂ group.

The term "oxo," as used herein, represents an =O group.

The term "thiol," as used herein, represents an -SH group.

The alkyl, alkenyl, alkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, carbocyclyl (e.g., cycloalkyl), aryl, heteroaryl, and heterocyclyl groups may be substituted or unsubstituted. When substituted, there will generally be 1 to 4 substituents present, unless otherwise specified. Substituents include, for example: alkyl (e.g., unsubstituted and substituted, where the substituents include any group described herein, e.g., aryl, halo, hydroxy), aryl (e.g., substituted and unsubstituted phenyl), carbocyclyl (e.g., substituted and unsubstituted cycloalkyl), halogen (e.g., fluoro), hydroxyl, heteroalkyl (e.g., substituted and unsubstituted methoxy, ethoxy, or thioalkoxy), heteroaryl, heterocyclyl, amino (e.g., NH₂ or mono- or dialkyl amino), azido, cyano, nitro, oxo, sulfonyl, or thiol. Aryl, carbocyclyl (e.g., cycloalkyl), heteroaryl, and heterocyclyl groups may also be substituted with alkyl (unsubstituted and substituted such as arylalkyl (e.g., substituted and unsubstituted benzyl)).

Compounds described herein (e.g., compounds of the invention) can have one or more asymmetric carbon atoms and can exist in the form of optically pure enantiomers, mixtures of enantiomers such as, for example, racemates, optically pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, or mixtures of diastereoisomeric racemates. The optically active forms can be obtained for example by resolution of the racemates, by asymmetric synthesis or asymmetric chromatography (chromatography with a chiral adsorbent or eluant). That is, certain of the disclosed compounds may exist in various stereoisomeric forms. Stereoisomers are compounds that differ only in their spatial arrangement. Enantiomers are pairs of stereoisomers whose mirror images are not superimposable, most commonly because they contain an asymmetrically substituted carbon atom that acts as a chiral center. "Enantiomer" means one of a pair of molecules that are mirror images of each other and are not superimposable. Diastereomers are stereoisomers that are not related as mirror images, most commonly because they contain two or more asymmetrically substituted carbon atoms and represent the configuration of substituents around one or more chiral carbon atoms. Enantiomers of a compound can be prepared, for example, by separating an enantiomer from a racemate using one or more well-known techniques and methods, such as, for example, chiral chromatography and separation methods based thereon. The appropriate technique and/or method for separating an enantiomer of a compound described herein from a racemic mixture can be readily determined by those of skill in the art. "Racemate" or "racemic mixture" means a compound containing two enantiomers, wherein such mixtures exhibit no optical activity; i.e., they do not rotate the plane of polarized light. "Geometric isomer" means isomers that differ in the orientation of substituent atoms in relationship to a carbon-carbon double bond, to a cycloalkyl ring, or to a bridged bicyclic system. Atoms (other than H) on each side of a carbon-carbon double bond may be in an E (substituents are on opposite sides of the carbon-carbon double bond) or Z (substituents are oriented on the same side) configuration. "R," "S," "S*," "R*," "E," "Z," "cis," and "trans," indicate configurations relative to the core molecule. Certain of the disclosed compounds may exist in atropisomeric forms. Atropisomers are stereoisomers resulting from hindered rotation about single bonds where the steric strain barrier to rotation is high enough to allow for the isolation of the conformers. The compounds described herein (e.g., the compounds of the invention) may be prepared as individual isomers by either isomer-specific synthesis or resolved from an isomeric mixture. Conventional resolution techniques include forming the salt of a free base of each isomer of an isomeric pair using an optically active acid (followed by fractional crystallization and regeneration of the free base), forming the salt of the acid form of each isomer of an

isomeric pair using an optically active amine (followed by fractional crystallization and regeneration of the free acid), forming an ester or amide of each of the isomers of an isomeric pair using an optically pure acid, amine or alcohol (followed by chromatographic separation and removal of the chiral auxiliary), or resolving an isomeric mixture of either a starting material or a final product using various well known chromatographic methods. When the stereochemistry of a disclosed compound is named or depicted by structure, the named or depicted stereoisomer is at least 60%, 70%, 80%, 90%, 99%, or 99.9% by weight relative to the other stereoisomers. When a single enantiomer is named or depicted by structure, the depicted or named enantiomer is at least 60%, 70%, 80%, 90%, 99%, or 99.9% by weight optically pure. When a single diastereomer is named or depicted by structure, the depicted or named diastereomer is at least 60%, 70%, 80%, 90%, 99%, or 99.9% by weight pure. Percent optical purity is the ratio of the weight of the enantiomer or over the weight of the enantiomer plus the weight of its optical isomer.

Diastereomeric purity by weight is the ratio of the weight of one diastereomer or over the weight of all the diastereomers. When the stereochemistry of a disclosed compound is named or depicted by structure, the named or depicted stereoisomer is at least 60%, 70%, 80%, 90%, 99%, or 99.9% by mole fraction pure relative to the other stereoisomers. When a single enantiomer is named or depicted by structure, the depicted or named enantiomer is at least 60%, 70%, 80%, 90%, 99%, or 99.9% by mole fraction pure. When a single diastereomer is named or depicted by structure, the depicted or named diastereomer is at least 60%, 70%, 80%, 90%, 99%, or 99.9% by mole fraction pure. Percent purity by mole fraction is the ratio of the moles of the enantiomer or over the moles of the enantiomer plus the moles of its optical isomer. Similarly, percent purity by moles fraction is the ratio of the moles of the diastereomer or over the moles of the diastereomer plus the moles of its isomer. When a disclosed compound is named or depicted by structure without indicating the stereochemistry, and the compound has at least one chiral center, it is to be understood that the name or structure encompasses either enantiomer of the compound free from the corresponding optical isomer, a racemic mixture of the compound, or mixtures enriched in one enantiomer relative to its corresponding optical isomer. When a disclosed compound is named or depicted by structure without indicating the stereochemistry and has two or more chiral centers, it is to be understood that the name or structure encompasses a diastereomer free of other diastereomers, a number of diastereomers free from other diastereomeric pairs, mixtures of diastereomers, mixtures of diastereomeric pairs, mixtures of diastereomers in which one diastereomer is enriched relative to the other diastereomer(s), or mixtures of diastereomers in which one or more diastereomer is enriched relative to the other diastereomers. The invention embraces all of these forms.

Compounds of the present disclosure also include all of the isotopes of the atoms occurring in the intermediate or final compounds. "Isotopes" refers to atoms having the same atomic number but different mass numbers resulting from a different number of neutrons in the nuclei. For example, isotopes of hydrogen include tritium and deuterium.

Unless otherwise stated, structures depicted herein are also meant to include compounds that differ only in the presence of one or more isotopically enriched atoms. Exemplary isotopes that can be incorporated into compounds of the present invention include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorus, sulfur, fluorine, chlorine, and iodine, such as ^2H , ^3H , ^{11}C , ^{13}C , ^{14}C , ^{13}N , ^{15}N , ^{15}O , ^{17}O , ^{18}O , ^{32}P , ^{33}P , ^{35}S , ^{18}F , ^{36}Cl , ^{123}I and ^{125}I . Isotopically-labeled compounds (e.g., those labeled with ^3H and ^{14}C) can be useful in compound or substrate tissue distribution assays. Tritiated (i.e., ^3H) and carbon-14

(i.e., ^{14}C) isotopes can be useful for their ease of preparation and detectability. Further, substitution with heavier isotopes such as deuterium (i.e., ^2H) may afford certain therapeutic advantages resulting from greater metabolic stability (e.g., increased in vivo half-life or reduced dosage requirements). In some embodiments, one or more hydrogen atoms are replaced by ^2H or ^3H , or one or more carbon atoms are replaced by ^{13}C - or ^{14}C -enriched carbon. Positron emitting isotopes such as ^{15}O , ^{13}N , ^{11}C , and ^{18}F are useful for positron emission tomography (PET) studies to examine substrate receptor occupancy. Preparations of isotopically labelled compounds are known to those of skill in the art. For example, isotopically labeled compounds can generally be prepared by following procedures analogous to those disclosed for compounds of the present invention described herein, by substituting an isotopically labeled reagent for a non-isotopically labeled reagent.

As is known in the art, many chemical entities can adopt a variety of different solid forms such as, for example, amorphous forms or crystalline forms (e.g., polymorphs, hydrates, solvate). In some embodiments, compounds of the present invention may be utilized in any such form, including in any solid form. In some embodiments, compounds described or depicted herein may be provided or utilized in hydrate or solvate form.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Methods and materials are described herein for use in the present disclosure; other, suitable methods and materials known in the art can also be used. The materials, methods, and examples are illustrative only and not intended to be limiting. All publications, patent applications, patents, sequences, database entries, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control.

Definitions

In this application, unless otherwise clear from context, (i) the term “a” may be understood to mean “at least one”; (ii) the term “or” may be understood to mean “and/or”; and (iii) the terms “including” and “including” may be understood to encompass itemized components or steps whether presented by themselves or together with one or more additional components or steps.

As used herein, the terms “about” and “approximately” refer to a value that is within 10% above or below the value being described. For example, the term “about 5 nM” indicates a range of from 4.5 to 5.5 nM.

As used herein, the term “administration” refers to the administration of a composition (e.g., a compound or a preparation that includes a compound as described herein) to a subject or system. Administration to an animal subject (e.g., to a human) may be by any appropriate route. For example, in some embodiments, administration may be bronchial (including by bronchial instillation), buccal, enteral, interdermal, intra-arterial, intradermal, intragastric, intramedullary, intramuscular, intranasal, intraperitoneal, intrathecal, intratumoral, intravenous, intraventricular, mucosal, nasal, oral, rectal, subcutaneous, sublingual, topical, tracheal (including by intratracheal instillation), transdermal, vaginal, and vitreal.

As used herein, the term “adult soft tissue sarcoma” refers to a sarcoma that develops in the soft tissues of the body, typically in adolescent and adult subjects (e.g., subjects who are at least 10 years

old, 11 years old, 12 years old, 13 years old, 14 years old, 15 years old, 16 years old, 17 years old, 18 years old, or 19 years old). Non-limiting examples of adult soft tissue sarcoma include, but are not limited to, synovial sarcoma, fibrosarcoma, malignant fibrous histiocytoma, dermatofibrosarcoma, liposarcoma, leiomyosarcoma, hemangiosarcoma, Kaposi's sarcoma, lymphangiosarcoma, malignant peripheral nerve sheath tumor/neurofibrosarcoma, extraskelatal chondrosarcoma, extraskelatal osteosarcoma, extraskelatal myxoid chondrosarcoma, and extraskelatal mesenchymal.

The term "antisense," as used herein, refers to a nucleic acid comprising a polynucleotide that is sufficiently complementary to all or a portion of a gene, primary transcript, or processed mRNA, so as to interfere with expression of the endogenous gene (e.g., BRD9). "Complementary" polynucleotides are those that are capable of base pairing according to the standard Watson-Crick complementarity rules. Specifically, purines will base pair with pyrimidines to form a combination of guanine paired with cytosine (G:C) and adenine paired with either thymine (A:T) in the case of DNA, or adenine paired with uracil (A:U) in the case of RNA. It is understood that two polynucleotides may hybridize to each other even if they are not completely complementary to each other, provided that each has at least one region that is substantially complementary to the other.

The term "antisense nucleic acid" includes single-stranded RNA as well as double-stranded DNA expression cassettes that can be transcribed to produce an antisense RNA. "Active" antisense nucleic acids are antisense RNA molecules that are capable of selectively hybridizing with a primary transcript or mRNA encoding a polypeptide having at least 80% sequence identity (e.g., 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.9% identity, or more) with the targeted polypeptide sequence (e.g., a BRD9 polypeptide sequence). The antisense nucleic acid can be complementary to an entire coding strand, or to only a portion thereof. In some embodiments, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence. The term "coding region" refers to the region of the nucleotide sequence comprising codons that are translated into amino acid residues. In some embodiments, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence. The term "noncoding region" refers to 5' and 3' sequences that flank the coding region that are not translated into amino acids (i.e., also referred to as 5' and 3' untranslated regions). The antisense nucleic acid molecule can be complementary to the entire coding region of mRNA, or can be antisense to only a portion of the coding or noncoding region of an mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site. An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45, or 50 nucleotides in length.

As used herein, the term "BAF complex" refers to the BRG1- or HRBM-associated factors complex in a human cell.

As used herein, the term "BAF complex-related disorder" refers to a disorder that is caused or affected by the level and/or activity of a BAF complex.

As used herein, the terms "GBAF complex" and "GBAF" refer to a SWI/SNF ATPase chromatin remodeling complex in a human cell. GBAF complex subunits may include, but are not limited to, ACTB, ACTL6A, ACTL6B, BICRA, BICRAL, BRD9, SMARCA2, SMARCA4, SMARCC1, SMARCD1, SMARCD2, SMARCD3, and SS18. The term "cancer" refers to a condition caused by the proliferation of malignant neoplastic cells, such as tumors, neoplasms, carcinomas, sarcomas, leukemias, and lymphomas.

As used herein, the term “BRD9” refers to bromodomain-containing protein 9, a component of the BAF (BRG1- or BRM-associated factors) complex, a SWI/SNF ATPase chromatin remodeling complex, and belongs to family IV of the bromodomain-containing proteins. BRD9 is encoded by the *BRD9* gene, the nucleic acid sequence of which is set forth in SEQ ID NO: 1. The term “BRD9” also refers to natural
5 variants of the wild-type BRD9 protein, such as proteins having at least 85% identity (e.g., 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.9% identity, or more) to the amino acid sequence of wild-type BRD9, which is set forth in SEQ ID NO: 2.

As used herein, the term “BRD9-related disorder” refers to a disorder that is caused or affected by the level and/or activity of BRD9. The term “cancer” refers to a condition caused by the proliferation of
10 malignant neoplastic cells, such as tumors, neoplasms, carcinomas, sarcomas, leukemias, and lymphomas.

As used herein, a “combination therapy” or “administered in combination” means that two (or more) different agents or treatments are administered to a subject as part of a defined treatment regimen for a particular disease or condition. The treatment regimen defines the doses and periodicity of
15 administration of each agent such that the effects of the separate agents on the subject overlap. In some embodiments, the delivery of the two or more agents is simultaneous or concurrent and the agents may be co-formulated. In some embodiments, the two or more agents are not co-formulated and are administered in a sequential manner as part of a prescribed regimen. In some embodiments, administration of two or more agents or treatments in combination is such that the reduction in a
20 symptom, or other parameter related to the disorder is greater than what would be observed with one agent or treatment delivered alone or in the absence of the other. The effect of the two treatments can be partially additive, wholly additive, or greater than additive (e.g., synergistic). Sequential or substantially simultaneous administration of each therapeutic agent can be effected by any appropriate route including, but not limited to, oral routes, intravenous routes, intramuscular routes, and direct absorption through
25 mucous membrane tissues. The therapeutic agents can be administered by the same route or by different routes. For example, a first therapeutic agent of the combination may be administered by intravenous injection while a second therapeutic agent of the combination may be administered orally.

A “compound of the present invention” and similar terms as used herein, whether explicitly noted or not, refers to compounds useful for treating BAF-related disorders (e.g., cancer or infection) described
30 herein, including, e.g., compounds of **Formula I** or **Formula II** (e.g., compounds of Table 2A, Table 2B, and Table 2C), as well as salts (e.g., pharmaceutically acceptable salts), solvates, hydrates, stereoisomers (including atropisomers), and tautomers thereof. Those skilled in the art will appreciate that certain compounds described herein can exist in one or more different isomeric (e.g., stereoisomers, geometric isomers, atropisomers, and tautomers) or isotopic (e.g., in which one or more atoms has been
35 substituted with a different isotope of the atom, such as hydrogen substituted for deuterium) forms. Unless otherwise indicated or clear from context, a depicted structure can be understood to represent any such isomeric or isotopic form, individually or in combination. Compounds described herein can be asymmetric (e.g., having one or more stereocenters). All stereoisomers, such as enantiomers and diastereomers, are intended unless otherwise indicated. Compounds of the present disclosure that
40 contain asymmetrically substituted carbon atoms can be isolated in optically active or racemic forms. Methods on how to prepare optically active forms from optically active starting materials are known in the

art, such as by resolution of racemic mixtures or by stereoselective synthesis. Many geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds described herein, and all such stable isomers are contemplated in the present disclosure. Cis and trans geometric isomers of the compounds of the present disclosure are described and may be isolated as a mixture of isomers or as separated isomeric forms. In some embodiments, one or more compounds depicted herein may exist in different tautomeric forms. As will be clear from context, unless explicitly excluded, references to such compounds encompass all such tautomeric forms. In some embodiments, tautomeric forms result from the swapping of a single bond with an adjacent double bond and the concomitant migration of a proton. In certain embodiments, a tautomeric form may be a prototropic tautomer, which is an isomeric protonation states having the same empirical formula and total charge as a reference form. Examples of moieties with prototropic tautomeric forms are ketone - enol pairs, amide - imidic acid pairs, lactam - lactim pairs, amide - imidic acid pairs, enamine - imine pairs, and annular forms where a proton can occupy two or more positions of a heterocyclic system, such as, 1H- and 3H-imidazole, 1H-, 2H- and 4H-1,2,4-triazole, 1H- and 2H- isoindole, and 1H- and 2H-pyrazole. In some embodiments, tautomeric forms can be in equilibrium or sterically locked into one form by appropriate substitution. In certain embodiments, tautomeric forms result from acetal interconversion.

As used herein, the term “degrader” refers to a small molecule compound including a degradation moiety, wherein the compound interacts with a protein (e.g., BRD9) in a way which results in degradation of the protein, e.g., binding of the compound results in at least 5% reduction of the level of the protein, e.g., in a cell or subject.

As used herein, the term “degradation moiety” refers to a moiety whose binding results in degradation of a protein, e.g., BRD9. In one example, the moiety binds to a protease or a ubiquitin ligase that metabolizes the protein, e.g., BRD9.

By “determining the level of a protein” is meant the detection of a protein, or an mRNA encoding the protein, by methods known in the art either directly or indirectly. “Directly determining” means performing a process (e.g., performing an assay or test on a sample or “analyzing a sample” as that term is defined herein) to obtain the physical entity or value. “Indirectly determining” refers to receiving the physical entity or value from another party or source (e.g., a third-party laboratory that directly acquired the physical entity or value). Methods to measure protein level generally include, but are not limited to, western blotting, immunoblotting, enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), immunoprecipitation, immunofluorescence, surface plasmon resonance, chemiluminescence, fluorescent polarization, phosphorescence, immunohistochemical analysis, matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry, liquid chromatography (LC)-mass spectrometry, microcytometry, microscopy, fluorescence activated cell sorting (FACS), and flow cytometry, as well as assays based on a property of a protein including, but not limited to, enzymatic activity or interaction with other protein partners. Methods to measure mRNA levels are known in the art.

As used herein, the terms “effective amount,” “therapeutically effective amount,” and “a sufficient amount” of an agent that reduces the level and/or activity of BRD9 (e.g., in a cell or a subject) described herein refer to a quantity sufficient to, when administered to the subject, including a human, effect beneficial or desired results, including clinical results, and, as such, an “effective amount” or synonym thereto depends on the context in which it is being applied. For example, in the context of treating

cancer, it is an amount of the agent that reduces the level and/or activity of BRD9 sufficient to achieve a treatment response as compared to the response obtained without administration of the agent that reduces the level and/or activity of BRD9. The amount of a given agent that reduces the level and/or activity of BRD9 described herein that will correspond to such an amount will vary depending upon various factors, such as the given agent, the pharmaceutical formulation, the route of administration, the type of disease or disorder, the identity of the subject (e.g., age, sex, and/or weight) or host being treated, and the like, but can nevertheless be routinely determined by one of skill in the art. Also, as used herein, a “therapeutically effective amount” of an agent that reduces the level and/or activity of BRD9 of the present disclosure is an amount which results in a beneficial or desired result in a subject as compared to a control. As defined herein, a therapeutically effective amount of an agent that reduces the level and/or activity of BRD9 of the present disclosure may be readily determined by one of ordinary skill by routine methods known in the art. Dosage regimen may be adjusted to provide the optimum therapeutic response.

As used herein, the term “inhibitor” refers to any agent which reduces the level and/or activity of a protein (e.g., BRD9). Non-limiting examples of inhibitors include small molecule inhibitors, degraders, antibodies, enzymes, or polynucleotides (e.g., siRNA).

The term “inhibitory RNA agent” refers to an RNA, or analog thereof, having sufficient sequence complementarity to a target RNA to direct RNA interference. Examples also include a DNA that can be used to make the RNA. RNA interference (RNAi) refers to a sequence-specific or selective process by which a target molecule (e.g., a target gene, protein, or RNA) is down-regulated. Generally, an interfering RNA (“iRNA”) is a double-stranded short-interfering RNA (siRNA), short hairpin RNA (shRNA), or single-stranded micro-RNA (miRNA) that results in catalytic degradation of specific mRNAs, and also can be used to lower or inhibit gene expression.

By “level” is meant a level of a protein, or mRNA encoding the protein, as compared to a reference. The reference can be any useful reference, as defined herein. By a “decreased level” or an “increased level” of a protein is meant a decrease or increase in protein level, as compared to a reference (e.g., a decrease or an increase by about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, about 150%, about 200%, about 300%, about 400%, about 500%, or more; a decrease or an increase of more than about 10%, about 15%, about 20%, about 50%, about 75%, about 100%, or about 200%, as compared to a reference; a decrease or an increase by less than about 0.01-fold, about 0.02-fold, about 0.1-fold, about 0.3-fold, about 0.5-fold, about 0.8-fold, or less; or an increase by more than about 1.2-fold, about 1.4-fold, about 1.5-fold, about 1.8-fold, about 2.0-fold, about 3.0-fold, about 3.5-fold, about 4.5-fold, about 5.0-fold, about 10-fold, about 15-fold, about 20-fold, about 30-fold, about 40-fold, about 50-fold, about 100-fold, about 1000-fold, or more). A level of a protein may be expressed in mass/vol (e.g., g/dL, mg/mL, µg/mL, ng/mL) or percentage relative to total protein or mRNA in a sample.

The terms “miRNA” and “microRNA” refer to an RNA agent, preferably a single-stranded agent, of about 10-50 nucleotides in length, preferably between about 15-25 nucleotides in length, which is capable of directing or mediating RNA interference. Naturally-occurring miRNAs are generated from stem-loop precursor RNAs (i.e., pre-miRNAs) by Dicer. The term “Dicer” as used herein, includes Dicer as well as

any Dicer ortholog or homolog capable of processing dsRNA structures into siRNAs, miRNAs, siRNA-like or miRNA-like molecules. The term microRNA ("miRNA") is used interchangeably with the term "small temporal RNA" ("stRNA") based on the fact that naturally-occurring miRNAs have been found to be expressed in a temporal fashion (e.g., during development).

By "modulating the activity of a BAF complex," is meant altering the level of an activity related to a BAF complex (e.g., GBAF), or a related downstream effect. The activity level of a BAF complex may be measured using any method known in the art, e.g., the methods described in Kadoch et al, Cell 153:71-85 (2013), the methods of which are herein incorporated by reference.

"Percent (%) sequence identity" with respect to a reference polynucleotide or polypeptide sequence is defined as the percentage of nucleic acids or amino acids in a candidate sequence that are identical to the nucleic acids or amino acids in the reference polynucleotide or polypeptide sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity. Alignment for purposes of determining percent nucleic acid or amino acid sequence identity can be achieved in various ways that are within the capabilities of one of skill in the art, for example, using publicly available computer software such as BLAST, BLAST-2, or Megalign software. Those skilled in the art can determine appropriate parameters for aligning sequences, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared. For example, percent sequence identity values may be generated using the sequence comparison computer program BLAST. As an illustration, the percent sequence identity of a given nucleic acid or amino acid sequence, A, to, with, or against a given nucleic acid or amino acid sequence, B, (which can alternatively be phrased as a given nucleic acid or amino acid sequence, A that has a certain percent sequence identity to, with, or against a given nucleic acid or amino acid sequence, B) is calculated as follows:

$$100 \text{ multiplied by (the fraction } X/Y \text{)}$$

where X is the number of nucleotides or amino acids scored as identical matches by a sequence alignment program (e.g., BLAST) in that program's alignment of A and B, and where Y is the total number of nucleic acids in B. It will be appreciated that where the length of nucleic acid or amino acid sequence A is not equal to the length of nucleic acid or amino acid sequence B, the percent sequence identity of A to B will not equal the percent sequence identity of B to A.

A "pharmaceutically acceptable excipient," as used herein, refers any ingredient other than the compounds described herein (for example, a vehicle capable of suspending or dissolving the active compound) and having the properties of being substantially nontoxic and non-inflammatory in a patient. Excipients may include, for example: antiadherents, antioxidants, binders, coatings, compression aids, disintegrants, dyes (colors), emollients, emulsifiers, fillers (diluent), film formers or coatings, flavors, fragrances, glidants (flow enhancers), lubricants, preservatives, printing inks, sorbents, suspending or dispersing agents, sweeteners, and waters of hydration. Exemplary excipients include, but are not limited to: butylated hydroxytoluene (BHT), calcium carbonate, calcium phosphate (dibasic), calcium stearate, croscarmellose, crosslinked polyvinyl pyrrolidone, citric acid, crospovidone, cysteine, ethylcellulose, gelatin, hydroxypropyl cellulose, hydroxypropyl methylcellulose, lactose, magnesium stearate, maltitol, mannitol, methionine, methylcellulose, methyl paraben, microcrystalline cellulose, polyethylene glycol, polyvinyl pyrrolidone, povidone, pregelatinized starch, propyl paraben, retinyl palmitate, shellac, silicon

dioxide, sodium carboxymethyl cellulose, sodium citrate, sodium starch glycolate, sorbitol, starch (corn), stearic acid, sucrose, talc, titanium dioxide, vitamin A, vitamin E, vitamin C, and xylitol.

As used herein, the term "pharmaceutically acceptable salt" means any pharmaceutically acceptable salt of the compound of any of the compounds described herein. For example,

pharmaceutically acceptable salts of any of the compounds described herein include those that are within the scope of sound medical judgment, suitable for use in contact with the tissues of humans and animals without undue toxicity, irritation, allergic response and are commensurate with a reasonable benefit/risk ratio. Pharmaceutically acceptable salts are well known in the art. For example, pharmaceutically acceptable salts are described in: Berge et al., J. Pharmaceutical Sciences 66:1-19, 1977 and in Pharmaceutical Salts: Properties, Selection, and Use, (Eds. P.H. Stahl and C.G. Wermuth), Wiley-VCH, 2008. The salts can be prepared in situ during the final isolation and purification of the compounds described herein or separately by reacting a free base group with a suitable organic acid.

The compounds described herein may have ionizable groups so as to be capable of preparation as pharmaceutically acceptable salts. These salts may be acid addition salts involving inorganic or organic acids or the salts may, in the case of acidic forms of the compounds described herein, be prepared from inorganic or organic bases. Frequently, the compounds are prepared or used as pharmaceutically acceptable salts prepared as addition products of pharmaceutically acceptable acids or bases. Suitable pharmaceutically acceptable acids and bases and methods for preparation of the appropriate salts are well-known in the art. Salts may be prepared from pharmaceutically acceptable non-toxic acids and bases including inorganic and organic acids and bases. Representative acid addition salts include acetate, adipate, alginate, ascorbate, aspartate, benzenesulfonate, benzoate, bisulfate, borate, butyrate, camphorate, camphorsulfonate, citrate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, fumarate, glucoheptonate, glycerophosphate, hemisulfate, heptonate, hexanoate, hydrobromide, hydrochloride, hydroiodide, 2-hydroxy-ethanesulfonate, lactobionate, lactate, laurate, lauryl sulfate, malate, maleate, malonate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, nitrate, oleate, oxalate, palmitate, pamoate, pectinate, persulfate, 3-phenylpropionate, phosphate, picrate, pivalate, propionate, stearate, succinate, sulfate, tartrate, thiocyanate, toluenesulfonate, undecanoate, and valerate salts. Representative alkali or alkaline earth metal salts include sodium, lithium, potassium, calcium, and magnesium, as well as nontoxic ammonium, quaternary ammonium, and amine cations, including, but not limited to ammonium, tetramethylammonium, tetraethylammonium, methylamine, dimethylamine, trimethylamine, triethylamine, and ethylamine.

The term "pharmaceutical composition," as used herein, represents a composition containing a compound described herein formulated with a pharmaceutically acceptable excipient, and manufactured or sold with the approval of a governmental regulatory agency as part of a therapeutic regimen for the treatment of disease in a mammal. Pharmaceutical compositions can be formulated, for example, for oral administration in unit dosage form (e.g., a tablet, capsule, caplet, gelcap, or syrup); for topical administration (e.g., as a cream, gel, lotion, or ointment); for intravenous administration (e.g., as a sterile solution free of particulate emboli and in a solvent system suitable for intravenous use); or in any other pharmaceutically acceptable formulation.

By "reducing the activity of BRD9," is meant decreasing the level of an activity related to an BRD9, or a related downstream effect. A non-limiting example of inhibition of an activity of BRD9 is

decreasing the level of a BAF complex (e.g., GBAF) in a cell. The activity level of BRD9 may be measured using any method known in the art. In some embodiments, an agent which reduces the activity of BRD9 is a small molecule BRD9 inhibitor. In some embodiments, an agent which reduces the activity of BRD9 is a small molecule BRD9 degrader.

5 By “reducing the level of BRD9,” is meant decreasing the level of BRD9 in a cell or subject. The level of BRD9 may be measured using any method known in the art.

By a “reference” is meant any useful reference used to compare protein or mRNA levels. The reference can be any sample, standard, standard curve, or level that is used for comparison purposes. The reference can be a normal reference sample or a reference standard or level. A “reference sample”
10 can be, for example, a control, e.g., a predetermined negative control value such as a “normal control” or a prior sample taken from the same subject; a sample from a normal healthy subject, such as a normal cell or normal tissue; a sample (e.g., a cell or tissue) from a subject not having a disease; a sample from a subject that is diagnosed with a disease, but not yet treated with a compound described herein; a sample from a subject that has been treated by a compound described herein; or a sample of a purified
15 protein (e.g., any described herein) at a known normal concentration. By “reference standard or level” is meant a value or number derived from a reference sample. A “normal control value” is a pre-determined value indicative of non-disease state, e.g., a value expected in a healthy control subject. Typically, a normal control value is expressed as a range (“between X and Y”), a high threshold (“no higher than X”), or a low threshold (“no lower than X”). A subject having a measured value within the normal control value
20 for a particular biomarker is typically referred to as “within normal limits” for that biomarker. A normal reference standard or level can be a value or number derived from a normal subject not having a disease or disorder (e.g., cancer); a subject that has been treated with a compound described herein. In preferred embodiments, the reference sample, standard, or level is matched to the sample subject sample by at least one of the following criteria: age, weight, sex, disease stage, and overall health. A standard curve of
25 levels of a purified protein, e.g., any described herein, within the normal reference range can also be used as a reference.

The terms “short interfering RNA” and “siRNA” (also known as “small interfering RNAs”) refer to an RNA agent, preferably a double-stranded agent, of about 10-50 nucleotides in length, the strands optionally having overhanging ends comprising, for example 1, 2 or 3 overhanging nucleotides (or
30 nucleotide analogs), which is capable of directing or mediating RNA interference. Naturally-occurring siRNAs are generated from longer dsRNA molecules (e.g., >25 nucleotides in length) by a cell’s RNAi machinery (e.g., Dicer or a homolog thereof).

The term “shRNA”, as used herein, refers to an RNA agent having a stem-loop structure, comprising a first and second region of complementary sequence, the degree of complementarity and
35 orientation of the regions being sufficient such that base pairing occurs between the regions, the first and second regions being joined by a loop region, the loop resulting from a lack of base pairing between nucleotides (or nucleotide analogs) within the loop region.

As used herein, the term “subject” refers to any organism to which a composition in accordance with the invention may be administered, e.g., for experimental, diagnostic, prophylactic, and/or
40 therapeutic purposes. Typical subjects include any animal (e.g., mammals such as mice, rats, rabbits, non-human primates, and humans). A subject may seek or be in need of treatment, require treatment, be

receiving treatment, be receiving treatment in the future, or be a human or animal who is under care by a trained professional for a particular disease or condition.

As used herein, the term "SS18-SSX fusion protein-related disorder" refers to a disorder that is caused or affected by the level and/or activity of SS18-SSX fusion protein.

As used herein, the terms "treat," "treated," or "treating" mean both therapeutic treatment and prophylactic or preventative measures wherein the object is to prevent or slow down (lessen) an undesired physiological condition, disorder, or disease, or obtain beneficial or desired clinical results. Beneficial or desired clinical results include, but are not limited to, alleviation of symptoms; diminishment of the extent of a condition, disorder, or disease; stabilized (i.e., not worsening) state of condition, disorder, or disease; delay in onset or slowing of condition, disorder, or disease progression; amelioration of the condition, disorder, or disease state or remission (whether partial or total), whether detectable or undetectable; an amelioration of at least one measurable physical parameter, not necessarily discernible by the patient; or enhancement or improvement of condition, disorder, or disease. Treatment includes eliciting a clinically significant response without excessive levels of side effects. Treatment also includes prolonging survival as compared to expected survival if not receiving treatment.

As used herein, the terms "variant" and "derivative" are used interchangeably and refer to naturally-occurring, synthetic, and semi-synthetic analogues of a compound, peptide, protein, or other substance described herein. A variant or derivative of a compound, peptide, protein, or other substance described herein may retain or improve upon the biological activity of the original material.

The details of one or more embodiments of the invention are set forth in the description below. Other features, objects, and advantages of the invention will be apparent from the description and from the claims.

Brief Description of the Drawings

FIG. 1 is a series of graphs illustrating the effect of specific guide RNA (sgRNA) targeting of the BRD9 BAF complex subunit on synovial sarcoma cell growth. The Y-axis indicated the dropout ratio. The X-axis indicates the nucleotide position of the BRD9 gene. The grey box indicates the range of the negative control sgRNAs in the screen. The SYO1 cell line carries SS18-SSX2 fusion protein. The breakpoint joining the N-terminal region of SS18 to the C-terminal region of SSX2 are indicated by the black lines in their respective panel. The linear protein sequence is shown with BRD9 PFAM domains annotated from the PFAM database.

FIG. 2 is an image illustrating dose dependent depletion of BRD9 levels in a synovial sarcoma cell line (SYO1) in the presence of a BRD9 degrader.

FIG. 3 is an image illustrating sustained suppression of BRD9 levels in a synovial sarcoma cell line (SYO1) in the presence of a BRD9 degrader over 72 hours.

FIG. 4 is an image illustrating sustained suppression of BRD9 levels in two cell lines (293T and SYO1) in the presence of a BRD9 degrader over 5 days.

FIG. 5 is an image illustrating sustained suppression of BRD9 levels in synovial sarcoma cell lines (SYO1 and Yamato) in the presence of a BRD9 degrader over 7 days compared to the levels in cells treated with CRISPR reagents.

FIG. 6 is an image illustrating the effect on cell growth of six cell lines (SYO1, Yamato, A549, HS-SY-II, ASKA, and 293T) in the presence of a BRD9 degrader and a BRD9 inhibitor.

FIG. 7 is an image illustrating the effect on cell growth of two cell lines (SYO1 and G401) in the presence of a BRD9 degrader.

5 FIG. 8 is an image illustrating the effect on cell growth of three synovial sarcoma cell lines (SYO1, HS-SY-II, and ASKA) in the presence of a BRD9 degrader, BRD9 binder and E3 ligase binder.

FIG. 9 is an image illustrating the effect on cell growth of three non-synovial sarcoma cell lines (RD, HCT116, and Calu6) in the presence of a BRD9 degrader, BRD9 binder and E3 ligase binder.

10 FIG. 10 is a graph illustrating the percentage of SYO1 in various cell cycle phases following treatment with DMSO, Compound 1 at 200 nM, or Compound 1 at 1 μ M for 8 or 13 days.

FIG. 11 is a series of contour plots illustrating the percentage of SYO1 cells in various cell cycle phases following treatment with DMSO, Compound 1 at 200 nM, Compound 1 at 1 μ M, or lenalidomide at 200nM for 8 days. Numerical values corresponding to each contour plot are found in the table below.

15 FIG. 12 is a series of contour plots illustrating the percentage of SYO1 cells in various cell cycle phases following treatment with DMSO, Compound 1 at 200 nM, Compound 1 at 1 μ M, or lenalidomide at 200nM for 13 days. Numerical values corresponding to each contour plot are found in the table below.

FIG. 13 is a series of contour plots illustrating the percentage of early- and late-apoptotic SYO1 cells following treatment with DMSO, Compound 1 at 200 nM, Compound 1 at 1 μ M, or lenalidomide at 200nM for 8 days. Numerical values corresponding to each contour plot are found in the table below.

20 FIG. 14 is a graph illustrating the proteins present in BAF complexes including the SS18-SSX fusion protein.

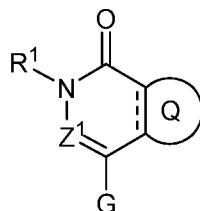
Detailed Description

25 The present disclosure features compositions and methods useful for the treatment of BAF-related disorders (e.g., cancer and infection). The disclosure further features compositions and methods useful for inhibition of the level and/or activity of BRD9, e.g., for the treatment of disorders such as cancer (e.g., sarcoma) and infection (e.g., viral infection), e.g., in a subject in need thereof.

Compounds

30 Compounds described herein reduce the level of an activity related to BRD9, or a related downstream effect, or reduce the level of BRD9 in a cell or subject. Exemplary compounds described herein have the structure according to **Formula I** or **Formula II**.

Formula I is:



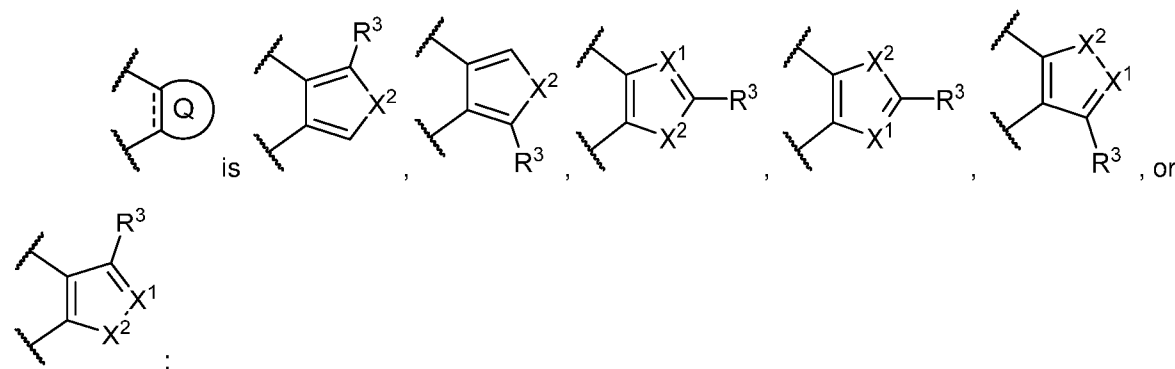
Formula I,

where

R¹ is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₁₀ carbocyclyl;

Z¹ is CR² or N;

R² is H, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, or optionally substituted C₂-C₉ heteroaryl;



X¹ is CR^{X1} or N;

X² is O or S;

R^{X1} is H or optionally substituted C₁-C₆ alkyl;

R³ is H, cyano, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₁-C₆ alkoxy, optionally substituted amino, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₃-C₁₀ heterocyclyl, or optionally substituted C₂-C₉ heteroaryl; and

G is optionally substituted C₃-C₁₀ carbocyclyl, C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, or optionally substituted C₂-C₉ heteroaryl, or a pharmaceutically acceptable salt thereof.

Formula II is:

A-L-B

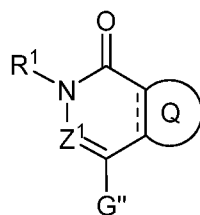
Formula II,

where

L is a linker;

B is a degradation moiety; and

A has the structure of **Formula III**:



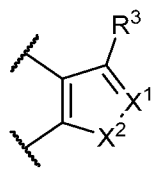
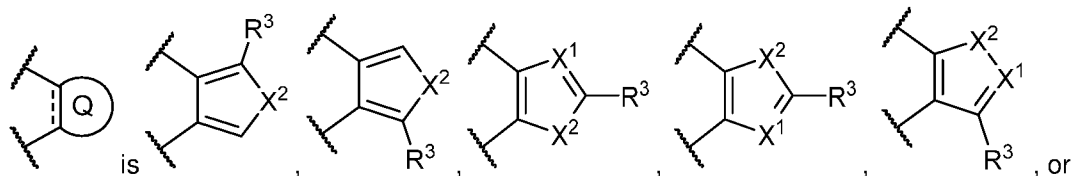
Formula III,

where

R¹ is, independently, H, optionally substituted C₁-C₆ alkyl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₁₀ carbocyclyl;

Z¹ is CR² or N;

R² is H, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, or optionally substituted C₂-C₉ heteroaryl;



X¹ is CR^{X1} or N;

X² is O or S;

R^{X1} is H or optionally substituted C₁-C₆ alkyl;

R³ is H, , cyano, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆

heteroalkyl, optionally substituted C₁-C₆ alkoxy, optionally substituted amino, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₃-C₁₀ heterocyclyl, or optionally substituted C₂-C₉ heteroaryl; and

R^{3'} is absent, optionally substituted C₁-C₆ alkylene, optionally substituted C₂-C₉ heteroarylene, or optionally substituted C₁-C₆ heteroalkylene;

G is , optionally substituted C₃-C₁₀ carbocyclyl, C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, or optionally substituted C₂-C₉ heteroaryl;

G' is optionally substituted C₃-C₁₀ carbocyclylene, C₂-C₉ heterocyclylene, optionally substituted C₆-C₁₀ arylene, or optionally substituted C₂-C₉ heteroarylene; and

A¹ is a bond between A and the linker,

where G is  or R³ is , or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound has the structure of any one of compounds B1-B10 in Table 1, or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound has the structure of any one of compounds D1-D15 in Table 2A, or a pharmaceutically acceptable salt thereof. In some embodiments, the compound has the

structure of any one of compounds D16-D90 in Table 2B, or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound has the structure of any one of compounds D91-D220 in Table 2C, or a pharmaceutically acceptable salt thereof.

Other embodiments, as well as exemplary methods for the synthesis of production of these compounds, are described herein.

Pharmaceutical Uses

The compounds described herein are useful in the methods of the invention and, while not bound by theory, are believed to exert their desirable effects through their ability to modulate the level, status, and/or activity of a BAF complex, e.g., by inhibiting the activity or level of the BRD9 protein in a cell within the BAF complex in a mammal.

An aspect of the present invention relates to methods of treating disorders related to BRD9 such as cancer in a subject in need thereof. In some embodiments, the compound is administered in an amount and for a time effective to result in one of (or more, e.g., two or more, three or more, four or more of): (a) reduced tumor size, (b) reduced rate of tumor growth, (c) increased tumor cell death (d) reduced tumor progression, (e) reduced number of metastases, (f) reduced rate of metastasis, (g) decreased tumor recurrence (h) increased survival of subject, and (i) increased progression free survival of a subject.

Treating cancer can result in a reduction in size or volume of a tumor. For example, after treatment, tumor size is reduced by 5% or greater (e.g., 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or greater) relative to its size prior to treatment. Size of a tumor may be measured by any reproducible means of measurement. For example, the size of a tumor may be measured as a diameter of the tumor.

Treating cancer may further result in a decrease in number of tumors. For example, after treatment, tumor number is reduced by 5% or greater (e.g., 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or greater) relative to number prior to treatment. Number of tumors may be measured by any reproducible means of measurement, e.g., the number of tumors may be measured by counting tumors visible to the naked eye or at a specified magnification (e.g., 2x, 3x, 4x, 5x, 10x, or 50x).

Treating cancer can result in a decrease in number of metastatic nodules in other tissues or organs distant from the primary tumor site. For example, after treatment, the number of metastatic nodules is reduced by 5% or greater (e.g., 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or greater) relative to number prior to treatment. The number of metastatic nodules may be measured by any reproducible means of measurement. For example, the number of metastatic nodules may be measured by counting metastatic nodules visible to the naked eye or at a specified magnification (e.g., 2x, 10x, or 50x).

Treating cancer can result in an increase in average survival time of a population of subjects treated according to the present invention in comparison to a population of untreated subjects. For example, the average survival time is increased by more than 30 days (more than 60 days, 90 days, or 120 days). An increase in average survival time of a population may be measured by any reproducible means. An increase in average survival time of a population may be measured, for example, by calculating for a population the average length of survival following initiation of treatment with the compound described herein. An increase in average survival time of a population may also be measured, for example, by calculating for a population the average length of survival following completion of a first round of treatment with a pharmaceutically acceptable salt of a compound described herein.

Treating cancer can also result in a decrease in the mortality rate of a population of treated subjects in comparison to an untreated population. For example, the mortality rate is decreased by more than 2% (e.g., more than 5%, 10%, or 25%). A decrease in the mortality rate of a population of treated

subjects may be measured by any reproducible means, for example, by calculating for a population the average number of disease-related deaths per unit time following initiation of treatment with a pharmaceutically acceptable salt of a compound described herein. A decrease in the mortality rate of a population may also be measured, for example, by calculating for a population the average number of disease-related deaths per unit time following completion of a first round of treatment with a pharmaceutically acceptable salt of a compound described herein.

Combination Therapies

A method of the invention can be used alone or in combination with an additional therapeutic agent, e.g., other agents that treat cancer or symptoms associated therewith, or in combination with other types of therapies to treat cancer. In combination treatments, the dosages of one or more of the therapeutic compounds may be reduced from standard dosages when administered alone. For example, doses may be determined empirically from drug combinations and permutations or may be deduced by isobolographic analysis (e.g., Black et al., *Neurology* 65:S3-S6 (2005)). In this case, dosages of the compounds when combined should provide a therapeutic effect.

In some embodiments, the second therapeutic agent is a chemotherapeutic agent (e.g., a cytotoxic agent or other chemical compound useful in the treatment of cancer). These include alkylating agents, antimetabolites, folic acid analogs, pyrimidine analogs, purine analogs and related inhibitors, vinca alkaloids, epipodophyllotoxins, antibiotics, L-Asparaginase, topoisomerase inhibitors, interferons, platinum coordination complexes, anthracenedione substituted urea, methyl hydrazine derivatives, adrenocortical suppressant, adrenocorticosteroides, progestins, estrogens, antiestrogen, androgens, antiandrogen, and gonadotropin-releasing hormone analog. Also included is 5-fluorouracil (5-FU), leucovorin (LV), irinotecan, oxaliplatin, capecitabine, paclitaxel, and doxorubicin. Non-limiting examples of chemotherapeutic agents include alkylating agents such as thiotepa and cyclophosphamide; alkyl sulfonates such as busulfan, improsulfan and piposulfan; aziridines such as benzodopa, carboquone, meturedopa, and uredopa; ethylenimines and methylamelamines including altretamine, triethylenemelamine, triethylenephosphoramide, triethylenethiophosphoramide and trimethylolomelamine; acetogenins (especially bullatacin and bullatacinone); a camptothecin (including the synthetic analogue topotecan); bryostatins; calyculin; CC-1065 (including its adozelesin, carzelesin and bizelesin synthetic analogues); cryptophycins (particularly cryptophycin 1 and cryptophycin 8); dolastatin; duocarmycin (including the synthetic analogues, KW-2189 and CB1-TM1); eleutherobin; pancratistatin; a sarcodictyin; spongistatin; nitrogen mustards such as chlorambucil, chlornaphazine, cholophosphamide, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard; nitrosureas such as carmustine, chlorozotocin, fotemustine, lomustine, nimustine, and ranimustine; antibiotics such as the enediyne antibiotics (e.g., calicheamicin, especially calicheamicin gammall and calicheamicin omegall (see, e.g., *Agnew, Chem. Intl. Ed Engl.* 33:183-186 (1994))); dynemicin, including dynemicin A; bisphosphonates, such as clodronate; an esperamicin; as well as neocarzinostatin chromophore and related chromoprotein enediyne antibiotic chromophores), aclacinomysins, actinomycin, anthramycin, azaserine, bleomycins, cactinomycin, carabycin, caminomycin, carzinophilin, chromomycinis, dactinomycin, daunorubicin, detorubicin, 6-diazo-5-oxo-L-norleucine, ADRIAMYCIN® (doxorubicin, including morpholino-doxorubicin, cyanomorpholino-

doxorubicin, 2-pyrrolino-doxorubicin and deoxydoxorubicin), epirubicin, esorubicin, idarubicin, marcellomycin, mitomycins such as mitomycin C, mycophenolic acid, nogalamycin, olivomycins, peplomycin, potfiromycin, puromycin, quelamycin, rodorubicin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin; anti-metabolites such as methotrexate and 5-fluorouracil (5-FU); folic acid analogues such as denopterin, methotrexate, pteropterin, trimetrexate; purine analogs such as fludarabine, 6-mercaptopurine, thiamiprine, thioguanine; pyrimidine analogs such as ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine; androgens such as calusterone, dromostanolone propionate, epitostanol, mepitiostane, testolactone; anti-adrenals such as aminogluthethimide, mitotane, trilostane; folic acid replenisher such as frolic acid; aceglatone; aldophosphamide glycoside; aminolevulinic acid; eniluracil; amsacrine; bestrabucil; bisantrene; edatraxate; defofamine; demecolcine; diaziquone; elfomithine; elliptinium acetate; an epothilone; etoglucid; gallium nitrate; hydroxyurea; lentinan; lonidainine; maytansinoids such as maytansine and ansamitocins; mitoguazone; mitoxantrone; mopidanmol; nitraerine; pentostatin; phenamet; pirarubicin; losoxantrone; podophyllinic acid; 2-ethylhydrazide; procarbazine; PSK® polysaccharide complex (JHS Natural Products, Eugene, OR); razoxane; rhizoxin; sizofuran; spirogermanium; tenuazonic acid; triaziquone; 2,2',2"-trichlorotriethylamine; trichothecenes (especially T-2 toxin, verracurin A, roridin A and anguidine); urethan; vindesine; dacarbazine; mannomustine; mitobronitol; mitolactol; pipobroman; gacytosine; arabinoside ("Ara-C"); cyclophosphamide; thiotepe; taxoids, e.g., TAXOL® (paclitaxel; Bristol-Myers Squibb Oncology, Princeton, NJ), ABRAXANE®, cremophor-free, albumin-engineered nanoparticle formulation of paclitaxel (American Pharmaceutical Partners, Schaumburg, IL), and TAXOTERE® doxetaxel (Rhone-Poulenc Rorer, Antony, France); chloranbucil; GEMZAR® gemcitabine; 6-thioguanine; mercaptopurine; methotrexate; platinum coordination complexes such as cisplatin, oxaliplatin and carboplatin; vinblastine; platinum; etoposide (VP-16); ifosfamide; mitoxantrone; vincristine; NAVELBINE® vinorelbine; novantrone; teniposide; edatrexate; daunomycin; aminopterin; xeloda; ibandronate; irinotecan (e.g., CPT-11); topoisomerase inhibitor RFS 2000; difluoromethylornithine (DMFO); retinoids such as retinoic acid; capecitabine; and pharmaceutically acceptable salts, acids or derivatives of any of the above. Two or more chemotherapeutic agents can be used in a cocktail to be administered in combination with the first therapeutic agent described herein. Suitable dosing regimens of combination chemotherapies are known in the art and described in, for example, Saltz et al., *Proc. Am. Soc. Clin. Oncol.* 18:233a (1999), and Douillard et al., *Lancet* 355(9209):1041-1047 (2000).

In some embodiments, the second therapeutic agent is a therapeutic agent which is a biologic such as a cytokine (e.g., interferon or an interleukin (e.g., IL-2)) used in cancer treatment. In some embodiments the biologic is an anti-angiogenic agent, such as an anti-VEGF agent, e.g., bevacizumab (AVASTIN®). In some embodiments the biologic is an immunoglobulin-based biologic, e.g., a monoclonal antibody (e.g., a humanized antibody, a fully human antibody, an Fc fusion protein or a functional fragment thereof) that agonizes a target to stimulate an anti-cancer response, or antagonizes an antigen important for cancer. Such agents include RITUXAN® (rituximab); ZENAPAX® (daclizumab); SIMULECT® (basiliximab); SYNAGIS® (palivizumab); REMICADE® (infliximab); HERCEPTIN® (trastuzumab); MYLOTARG® (gemtuzumab ozogamicin); CAMPATH® (alemtuzumab); ZEVALIN® (ibritumomab tiuxetan); HUMIRA® (adalimumab); XOLAIR® (omalizumab); BEXXAR® (tositumomab-I-

131); RAPTIVA® (efalizumab); ERBITUX® (cetuximab); AVASTIN® (bevacizumab); TYSABRI® (natalizumab); ACTEMRA® (tocilizumab); VECTIBIX® (panitumumab); LUCENTIS® (ranibizumab); SOLIRIS® (eculizumab); CIMZIA® (certolizumab pegol); SIMPONI® (golimumab); ILARIS® (canakinumab); STELARA® (ustekinumab); ARZERRA® (ofatumumab); PROLIA® (denosumab);
 5 NUMAX® (motavizumab); ABTHRAX® (raxibacumab); BENLYSTA® (belimumab); YERVOY® (ipilimumab); ADCETRIS® (brentuximab vedotin); PERJETA® (pertuzumab); KADCYLA® (ado-trastuzumab emtansine); and GAZYVA® (obinutuzumab). Also included are antibody-drug conjugates.

The second agent may be a therapeutic agent which is a non-drug treatment. For example, the second therapeutic agent is radiation therapy, cryotherapy, hyperthermia, and/or surgical excision of
 10 tumor tissue.

The second agent may be a checkpoint inhibitor. In one embodiment, the inhibitor of checkpoint is an inhibitory antibody (e.g., a monospecific antibody such as a monoclonal antibody). The antibody may be, e.g., humanized or fully human. In some embodiments, the inhibitor of checkpoint is a fusion protein, e.g., an Fc-receptor fusion protein. In some embodiments, the inhibitor of checkpoint is an agent,
 15 such as an antibody, that interacts with a checkpoint protein. In some embodiments, the inhibitor of checkpoint is an agent, such as an antibody, that interacts with the ligand of a checkpoint protein. In some embodiments, the inhibitor of checkpoint is an inhibitor (e.g., an inhibitory antibody or small molecule inhibitor) of CTLA-4 (e.g., an anti-CTLA4 antibody or fusion a protein such as
 20 ipilimumab/YERVOY® or tremelimumab). In some embodiments, the inhibitor of checkpoint is an inhibitor (e.g., an inhibitory antibody or small molecule inhibitor) of PD-1 (e.g., nivolumab/OPDIVO®; pembrolizumab/KEYTRUDA®; pidilizumab/CT-011). In some embodiments, the inhibitor of checkpoint is an inhibitor (e.g., an inhibitory antibody or small molecule inhibitor) of PDL1 (e.g., MPDL3280A/RG7446; MEDI4736; MSB0010718C; BMS 936559). In some embodiments, the inhibitor of checkpoint is an
 25 inhibitor (e.g., an inhibitory antibody or Fc fusion or small molecule inhibitor) of PDL2 (e.g., a PDL2/Ig fusion protein such as AMP 224). In some embodiments, the inhibitor of checkpoint is an inhibitor (e.g., an inhibitory antibody or small molecule inhibitor) of B7-H3 (e.g., MGA271), B7-H4, BTLA, HVEM, TIM3, GAL9, LAG3, VISTA, KIR, 2B4, CD160, CGEN-15049, CHK 1, CHK2, A2aR, B-7 family ligands, or a combination thereof.

In some embodiments, the anti-cancer therapy is a T cell adoptive transfer (ACT) therapy. In
 30 some embodiments, the T cell is an activated T cell. The T cell may be modified to express a chimeric antigen receptor (CAR). CAR modified T (CAR-T) cells can be generated by any method known in the art. For example, the CAR-T cells can be generated by introducing a suitable expression vector encoding the CAR to a T cell. Prior to expansion and genetic modification of the T cells, a source of T cells is obtained from a subject. T cells can be obtained from a number of sources, including peripheral blood
 35 mononuclear cells, bone marrow, lymph node tissue, cord blood, thymus tissue, tissue from a site of infection, ascites, pleural effusion, spleen tissue, and tumors. In certain embodiments of the present invention, any number of T cell lines available in the art, may be used. In some embodiments, the T cell is an autologous T cell. Whether prior to or after genetic modification of the T cells to express a desirable protein (e.g., a CAR), the T cells can be activated and expanded generally using methods as described,
 40 for example, in U.S. Patents 6,352,694; 6,534,055; 6,905,680; 6,692,964; 5,858,358; 6,887,466;

6,905,681; 7,144,575; 7,067,318; 7,172,869; 7,232,566; 7,175,843; 5,883,223; 6,905,874; 6,797,514; 6,867,041; and U.S. Patent Application Publication No. 20060121005.

In any of the combination embodiments described herein, the first and second therapeutic agents are administered simultaneously or sequentially, in either order. The first therapeutic agent may be administered immediately, up to 1 hour, up to 2 hours, up to 3 hours, up to 4 hours, up to 5 hours, up to 6 hours, up to 7 hours, up to 8 hours, up to 9 hours, up to 10 hours, up to 11 hours, up to 12 hours, up to 13 hours, 14 hours, up to 16 hours, up to 17 hours, up to 18 hours, up to 19 hours up to 20 hours, up to 21 hours, up to 22 hours, up to 23 hours up to 24 hours or up to 1-7, 1-14, 1-21 or 1-30 days before or after the second therapeutic agent.

Pharmaceutical Compositions

The pharmaceutical compositions described herein are preferably formulated into pharmaceutical compositions for administration to human subjects in a biologically compatible form suitable for administration in vivo.

The compounds described herein may be used in the form of the free base, in the form of salts, solvates, and as prodrugs. All forms are within the methods described herein. In accordance with the methods of the invention, the described compounds or salts, solvates, or prodrugs thereof may be administered to a patient in a variety of forms depending on the selected route of administration, as will be understood by those skilled in the art. The compounds described herein may be administered, for example, by oral, parenteral, buccal, sublingual, nasal, rectal, patch, pump, intratumoral, or transdermal administration and the pharmaceutical compositions formulated accordingly. Parenteral administration includes intravenous, intraperitoneal, subcutaneous, intramuscular, transepithelial, nasal, intrapulmonary, intrathecal, rectal, and topical modes of administration. Parenteral administration may be by continuous infusion over a selected period of time.

A compound described herein may be orally administered, for example, with an inert diluent or with an assimilable edible carrier, or it may be enclosed in hard or soft shell gelatin capsules, or it may be compressed into tablets, or it may be incorporated directly with the food of the diet. For oral therapeutic administration, a compound described herein may be incorporated with an excipient and used in the form of ingestible tablets, buccal tablets, troches, capsules, elixirs, suspensions, syrups, and wafers. A compound described herein may also be administered parenterally. Solutions of a compound described herein can be prepared in water suitably mixed with a surfactant, such as hydroxypropylcellulose. Dispersions can also be prepared in glycerol, liquid polyethylene glycols, DMSO, and mixtures thereof with or without alcohol, and in oils. Under ordinary conditions of storage and use, these preparations may contain a preservative to prevent the growth of microorganisms. Conventional procedures and ingredients for the selection and preparation of suitable formulations are described, for example, in Remington's Pharmaceutical Sciences (2012, 22nd ed.) and in The United States Pharmacopeia: The National Formulary (USP 41 NF36), published in 2018. The pharmaceutical forms suitable for injectable use include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions. In all cases the form must be sterile and must be fluid to the extent that may be easily administered via syringe. Compositions for nasal administration may conveniently be formulated as aerosols, drops, gels, and powders. Aerosol formulations typically include

a solution or fine suspension of the active substance in a physiologically acceptable aqueous or non-aqueous solvent and are usually presented in single or multidose quantities in sterile form in a sealed container, which can take the form of a cartridge or refill for use with an atomizing device. Alternatively, the sealed container may be a unitary dispensing device, such as a single dose nasal inhaler or an aerosol dispenser fitted with a metering valve which is intended for disposal after use. Where the dosage form includes an aerosol dispenser, it will contain a propellant, which can be a compressed gas, such as compressed air or an organic propellant, such as fluorochlorohydrocarbon. The aerosol dosage forms can also take the form of a pump-atomizer. Compositions suitable for buccal or sublingual administration include tablets, lozenges, and pastilles, where the active ingredient is formulated with a carrier, such as sugar, acacia, tragacanth, gelatin, and glycerine. Compositions for rectal administration are conveniently in the form of suppositories containing a conventional suppository base, such as cocoa butter. A compound described herein may be administered intratumorally, for example, as an intratumoral injection. Intratumoral injection is injection directly into the tumor vasculature and is specifically contemplated for discrete, solid, accessible tumors. Local, regional, or systemic administration also may be appropriate. A compound described herein may advantageously be contacted by administering an injection or multiple injections to the tumor, spaced for example, at approximately, 1 cm intervals. In the case of surgical intervention, the present invention may be used preoperatively, such as to render an inoperable tumor subject to resection. Continuous administration also may be applied where appropriate, for example, by implanting a catheter into a tumor or into tumor vasculature.

The compounds described herein may be administered to an animal, e.g., a human, alone or in combination with pharmaceutically acceptable carriers, as noted herein, the proportion of which is determined by the solubility and chemical nature of the compound, chosen route of administration, and standard pharmaceutical practice.

Dosages

The dosage of the compounds described herein, and/or compositions including a compound described herein, can vary depending on many factors, such as the pharmacodynamic properties of the compound; the mode of administration; the age, health, and weight of the recipient; the nature and extent of the symptoms; the frequency of the treatment, and the type of concurrent treatment, if any; and the clearance rate of the compound in the animal to be treated. One of skill in the art can determine the appropriate dosage based on the above factors. The compounds described herein may be administered initially in a suitable dosage that may be adjusted as required, depending on the clinical response. In general, satisfactory results may be obtained when the compounds described herein are administered to a human at a daily dosage of, for example, between 0.05 mg and 3000 mg (measured as the solid form). Dose ranges include, for example, between 10-1000 mg (e.g., 50-800 mg). In some embodiments, 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, or 1000 mg of the compound is administered.

Alternatively, the dosage amount can be calculated using the body weight of the patient. For example, the dose of a compound, or pharmaceutical composition thereof, administered to a patient may range from 0.1-100 mg/kg (e.g., 0.1-50 mg/kg (e.g., 0.25-25 mg/kg)). In exemplary, non-limiting embodiments, the dose may range from 0.5-5.0 mg/kg (e.g., 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, or

5.0 mg/kg) or from 5.0-20 mg/kg (e.g., 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, 8.5, 9.0, 9.5, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 mg/kg).

Kits

5 The invention also features kits including (a) a pharmaceutical composition including an agent that reduces the level and/or activity of BRD9 in a cell or subject described herein, and (b) a package insert with instructions to perform any of the methods described herein. In some embodiments, the kit includes (a) a pharmaceutical composition including an agent that reduces the level and/or activity of BRD9 in a cell or subject described herein, (b) an additional therapeutic agent (e.g., an anti-cancer agent), and (c) a package insert with instructions to perform any of the methods described herein.

Examples

Example 1 – High density tiling sgRNA screen against human BAF complex subunits in synovial sarcoma cell line SYO1

15 The following example shows that BRD9 sgRNA inhibits cell growth in synovial sarcoma cells.

Procedure: To perform high density sgRNA tiling screen, an sgRNA library against BAF complex subunits was custom synthesized at Cellesta (Mountain View, CA). Sequences of DNA encoding the BRD9-targeting sgRNAs used in this screen are listed in Table 3. Negative and positive control sgRNA were included in the library. Negative controls consisted of 200 sgRNAs that do not target human genome. The positive controls are sgRNAs targeting essential genes (CDC16, GTF2B, HSPA5, HSPA9, PAFAH1B1, PCNA, POLR2L, RPL9, and SF3A3). DNA sequences encoding all positive and negative control sgRNAs are listed in Table 4. Procedures for virus production, cell infection, and performing the sgRNA screen were previously described (Tsherniak et al, *Cell* 170:564-576 (2017); Munoz et al, *Cancer Discovery* 6:900-913 (2016)). For each sgRNA, 50 counts were added to the sequencing counts and for each time point the resulting counts were normalized to the total number of counts. The log2 of the ratio between the counts (defined as dropout ratio) at day 24 and day 1 post-infection was calculated. For negative control sgRNAs, the 2.5 and 97.5 percentile of the log2 dropout ratio of all non-targeting sgRNAs was calculated and considered as background (grey box in the graph). Protein domains were obtained from PFAM regions defined for the UNIPROT identifier: Q9H8M2.

30 **Results:** As shown in FIG. 1, targeted inhibition of the GBAF complex component BRD9 by sgRNA resulted in growth inhibition of the SYO1 synovial sarcoma cell line. sgRNAs against other components of the BAF complexes resulted in increased proliferation of cells, inhibition of cell growth, or had no effect on SYO1 cells. These data show that targeting various subunits of the GBAF complex represents a therapeutic strategy for the treatment of synovial sarcoma.

Table 3. BRD9 sgRNA Library

SEQ ID NO	Nucleic Acid Sequence	SEQ ID NO	Nucleic Acid Sequence
203	CAAGAAGCACAAGAAGCACA	319	GCTCTACAGCGTGGTCAACA
204	CTTGTGCTTCTTGCCCATGG	320	CGGGAGCCTGCTCTACAGCG
205	CTTCTTGTGCTTCTTGCCCA	321	CGTGGTCAACACGGCCGAGC

SEQ ID NO	Nucleic Acid Sequence	SEQ ID NO	Nucleic Acid Sequence
206	ACAAGAAGCACAAGGCCGAG	322	CCCACCATCAGCGTCCGGCT
207	CTCGTAGGACGAGCGCCACT	323	ACGGCCGAGCCGGACGCTGA
208	CGAGTGGCGCTCGTCCTACG	324	GGGCACCCACCATCAGCGTC
209	GAGTGGCGCTCGTCCTACGA	325	GCCGAGCCGGACGCTGATGG
210	AGGCTTCTCCAGGGGCTTGT	326	CCATGTCCGTGTTGCAGAGG
211	AGATTATGCCGACAAGCCCC	327	CCGAGCCGGACGCTGATGGT
212	ACCTTCAGGACTAGCTTTAG	328	CGAGCTCAAGTCCACCGGGT
213	AGCTTTAGAGGCTTCTCCAG	329	GCGAGCTCAAGTCCACCGGG
214	CTAGCTTTAGAGGCTTCTCC	330	AGAGCGAGCTCAAGTCCACC
215	TAGCTTTAGAGGCTTCTCCA	331	GAGAGCGAGCTCAAGTCCAC
216	CTAAAGCTAGTCCTGAAGGT	332	GAAGCCTGGGAGTAGCTTAC
217	GCCTCTAAAGCTAGTCCTGA	333	CTCTCCAGTAAGCTACTCCC
218	CTTCACTTCCTCCGACCTTC	334	AGCCCAGCGTGGTGAAGCCT
219	AAGCTAGTCCTGAAGGTCCG	335	AAGCCCAGCGTGGTGAAGCC
220	AGTGAAGTGAAGTGAAGTCTC	336	ACTCCCAGGCTTCACCACGC
221	GTGACTGAAGTCTCAGGATC	337	CTCCCAGGCTTCACCACGCT
222	ATAGTAACTGGAGTCGTGGC	338	CTCGTCTTTGAAGCCCAGCG
223	CATCATAGTAACTGGAGTCG	339	CACTGGAGAGAAAGGTGACT
224	TGACCTGTCATCATAGTAAC	340	GCACTGGAGAGAAAGGTGAC
225	ACTCCAGTTACTATGATGAC	341	AGTAGTGGCACTGGAGAGAA
226	CTTTGTGCCTCTCTCGCTCA	342	CGAAAGCGCAGTAGTGGCAC
227	GGTCAGACCATGAGCGAGAG	343	CTGCATCGAAAGCGCAGTAG
228	GAAGAAGAAGAAGTCCGAGA	344	ATGCAGAATAATTCAGTATT
229	GTCCAGATGCTTCTCCTTCT	345	AGTATTTGGCGACTTGAAGT
230	GTCCGAGAAGGAGAAGCATC	346	CGACTTGAAGTCGGACGAGA
231	GGAGAAGCATCTGGACGATG	347	GAGCTGCTCTACTCAGCCTA
232	TGAGGAAAGAAGGAAGCGAA	348	CACGCCTGTCTCATCTCCGT
233	ATCTGGACGATGAGGAAAGA	349	TCAGCCTACGGAGATGAGAC
234	AGAAGAAGCGGAAGCGAGAG	350	CAGGCGTGCAGTGTGCGCTG
235	GAAGAAGCGGAAGCGAGAGA	351	CCGCGGCCCTCTAGCCTGC
236	CCGCCCAGGAAGAGAAGAAG	352	CATCCTTCACAACTCCTGC
237	AGAGAGGGAGCACTGTGACA	353	TAGCCTGCAGGAGTTTGTGA
238	AGGGAGCACTGTGACACGGA	354	CAGGAGTTTGTGAAGGATGC
239	GAGGGAGCACTGTGACACGG	355	AGGAGTTTGTGAAGGATGCT
240	GCACTGTGACACGGAGGGAG	356	TGGGAGCTACAGCAAGAAAG
241	GAGGCTGACGACTTTGATCC	357	GAGCTACAGCAAGAAAGTGG

SEQ ID NO	Nucleic Acid Sequence	SEQ ID NO	Nucleic Acid Sequence
242	AGGCTGACGACTTTGATCCT	358	GAAAGTGGTGGACGACCTCC
243	TCCACCTCCACCTTCTTCCC	359	CGCCTGTGATCTGGTCCAGG
244	CGACTTTGATCCTGGGAAGA	360	CTCCGCCTGTGATCTGGTCC
245	CTTTGATCCTGGGAAGAAGG	361	GACCTCCTGGACCAGATCAC
246	TGATCCTGGGAAGAAGGTGG	362	CTCCTGGACCAGATCACAGG
247	TCCTGGGAAGAAGGTGGAGG	363	GCTGGAAGAGCGTCCTAGAG
248	CGGACTGGCCGATCTGGGGG	364	TGCAGCCCACCTGCTTCAGC
249	ACGCTCGGACTGGCCGATCT	365	GACGCTCTTCCAGCTGAAGC
250	AGGTGGAGCCGCCCCAGAT	366	CTCTTCCAGCTGAAGCAGGT
251	CGCTCGGACTGGCCGATCTG	367	GCTCTTCCAGCTGAAGCAGG
252	GCTCGGACTGGCCGATCTGG	368	CCTCCAGATGAAGCCAAGGT
253	CACGCTCGGACTGGCCGATC	369	GCTTCATCTGGAGGCTTCAT
254	TGTGTCCGGCACGCTCGGAC	370	GGCTTCATCTGGAGGCTTCA
255	CTGGCTGTGTCCGGCACGCT	371	CTTACCTTGGCTTCATCTGG
256	ATCGGCCAGTCCGAGCGTGC	372	AAACTTACCTTGGCTTCATC
257	CACCCTTGCCTGGCTGTGTC	373	GAAGCCTCCAGATGAAGCCA
258	CGAGCGTGCCGGACACAGCC	374	TCCTAGGGTGTCCCCAACCT
259	TGTTCCAGGAGTTGCTGAAT	375	CCTAGGGTGTCCCCAACCTG
260	CACACCTATTCAGCAACTCC	376	GTGTCTGTCTCCACAGGTTG
261	GCTGGCGGAGGAAGTGTTCC	377	TGTGTCTGTCTCCACAGGTT
262	TTTACCTCTGAAGCTGGCGG	378	CCACAGGTTGGGGACACCCT
263	CCCCGGTTTACCTCTGAAGC	379	AGAGCTGCTGCTGTCTCCTA
264	ACTTCCTCCGCCAGCTTCAG	380	CAGAGCTGCTGCTGTCTCCT
265	CAGGAAAAGCAAAAAATCCA	381	AGACAGCAGCAGCTCTGTTC
266	GCTTTCAGAAAAGATCCCCA	382	ATCCACAGAAACGTCGGGAT
267	AGGAAAAGCAAAAAATCCAT	383	GAGATATCCACAGAAACGTC
268	GGAAAAGCAAAAAATCCATG	384	GGAGATATCCACAGAAACGT
269	GGAGCAATTGCATCCGTGAC	385	GTCCTATCCCGACGTTTCTG
270	GTCACGGATGCAATTGCTCC	386	TCTCCATGCTCAGCTCTCTG
271	TTTATTATCATTGAATATCC	387	CTCACCCAGAGAGCTGAGCA
272	AATGATAATAAACATCCCA	388	ATCTCCATGCTCAGCTCTCT
273	ATAAACATCCCATGGATTT	389	TATCTCCATGCTCAGCTCTC
274	TTCATGGTGCCAAAATCCAT	390	ATGTCCTGTTTACACAGGGA
275	TTTCATGGTGCCAAAATCCA	391	TTACACAGGGAAGGTGAAGA
276	TAATGAATACAAGTCAGTTA	392	AGTTCAAATGGCTGTCGTCA
277	CAAGTCAGTTACGGAATTTA	393	TGACGACAGCCATTTGAACT

SEQ ID NO	Nucleic Acid Sequence	SEQ ID NO	Nucleic Acid Sequence
278	ATAATGCAATGACATACAAT	394	AAGTTCAAATGGCTGTGCTC
279	AAC TTGTAGTACACGGTATC	395	TCGTCTCATCCAAGTTCAAA
280	CTTCGCCAACTTGTAGTACA	396	TGAGACGACGAAGCTCCTGC
281	AGATACCGTGTACTACAAGT	397	GTGCTTCGTGCAGGTCCTGC
282	GCGAAGAAGATCCTTCACGC	398	GCAGGACCTGCACGAAGCAC
283	TCATCTTAAAGCCTGCGTGA	399	GCTCCGCCTGTGCTTCGTGC
284	TTCTCAGCAGGCAGCTCTTT	400	GGACCTGCACGAAGCACAGG
285	CAATGAAGATACAGCTGTTG	401	CACGAAGCACAGGCGGAGCG
286	ACTGGTACAACCTTCAGGGAC	402	AGGCGGAGCGCGGCGGCTCT
287	CTTG TACTGGTACAACCTTCA	403	AGGGAGCTGAGGTTGGACGA
288	ACTTG TACTGGTACAACCTTC	404	GTTGGACAGGGAGCTGAGGT
289	TTGGCAGTTTCTACTTGTAC	405	AGGCGTTGGACAGGGAGCTG
290	TACCTGATAACTTCTCTACT	406	CCCTCTCGGAGGCGTTGGAC
291	AGCCGAGTAGAGAAGTTATC	407	CCTCTCGGAGGCGTTGGACA
292	AGCTGCATGTTTGAGCCTGA	408	CTGGTCCCTCTCGGAGGCGT
293	GCTGCATGTTTGAGCCTGAA	409	CCCTGTCCAACGCCTCCGAG
294	AAGCTGCAGGCATTCCCTTC	410	CCTGTCCAACGCCTCCGAGA
295	GGTACTGTCCGTCAAGCTGC	411	GTGGTGCTGGTCCCTCTCGG
296	AGGGAATGCCTGCAGCTTGA	412	CAGGTGGTGCTGGTCCCTCT
297	CTTGACGGACAGTACCGCAG	413	GCATCTCACCAGGTGGTGC
298	CGCCAGCACGTGCTCCTCTG	414	CGAGAGGGACCAGCACCACC
299	TACCGCAGAGGAGCACGTGC	415	GAGAGGGACCAGCACCACCT
300	AGAGGAGCACGTGCTGGCGC	416	GTGGGGGCATCTCACCAGG
301	GGAGCACGTGCTGGCGCTGG	417	CCCCGACACTCAGGCGAGAA
302	AGCACGCAGCTGACGAAGCT	418	TCCCCGACACTCAGGCGAGA
303	GCACGCAGCTGACGAAGCTC	419	AGCCCTTCTCGCCTGAGTGT
304	CAGCTGACGAAGCTCGGGAC	420	CTGGCTGCTCCCCGACACTC
305	AAGCTCGGGACAGGATCAAC	421	CCCTTCTCGCCTGAGTGTG
306	CCTTGCCGCCTGGGAGGAAC	422	GCCCTTCTCGCCTGAGTGTG
307	AGGATCAACCGGTTCTCCC	423	TAGGGGTCGTGGGTGACGTC
308	ATCAACCGGTTCTCCAGG	424	AAGAAACTCATAGGGGTCTG
309	GCACTACCTTGCCGCCTGGG	425	GAAGAAACTCATAGGGGTCTG
310	AGAGCACTACCTTGCCGCCT	426	GAGACTGAAGAAACTCATAG
311	CCGGTTCTCCAGGCGGCA	427	GGAGACTGAAGAAACTCATA
312	TCCTCTTCAGATAGCCATC	428	TGGAGACTGAAGAAACTCAT
313	ATGGGCTATCTGAAGAGGAA	429	TCTTCAGTCTCCAGAGCCTG

SEQ ID NO	Nucleic Acid Sequence	SEQ ID NO	Nucleic Acid Sequence
314	GGGCTATCTGAAGAGGAACG	430	TTGGCAGAGGCCGCGAGGCTC
315	TGGGCTATCTGAAGAGGAAC	431	TAGGTCTTGGCAGAGGCCGC
316	TATCTGAAGAGGAACGGGGA	432	CTAGAGTTAGGTCTTGGCAG
317	ATCTGAAGAGGAACGGGGAC	433	GGTGGTCTAGAGTTAGGTCT
318	TGTTGACCACGCTGTAGAGC		

Table 4. Control sgRNA Library

SEQ ID NO.	gRNA Label	Gene	Nucleic Acid Sequence
434	1 sg_Non_Targeting_Human_001 Non_Targeting_Human	Non_Targeting_Human	GTAGCGAACGTGTCCGGCGT
435	1 sg_Non_Targeting_Human_002 Non_Targeting_Human	Non_Targeting_Human	GACCGGAACGATCTCGCGTA
436	1 sg_Non_Targeting_Human_003 Non_Targeting_Human	Non_Targeting_Human	GGCAGTCGTTGCGTTGATAT
437	1 sg_Non_Targeting_Human_004 Non_Targeting_Human	Non_Targeting_Human	GCTTGAGCACATACGCGAAT
438	1 sg_Non_Targeting_Human_005 Non_Targeting_Human	Non_Targeting_Human	GTGGTAGAATAACGTATTAC
439	1 sg_Non_Targeting_Human_006 Non_Targeting_Human	Non_Targeting_Human	GTCATACATGGATAAGGCTA
440	1 sg_Non_Targeting_Human_007 Non_Targeting_Human	Non_Targeting_Human	GATACACGAAGCATCACTAG
441	1 sg_Non_Targeting_Human_008 Non_Targeting_Human	Non_Targeting_Human	GAACGTTGGCACTACTTCAC
442	1 sg_Non_Targeting_Human_009 Non_Targeting_Human	Non_Targeting_Human	GATCCATGTAATGCGTTCGA
443	1 sg_Non_Targeting_Human_010 Non_Targeting_Human	Non_Targeting_Human	GTCGTGAAGTGCATTGATC
444	1 sg_Non_Targeting_Human_011 Non_Targeting_Human	Non_Targeting_Human	GTTGCGACTCGCGTGACCGTA
445	1 sg_Non_Targeting_Human_012 Non_Targeting_Human	Non_Targeting_Human	GAATCTACCGCAGCGGTTTCG
446	1 sg_Non_Targeting_Human_013 Non_Targeting_Human	Non_Targeting_Human	GAAGTGACGTCGATTGCGATA
447	1 sg_Non_Targeting_Human_014 Non_Targeting_Human	Non_Targeting_Human	GCGGTGTATGACAACCGCCG

SEQ ID NO.	gRNA Label	Gene	Nucleic Acid Sequence
448	1 sg_Non_Targeting_Human_0015 Non_Targeting_Human	Non_Targeting_Human	GTACCGCGCCTGAAGTTCGC
449	1 sg_Non_Targeting_Human_0016 Non_Targeting_Human	Non_Targeting_Human	GCAGCTCGTGTGTCGTA CT C
450	1 sg_Non_Targeting_Human_0017 Non_Targeting_Human	Non_Targeting_Human	GCGCCTTAAGAGTACTCATC
451	1 sg_Non_Targeting_Human_0018 Non_Targeting_Human	Non_Targeting_Human	GAGTGTGTCGTCGTTGCTCCTA
452	1 sg_Non_Targeting_Human_0019 Non_Targeting_Human	Non_Targeting_Human	GCAGCTCGACCTCAAGCCGT
453	1 sg_Non_Targeting_Human_0020 Non_Targeting_Human	Non_Targeting_Human	GTATCCTGACCTACGCGCTG
454	1 sg_Non_Targeting_Human_0021 Non_Targeting_Human	Non_Targeting_Human	GTGTATCTCAGCACGCTAAC
455	1 sg_Non_Targeting_Human_0022 Non_Targeting_Human	Non_Targeting_Human	GTCGTCATACAACGGCAACG
456	1 sg_Non_Targeting_Human_0023 Non_Targeting_Human	Non_Targeting_Human	GTCGTGCGCTTCCGGCGGTA
457	1 sg_Non_Targeting_Human_0024 Non_Targeting_Human	Non_Targeting_Human	GCGGTCCTCAGTAAGCGCGT
458	1 sg_Non_Targeting_Human_0025 Non_Targeting_Human	Non_Targeting_Human	GCTCTGCTGCGGAAGGATTC
459	1 sg_Non_Targeting_Human_0026 Non_Targeting_Human	Non_Targeting_Human	GCATGGAGGAGCGTCGCAGA
460	1 sg_Non_Targeting_Human_0027 Non_Targeting_Human	Non_Targeting_Human	GTAGCGCGCGTAGGAGTGGC
461	1 sg_Non_Targeting_Human_0028 Non_Targeting_Human	Non_Targeting_Human	GATCACCTGCATTCGTACAC
462	1 sg_Non_Targeting_Human_0029 Non_Targeting_Human	Non_Targeting_Human	GCACACCTAGATATCGAATG
463	1 sg_Non_Targeting_Human_0030 Non_Targeting_Human	Non_Targeting_Human	GTTGATCAACGCGCTTCGCG
464	1 sg_Non_Targeting_Human_0031 Non_Targeting_Human	Non_Targeting_Human	GCGTCTCACTCACTCCATCG
465	1 sg_Non_Targeting_Human_0032 Non_Targeting_Human	Non_Targeting_Human	GCCGACCAACGTCAGCGGTA

SEQ ID NO.	gRNA Label	Gene	Nucleic Acid Sequence
466	1 sg_Non_Targeting_Human_0033 Non_Targeting_Human	Non_Targeting_Human	GGATACGGTGCGTCAATCTA
467	1 sg_Non_Targeting_Human_0034 Non_Targeting_Human	Non_Targeting_Human	GAATCCAGTGGCGGCGACAA
468	1 sg_Non_Targeting_Human_0035 Non_Targeting_Human	Non_Targeting_Human	GCACTGTCAGTGCAACGATA
469	1 sg_Non_Targeting_Human_0036 Non_Targeting_Human	Non_Targeting_Human	GCGATCCTCAAGTATGCTCA
470	1 sg_Non_Targeting_Human_0037 Non_Targeting_Human	Non_Targeting_Human	GCTAATATCGACACGGCCGC
471	1 sg_Non_Targeting_Human_0038 Non_Targeting_Human	Non_Targeting_Human	GGAGATGCATCGAAGTCGAT
472	1 sg_Non_Targeting_Human_0039 Non_Targeting_Human	Non_Targeting_Human	GGATGCACTCCATCTCGTCT
473	1 sg_Non_Targeting_Human_0040 Non_Targeting_Human	Non_Targeting_Human	GTGCCGAGTAATAACGCGAG
474	1 sg_Non_Targeting_Human_0041 Non_Targeting_Human	Non_Targeting_Human	GAGATTCCGATGTAACGTAC
475	1 sg_Non_Targeting_Human_0042 Non_Targeting_Human	Non_Targeting_Human	GTCGTCACGAGCAGGATTGC
476	1 sg_Non_Targeting_Human_0043 Non_Targeting_Human	Non_Targeting_Human	GCGTTAGTCACTTAGCTCGA
477	1 sg_Non_Targeting_Human_0044 Non_Targeting_Human	Non_Targeting_Human	G TTCACACGGTGTCCGATAG
478	1 sg_Non_Targeting_Human_0045 Non_Targeting_Human	Non_Targeting_Human	GGATAGGTGACCTTAGTACG
479	1 sg_Non_Targeting_Human_0046 Non_Targeting_Human	Non_Targeting_Human	GTATGAGTCAAGCTAATGCG
480	1 sg_Non_Targeting_Human_0047 Non_Targeting_Human	Non_Targeting_Human	GCAACTATTGGAATACGTGA
481	1 sg_Non_Targeting_Human_0048 Non_Targeting_Human	Non_Targeting_Human	GTTACCTTCGCTCGTCTATA
482	1 sg_Non_Targeting_Human_0049 Non_Targeting_Human	Non_Targeting_Human	GTACCGAGCACCACAGGCCG
483	1 sg_Non_Targeting_Human_0050 Non_Targeting_Human	Non_Targeting_Human	GTCAGCCATCGGATAGAGAT

SEQ ID NO.	gRNA Label	Gene	Nucleic Acid Sequence
484	1 sg_Non_Targeting_Human_0051 Non_Targeting_Human	Non_Targeting_Human	GTACGGCACTCCTAGCCGCT
485	1 sg_Non_Targeting_Human_0052 Non_Targeting_Human	Non_Targeting_Human	GGTCCTGTCTGATGCTTGCA
486	1 sg_Non_Targeting_Human_0053 Non_Targeting_Human	Non_Targeting_Human	GCCGCAATATATGCGGTAAG
487	1 sg_Non_Targeting_Human_0054 Non_Targeting_Human	Non_Targeting_Human	GCGCACGTATAATCCTGCGT
488	1 sg_Non_Targeting_Human_0055 Non_Targeting_Human	Non_Targeting_Human	GTGCACAACACGATCCACGA
489	1 sg_Non_Targeting_Human_0056 Non_Targeting_Human	Non_Targeting_Human	GCACAATGTTGACGTAAGTG
490	1 sg_Non_Targeting_Human_0057 Non_Targeting_Human	Non_Targeting_Human	GTAAGATGCTGCTCACCGTG
491	1 sg_Non_Targeting_Human_0058 Non_Targeting_Human	Non_Targeting_Human	GTCGGTGATCCAACGTATCG
492	1 sg_Non_Targeting_Human_0059 Non_Targeting_Human	Non_Targeting_Human	GAGCTAGTAGGACGCAAGAC
493	1 sg_Non_Targeting_Human_0060 Non_Targeting_Human	Non_Targeting_Human	GTACGTGGAAGCTTGTGGCC
494	1 sg_Non_Targeting_Human_0061 Non_Targeting_Human	Non_Targeting_Human	GAGAACTGCCAGTTCTCGAT
495	1 sg_Non_Targeting_Human_0062 Non_Targeting_Human	Non_Targeting_Human	GCCATTCGGCGCGGCACTTC
496	1 sg_Non_Targeting_Human_0063 Non_Targeting_Human	Non_Targeting_Human	GCACACGACCAATCCGCTTC
497	1 sg_Non_Targeting_Human_0064 Non_Targeting_Human	Non_Targeting_Human	GAGGTGATCGATTAAGTACA
498	1 sg_Non_Targeting_Human_0065 Non_Targeting_Human	Non_Targeting_Human	GTCACTCGCAGACGCCTAAC
499	1 sg_Non_Targeting_Human_0066 Non_Targeting_Human	Non_Targeting_Human	GCGCTACGGAATCATACGTT
500	1 sg_Non_Targeting_Human_0067 Non_Targeting_Human	Non_Targeting_Human	GGTAGGACCTCACGGCGCGC
501	1 sg_Non_Targeting_Human_0068 Non_Targeting_Human	Non_Targeting_Human	GAAGTGCATCTTGTTGTAGT

SEQ ID NO.	gRNA Label	Gene	Nucleic Acid Sequence
502	1 sg_Non_Targeting_Human_0069 Non_Targeting_Human	Non_Targeting_Human	GATCCTGATCCGGCGGCGCG
503	1 sg_Non_Targeting_Human_0070 Non_Targeting_Human	Non_Targeting_Human	GGTATGCGCGATCCTGAGTT
504	1 sg_Non_Targeting_Human_0071 Non_Targeting_Human	Non_Targeting_Human	GCGGAGCTAGAGAGCGGTCA
505	1 sg_Non_Targeting_Human_0072 Non_Targeting_Human	Non_Targeting_Human	GAATGGCAATTACGGCTGAT
506	1 sg_Non_Targeting_Human_0073 Non_Targeting_Human	Non_Targeting_Human	GTATGGTGAGTAGTCGCTTG
507	1 sg_Non_Targeting_Human_0074 Non_Targeting_Human	Non_Targeting_Human	GTGTAATTGCGTCTAGTCGG
508	1 sg_Non_Targeting_Human_0075 Non_Targeting_Human	Non_Targeting_Human	GGTCCTGGCGAGGAGCCTTG
509	1 sg_Non_Targeting_Human_0076 Non_Targeting_Human	Non_Targeting_Human	GAAGATAAGTCGCTGTCTCG
510	1 sg_Non_Targeting_Human_0077 Non_Targeting_Human	Non_Targeting_Human	GTCGGCGTTCTGTTGTGACT
511	1 sg_Non_Targeting_Human_0078 Non_Targeting_Human	Non_Targeting_Human	GAGGCAAGCCGTTAGGTGTA
512	1 sg_Non_Targeting_Human_0079 Non_Targeting_Human	Non_Targeting_Human	GCGGATCCAGATCTCATTCG
513	1 sg_Non_Targeting_Human_0080 Non_Targeting_Human	Non_Targeting_Human	GGAACATAGGAGCACGTAGT
514	1 sg_Non_Targeting_Human_0081 Non_Targeting_Human	Non_Targeting_Human	GTCATCATTATGGCGTAAGG
515	1 sg_Non_Targeting_Human_0082 Non_Targeting_Human	Non_Targeting_Human	GCGACTAGCGCCATGAGCGG
516	1 sg_Non_Targeting_Human_0083 Non_Targeting_Human	Non_Targeting_Human	GGCGAAGTTCGACATGACAC
517	1 sg_Non_Targeting_Human_0084 Non_Targeting_Human	Non_Targeting_Human	GCTGTCTGTGTGGAGGCTATG
518	1 sg_Non_Targeting_Human_0085 Non_Targeting_Human	Non_Targeting_Human	GCGGAGAGCATTGACCTCAT
519	1 sg_Non_Targeting_Human_0086 Non_Targeting_Human	Non_Targeting_Human	GACTAATGGACCAAGTCAGT

SEQ ID NO.	gRNA Label	Gene	Nucleic Acid Sequence
520	1 sg_Non_Targeting_Human_0087 Non_Targeting_Human	Non_Targeting_Human	GCGGATTAGAGGTAATGCGG
521	1 sg_Non_Targeting_Human_0088 Non_Targeting_Human	Non_Targeting_Human	GCCGACGGCAATCAGTACGC
522	1 sg_Non_Targeting_Human_0089 Non_Targeting_Human	Non_Targeting_Human	GTAACCTCTCGAGCGATAGA
523	1 sg_Non_Targeting_Human_0090 Non_Targeting_Human	Non_Targeting_Human	GACTTGTATGTGGCTTACGG
524	1 sg_Non_Targeting_Human_0091 Non_Targeting_Human	Non_Targeting_Human	GTCACTGTGGTCAACATGT
525	1 sg_Non_Targeting_Human_0092 Non_Targeting_Human	Non_Targeting_Human	GTACTCCAATCCGCGATGAC
526	1 sg_Non_Targeting_Human_0093 Non_Targeting_Human	Non_Targeting_Human	GCGTTGGCACGATGTTACGG
527	1 sg_Non_Targeting_Human_0094 Non_Targeting_Human	Non_Targeting_Human	GAACCAGCCGGCTAGTATGA
528	1 sg_Non_Targeting_Human_0095 Non_Targeting_Human	Non_Targeting_Human	GTATACTAGCTAACCACACG
529	1 sg_Non_Targeting_Human_0096 Non_Targeting_Human	Non_Targeting_Human	GAATCGGAATAGTTGATTCTG
530	1 sg_Non_Targeting_Human_0097 Non_Targeting_Human	Non_Targeting_Human	GAGCACTTGCATGAGGCGGT
531	1 sg_Non_Targeting_Human_0098 Non_Targeting_Human	Non_Targeting_Human	GAACGGCGATGAAGCCAGCC
532	1 sg_Non_Targeting_Human_0099 Non_Targeting_Human	Non_Targeting_Human	GCAACCGAGATGAGAGGTTC
533	1 sg_Non_Targeting_Human_0100 Non_Targeting_Human	Non_Targeting_Human	GCAAGATCAATATGCGTGAT
534	1 sg_Non_Targeting_Human_GA_0101 Non_Targeting_Human	Non_Targeting_Human	ACGGAGGCTAAGCGTCGCAA
535	1 sg_Non_Targeting_Human_GA_0102 Non_Targeting_Human	Non_Targeting_Human	CGCTTCCGCGGCCCGTTCAA
536	1 sg_Non_Targeting_Human_GA_0103 Non_Targeting_Human	Non_Targeting_Human	ATCGTTTCCGCTTAACGGCG
537	1 sg_Non_Targeting_Human_GA_0104 Non_Targeting_Human	Non_Targeting_Human	GTAGGCGCGCCGCTCTCTAC

SEQ ID NO.	gRNA Label	Gene	Nucleic Acid Sequence
538	1 sg_Non_Targeting_Human_GA_0105 Non_Targeting_Human	Non_Targeting_Human	CCATATCGGGGCGAGACATG
539	1 sg_Non_Targeting_Human_GA_0106 Non_Targeting_Human	Non_Targeting_Human	TACTAACGCCGCTCCTACAG
540	1 sg_Non_Targeting_Human_GA_0107 Non_Targeting_Human	Non_Targeting_Human	TGAGGATCATGTGAGCGCC
541	1 sg_Non_Targeting_Human_GA_0108 Non_Targeting_Human	Non_Targeting_Human	GGGCCCCGCATAGGATATCGC
542	1 sg_Non_Targeting_Human_GA_0109 Non_Targeting_Human	Non_Targeting_Human	TAGACAACCGCGGAGAATGC
543	1 sg_Non_Targeting_Human_GA_0110 Non_Targeting_Human	Non_Targeting_Human	ACGGGCGGCTATCGCTGACT
544	1 sg_Non_Targeting_Human_GA_0111 Non_Targeting_Human	Non_Targeting_Human	CGCGGAAATTTTACCGACGA
545	1 sg_Non_Targeting_Human_GA_0112 Non_Targeting_Human	Non_Targeting_Human	CTTACAATCGTCGGTCCAAT
546	1 sg_Non_Targeting_Human_GA_0113 Non_Targeting_Human	Non_Targeting_Human	GCGTGCGTCCCGGGTTACCC
547	1 sg_Non_Targeting_Human_GA_0114 Non_Targeting_Human	Non_Targeting_Human	CGGAGTAACAAGCGGACGGA
548	1 sg_Non_Targeting_Human_GA_0115 Non_Targeting_Human	Non_Targeting_Human	CGAGTGTTATACGCACCGTT
549	1 sg_Non_Targeting_Human_GA_0116 Non_Targeting_Human	Non_Targeting_Human	CGACTAACCGGAACTTTTT
550	1 sg_Non_Targeting_Human_GA_0117 Non_Targeting_Human	Non_Targeting_Human	CAACGGGTTCTCCCGGCTAC
551	1 sg_Non_Targeting_Human_GA_0118 Non_Targeting_Human	Non_Targeting_Human	CAGGAGTCGCCGATACGCGT
552	1 sg_Non_Targeting_Human_GA_0119 Non_Targeting_Human	Non_Targeting_Human	TTCACGTCGTCTCGCGACCA
553	1 sg_Non_Targeting_Human_GA_0120 Non_Targeting_Human	Non_Targeting_Human	GTGTGCGATTCCGCCGCTTA
554	1 sg_Non_Targeting_Human_GA_0121 Non_Targeting_Human	Non_Targeting_Human	CACGAACTCACACCGCGCGA
555	1 sg_Non_Targeting_Human_GA_0122 Non_Targeting_Human	Non_Targeting_Human	CGCTAGTACGCTCCTCTATA

SEQ ID NO.	gRNA Label	Gene	Nucleic Acid Sequence
556	1 sg_Non_Targeting_Human_GA_0123 Non_Targeting_Human	Non_Targeting_Human	TCGCGCTTGGGTTATACGCT
557	1 sg_Non_Targeting_Human_GA_0124 Non_Targeting_Human	Non_Targeting_Human	CTATCTCGAGTGGTAATGCG
558	1 sg_Non_Targeting_Human_GA_0125 Non_Targeting_Human	Non_Targeting_Human	AATCGACTCGAACTTCGTGT
559	1 sg_Non_Targeting_Human_GA_0126 Non_Targeting_Human	Non_Targeting_Human	CCCGATGGACTATACCGAAC
560	1 sg_Non_Targeting_Human_GA_0127 Non_Targeting_Human	Non_Targeting_Human	ACGTTTCGAGTACGACCAGCT
561	1 sg_Non_Targeting_Human_GA_0128 Non_Targeting_Human	Non_Targeting_Human	CGCGACGACTCAACCTAGTC
562	1 sg_Non_Targeting_Human_GA_0129 Non_Targeting_Human	Non_Targeting_Human	GGTCACCGATCGAGAGCTAG
563	1 sg_Non_Targeting_Human_GA_0130 Non_Targeting_Human	Non_Targeting_Human	CTCAACCGACCGTATGGTCA
564	1 sg_Non_Targeting_Human_GA_0131 Non_Targeting_Human	Non_Targeting_Human	CGTATTCGACTCTCAACGCG
565	1 sg_Non_Targeting_Human_GA_0132 Non_Targeting_Human	Non_Targeting_Human	CTAGCCGCCCAGATCGAGCC
566	1 sg_Non_Targeting_Human_GA_0133 Non_Targeting_Human	Non_Targeting_Human	GAATCGACCGACACTAATGT
567	1 sg_Non_Targeting_Human_GA_0134 Non_Targeting_Human	Non_Targeting_Human	ACTTCAGTTCGGCGTAGTCA
568	1 sg_Non_Targeting_Human_GA_0135 Non_Targeting_Human	Non_Targeting_Human	GTGCGATGTCGCTTCAACGT
569	1 sg_Non_Targeting_Human_GA_0136 Non_Targeting_Human	Non_Targeting_Human	CGCCTAATTTCCGGATCAAT
570	1 sg_Non_Targeting_Human_GA_0137 Non_Targeting_Human	Non_Targeting_Human	CGTGGCCGGAACCGTCATAG
571	1 sg_Non_Targeting_Human_GA_0138 Non_Targeting_Human	Non_Targeting_Human	ACCCTCCGAATCGTAACGGA
572	1 sg_Non_Targeting_Human_GA_0139 Non_Targeting_Human	Non_Targeting_Human	AAACGGTACGACAGCGTGTG
573	1 sg_Non_Targeting_Human_GA_0140 Non_Targeting_Human	Non_Targeting_Human	ACATAGTCGACGGCTCGATT

SEQ ID NO.	gRNA Label	Gene	Nucleic Acid Sequence
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576	1 sg_Non_Targeting_Human_GA_0143 Non_Targeting_Human	Non_Targeting_Human	CGCCGGGCTGACAATTAACG
577	1 sg_Non_Targeting_Human_GA_0144 Non_Targeting_Human	Non_Targeting_Human	CGTCGCCATATGCCGGTGGC
578	1 sg_Non_Targeting_Human_GA_0145 Non_Targeting_Human	Non_Targeting_Human	CGGGCCTATAACACCATCGA
579	1 sg_Non_Targeting_Human_GA_0146 Non_Targeting_Human	Non_Targeting_Human	CGCCGTTCCGAGATACTTGA
580	1 sg_Non_Targeting_Human_GA_0147 Non_Targeting_Human	Non_Targeting_Human	CGGGACGTCGCGAAAATGTA
581	1 sg_Non_Targeting_Human_GA_0148 Non_Targeting_Human	Non_Targeting_Human	TCGGCATACGGGACACACGC
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584	1 sg_Non_Targeting_Human_GA_0151 Non_Targeting_Human	Non_Targeting_Human	TCGATCGAGGTTGCATTCCG
585	1 sg_Non_Targeting_Human_GA_0152 Non_Targeting_Human	Non_Targeting_Human	CTCGACAGTTCGTCCCGAGC
586	1 sg_Non_Targeting_Human_GA_0153 Non_Targeting_Human	Non_Targeting_Human	CGGTAGTATTAATCGCTGAC
587	1 sg_Non_Targeting_Human_GA_0154 Non_Targeting_Human	Non_Targeting_Human	TGAACGCGTGTTTCCTTGCA
588	1 sg_Non_Targeting_Human_GA_0155 Non_Targeting_Human	Non_Targeting_Human	CGACGCTAGGTAACGTAGAG
589	1 sg_Non_Targeting_Human_GA_0156 Non_Targeting_Human	Non_Targeting_Human	CATTGTTGAGCGGGCGCGCT
590	1 sg_Non_Targeting_Human_GA_0157 Non_Targeting_Human	Non_Targeting_Human	CCGCTATTGAAACCGCCAC
591	1 sg_Non_Targeting_Human_GA_0158 Non_Targeting_Human	Non_Targeting_Human	AGACACGTCACCGGTCAAAA

SEQ ID NO.	gRNA Label	Gene	Nucleic Acid Sequence
592	1 sg_Non_Targeting_Human_GA_0159 Non_Targeting_Human	Non_Targeting_Human	TTTACGATCTAGCGGCGTAG
593	1 sg_Non_Targeting_Human_GA_0160 Non_Targeting_Human	Non_Targeting_Human	TTCGCACGATTGCACCTTGG
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595	1 sg_Non_Targeting_Human_GA_0162 Non_Targeting_Human	Non_Targeting_Human	CCTCCGTGCTAACGCGGACG
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598	1 sg_Non_Targeting_Human_GA_0165 Non_Targeting_Human	Non_Targeting_Human	CGCGGCCACGCGTCATCGC
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600	1 sg_Non_Targeting_Human_GA_0167 Non_Targeting_Human	Non_Targeting_Human	AACTAGCCCGAGCAGCTTCG
601	1 sg_Non_Targeting_Human_GA_0168 Non_Targeting_Human	Non_Targeting_Human	CGCAAGGTGTGCGTAACCCT
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605	1 sg_Non_Targeting_Human_GA_0172 Non_Targeting_Human	Non_Targeting_Human	GTCGTCCGGGATTACAAAAT
606	1 sg_Non_Targeting_Human_GA_0173 Non_Targeting_Human	Non_Targeting_Human	TAATGCTGCACACGCCGAAT
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609	1 sg_Non_Targeting_Human_GA_0176 Non_Targeting_Human	Non_Targeting_Human	TAAGATCCGCGGGTGGCAAC

SEQ ID NO.	gRNA Label	Gene	Nucleic Acid Sequence
610	1 sg_Non_Targeting_Human_GA_0177 Non_Targeting_Human	Non_Targeting_Human	GTAGACGTCGTGAGCTTCAC
611	1 sg_Non_Targeting_Human_GA_0178 Non_Targeting_Human	Non_Targeting_Human	TCGCGGACATAGGGCTCTAA
612	1 sg_Non_Targeting_Human_GA_0179 Non_Targeting_Human	Non_Targeting_Human	AGCGCAGATAGCGCGTATCA
613	1 sg_Non_Targeting_Human_GA_0180 Non_Targeting_Human	Non_Targeting_Human	GTTCTGCTTCGTAACGAGGAA
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615	1 sg_Non_Targeting_Human_GA_0182 Non_Targeting_Human	Non_Targeting_Human	ACGTCCATACTGTCTGGCTAC
616	1 sg_Non_Targeting_Human_GA_0183 Non_Targeting_Human	Non_Targeting_Human	GTACCATTGCCGGCTCCCTA
617	1 sg_Non_Targeting_Human_GA_0184 Non_Targeting_Human	Non_Targeting_Human	TGGTTCCGTAGGTCGGTATA
618	1 sg_Non_Targeting_Human_GA_0185 Non_Targeting_Human	Non_Targeting_Human	TCTGGCTTGACACGACCGTT
619	1 sg_Non_Targeting_Human_GA_0186 Non_Targeting_Human	Non_Targeting_Human	CGCTAGGTCCGGTAAGTGCG
620	1 sg_Non_Targeting_Human_GA_0187 Non_Targeting_Human	Non_Targeting_Human	AGCACGTAATGTCCGTGGAT
621	1 sg_Non_Targeting_Human_GA_0188 Non_Targeting_Human	Non_Targeting_Human	AAGGCGCGCGAATGTGGCAG
622	1 sg_Non_Targeting_Human_GA_0189 Non_Targeting_Human	Non_Targeting_Human	ACTGCGGAGCGCCCAATATC
623	1 sg_Non_Targeting_Human_GA_0190 Non_Targeting_Human	Non_Targeting_Human	CGTCGAGTGCTCGAACTCCA
624	1 sg_Non_Targeting_Human_GA_0191 Non_Targeting_Human	Non_Targeting_Human	TCGCAGCGGCGTGGGATCGG
625	1 sg_Non_Targeting_Human_GA_0192 Non_Targeting_Human	Non_Targeting_Human	ATCTGTCCTAATTCGGATCG
626	1 sg_Non_Targeting_Human_GA_0193 Non_Targeting_Human	Non_Targeting_Human	TGCGGCGTAATGCTTGAAAG
627	1 sg_Non_Targeting_Human_GA_0194 Non_Targeting_Human	Non_Targeting_Human	CGAACTTAATCCCGTGGCAA

SEQ ID NO.	gRNA Label	Gene	Nucleic Acid Sequence
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630	1 sg_Non_Targeting_Human_GA_0197 Non_Targeting_Human	Non_Targeting_Human	CCGTTGGACTATGGCGGGTC
631	1 sg_Non_Targeting_Human_GA_0198 Non_Targeting_Human	Non_Targeting_Human	GTACGGGGCGATCATCCACA
632	1 sg_Non_Targeting_Human_GA_0199 Non_Targeting_Human	Non_Targeting_Human	AAGAGTAGTAGACGCCCGGG
633	1 sg_Non_Targeting_Human_GA_0200 Non_Targeting_Human	Non_Targeting_Human	AAGAGCGAATCGATTTCTGTG
634	3 sg_hCDC16_CC_1 CDC16	CDC16	TCAACACCAGTGCCTGACGG
635	3 sg_hCDC16_CC_2 CDC16	CDC16	AAAGTAGCTTCACTCTCTCG
636	3 sg_hCDC16_CC_3 CDC16	CDC16	GAGCCAACCAATAGATGTCC
637	3 sg_hCDC16_CC_4 CDC16	CDC16	GCGCCGCCATGAACCTAGAG
638	3 sg_hGTF2B_CC_1 GTF2B	GTF2B	ACAAAGGTTGGAACAGAACC
639	3 sg_hGTF2B_CC_2 GTF2B	GTF2B	GGTGACCGGGTTATTGATGT
640	3 sg_hGTF2B_CC_3 GTF2B	GTF2B	TTAGTGGAGGACTACAGAGC
641	3 sg_hGTF2B_CC_4 GTF2B	GTF2B	ACATATAGCCCGTAAAGCTG
642	3 sg_hHSPA5_CC_1 HSPA5	HSPA5	CGTTGGCGATGATCTCCACG
643	3 sg_hHSPA5_CC_2 HSPA5	HSPA5	TGGCCTTTTCTACCTCGCGC
644	3 sg_hHSPA5_CC_3 HSPA5	HSPA5	AATGGAGATACTCATCTGGG
645	3 sg_hHSPA5_CC_4 HSPA5	HSPA5	GAAGCCCGTCCAGAAAGTGT
646	3 sg_hHSPA9_CC_1 HSPA9	HSPA9	CAATCTGAGGAACTCCACGA
647	3 sg_hHSPA9_CC_2 HSPA9	HSPA9	AGGCTGCGGCGCCCACGAGA
648	3 sg_hHSPA9_CC_3 HSPA9	HSPA9	ACTTTGACCAGGCCTTGCTA

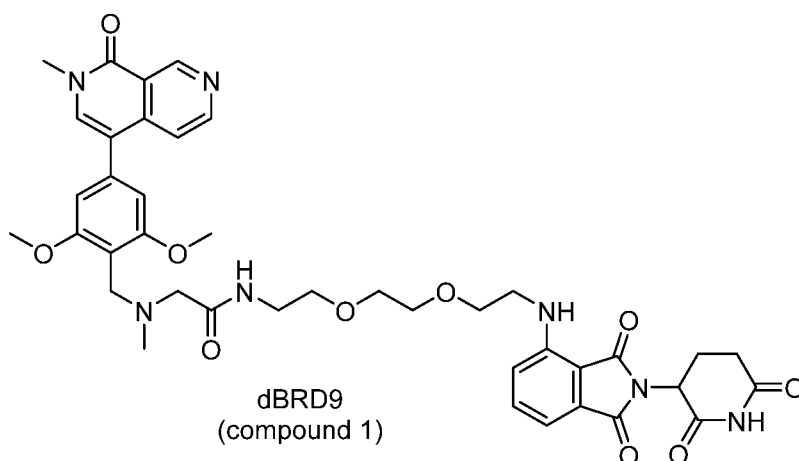
SEQ ID NO.	gRNA Label	Gene	Nucleic Acid Sequence
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650	3 sg_hPAFAH1B1_CC_1 PAFAH1B1	PAFAH1B1	CGAGGCGTACATACCCAAGG
651	3 sg_hPAFAH1B1_CC_2 PAFAH1B1	PAFAH1B1	ATGGTACGGCCAAATCAAGA
652	3 sg_hPAFAH1B1_CC_3 PAFAH1B1	PAFAH1B1	TCTTGTAATCCCATACGCGT
653	3 sg_hPAFAH1B1_CC_4 PAFAH1B1	PAFAH1B1	ATTCACAGGACACAGAGAAT
654	3 sg_hPCNA_CC_1 PCNA	PCNA	CCAGGGCTCCATCCTCAAGA
655	3 sg_hPCNA_CC_2 PCNA	PCNA	TGAGCTGCACCAAAGAGACG
656	3 sg_hPCNA_CC_3 PCNA	PCNA	ATGTCTGCAGATGTACCCCT
657	3 sg_hPCNA_CC_4 PCNA	PCNA	CGAAGATAACGCGGATACCT
658	3 sg_hPOLR2L_CC_1 POLR2L	POLR2L	GCTGCAGGCCGAGTACACCG
659	3 sg_hPOLR2L_CC_2 POLR2L	POLR2L	ACAAGTGGGAGGCTTACCTG
660	3 sg_hPOLR2L_CC_3 POLR2L	POLR2L	GCAGCGTACAGGGATGATCA
661	3 sg_hPOLR2L_CC_4 POLR2L	POLR2L	GCAGTAGCGCTTCAGGCCCA
662	3 sg_hRPL9_CC_1 RPL9	RPL9	CAAATGGTGGGGTAACAGAA
663	3 sg_hRPL9_CC_2 RPL9	RPL9	GAAAGGAACTGGCTACCGTT
664	3 sg_hRPL9_CC_3 RPL9	RPL9	AGGGCTTCCGTTACAAGATG
665	3 sg_hRPL9_CC_4 RPL9	RPL9	GAACAAGCAACACCTAAAAG
666	3 sg_hSF3A3_CC_1 SF3A3	SF3A3	TGAGGAGAAGGAACGGCTCA
667	3 sg_hSF3A3_CC_2 SF3A3	SF3A3	GGAAGAATGCAGAGTATAAG
668	3 sg_hSF3A3_CC_3 SF3A3	SF3A3	GGAATTTGAGGAACTCCTGA
669	3 sg_hSF3A3_CC_4 SF3A3	SF3A3	GCTCACCGGCCATCCAGGAA

SEQ ID NO.	gRNA Label	Gene	Nucleic Acid Sequence
670	3 sg_hSF3B3_CC_1 SF3B3	SF3B3	ACTGGCCAGGAACGATGCGA
671	3 sg_hSF3B3_CC_2 SF3B3	SF3B3	GCAGCTCCAAGATCTTCCCA
672	3 sg_hSF3B3_CC_3 SF3B3	SF3B3	GAATGAGTACACAGAACGGA
673	3 sg_hSF3B3_CC_4 SF3B3	SF3B3	GGAGCAGGACAAGGTCGGGG

Example 2 – BRD9 degrader depletes BRD9 protein

The following example demonstrates the depletion of the BRD9 protein in synovial sarcoma cells treated with a BRD9 degrader.

- 5 **Procedure:** Cells were treated with DMSO or the BRD9 degrader, Compound 1 (also known as dBRD9, see Remillard et al, *Angew. Chem. Int. Ed. Engl.* 56(21):5738-5743 (2017); see structure of compound 1 below), for indicated doses and timepoints.



- Whole cell extracts were fractionated by SDS-PAGE and transferred to a polyvinylidene difluoride
 10 membrane using a transfer apparatus according to the manufacturer's protocols (Bio-Rad). After incubation with 5% nonfat milk in TBST (10 mM Tris, pH 8.0, 150 mM NaCl, 0.5% Tween 20) for 60 min, the membrane was incubated with antibodies against BRD9 (1:1,000, Bethyl laboratory A303-781A), GAPDH (1:5,000, Cell Signaling Technology), and/or MBP (1:1,000, BioRad) overnight at 4°C. Membranes were washed three times for 10 minutes and incubated with anti-mouse or anti-rabbit
 15 antibodies conjugated with either horseradish peroxidase (HRP, FIGS. 2-3) or IRDye (FIG. 4, 1:20,000, LI-COR) for at least 1h. Blots were washed with TBST three times and developed with either the ECL system according to the manufacturer's protocols (FIGS. 2-3) or scanned on an Odyssey CLx Imaging system (FIG. 4).

- Results:** Treatment of SYO1 synovial sarcoma cells with the BRD9 degrader Compound 1
 20 results in dose dependent (FIG. 2) and time dependent (FIG. 3) depletion of BRD9 in the cells. Further, as shown in FIG. 4, the depletion of BRD9 by Compound 1 is replicated in a non-synovial sarcoma cell line (293T) and may be sustained for at least 5 days.

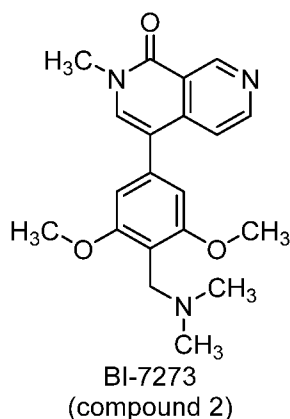
Example 3 – Inhibition of growth of synovial cell lines by BRD9 inhibitors and BRD9 degraders

The following example demonstrates that BRD9 degraders and inhibitors selectively inhibit growth of synovial sarcoma cells.

Procedures:

Cells were treated with DMSO or the BRD9 degrader, Compound 1, at indicated concentrations, and proliferation was monitored from day 7 to day 14 by measuring confluency over time using an IncuCyte live cell analysis system (FIG. 5). Growth medium and compounds were refreshed every 3-4 days.

Cells were seeded into 12-well plates and treated with DMSO, 1 μ M BRD9 inhibitor, Compound 2 (also known as BI-7273, see Martin et al, *J Med Chem.* 59(10):4462-4475 (2016); see structure of compound 2 below), or 1 μ M BRD9 degrader, Compound 1.



The number of cells was optimized for each cell line. Growth medium and compounds were refreshed every 3-5 days. SYO1, Yamato, A549, 293T and HS-SY-II cells were fixed and stained at day 11. ASKA cells were fixed and stained at day 23. Staining was done by incubation with crystal violet solution (0.5 g Crystal Violet, 27 ml 37% Formaldehyde, 100 mL 10X PBS, 10 mL Methanol, 863 dH2O to 1L) for 30 minutes followed by 3x washes with water and drying the plates for at least 24h at room temperature. Subsequently plates were scanned on an Odyssey CLx Imaging system (FIG. 6).

Cells were seeded into 96-well ultra low cluster plate (Costar, #7007) in 200 μ L complete media and treated at day 2 with DMSO, Staurosporin, or BRD9 degrader, Compound 1, at indicated doses (FIG. 7). Media and compounds were changed every 5 d and cell colonies were imaged at day 14.

Results: As shown in FIGS. 5, 6, and 7, treatment of synovial sarcoma cell lines (SYO1, Yamato, HS-SY-II, and ASKA) with a BRD9 inhibitor, Compound 2, or a BRD9 degrader, Compound 1, results in inhibition of the growth of the cells, but does not result in inhibition of the growth of non-synovial control cancer cell lines (293T, A549, G401).

Example 4 – Selective inhibition of growth of synovial cell lines by BRD9 degraders and BRD9 binders

The following example demonstrates that BRD9 degraders and binders selectively inhibit growth of synovial sarcoma cells.

Procedure: Cells were seeded into 6-well or 12-well plates and were treated daily with a BRD9 degrader (Compound 1), a bromo-domain BRD9 binder (Compound 2), E3 ligase binder (lenalidomide),

DMSO, or staurosporin (positive control for cell killing), at indicated concentrations. The number of cells was optimized for each cell line. Growth media was refreshed every 5 days. By day 14, medium was removed, cells were washed with PBS, and stained using 500 μ L of 0.005% (w/v) crystal violet solution in 25% (v/v) methanol for at least 1 hour at room temperature. Subsequently plates were scanned on an Odyssey CLx Imaging system.

Results: As shown in FIGS. 8 and 9, treatment of synovial sarcoma cell lines (SYO1, HS-SY-II, and ASKA) with Compound 1 or Compound 2 resulted in inhibition of the growth of the cells, but did not result in inhibition of the growth of non-synovial control cancer cell lines (RD, HCT116, and Calu6). Overall, Compound 1 showed most significant growth inhibition in all synovial cell lines.

Example 5 – Inhibition of cell growth in synovial sarcoma cells

The following example shows that BRD9 degraders inhibit cell growth and induce apoptosis in synovial sarcoma cells.

Procedure: SYO1 cells were treated for 8 or 13 days with DMSO, a BRD9 degrader (Compound 1) at 200nM or 1 μ M, or an E3 ligase binder (lenalidomide) at 200nM. Compounds were refreshed every 5 days. Cell cycle analysis was performed using the Click-iT™ Plus EdU Flow Cytometry Assay (Invitrogen). The apoptosis assay was performed using the Annexin V-FITC Apoptosis Detection Kit (Sigma A9210). Assays were performed according to the manufacturer's protocol.

Results: As shown in FIGS. 10-13, treatment with Compound 1 for 8 or 13 days resulted in reduced numbers of cells in the S-phase of the cell cycle as compared to DMSO and lenalidomide. Treatment with Compound 1 for 8 days also resulted in increased numbers of early- and late-apoptotic cells as compared to DMSO controls.

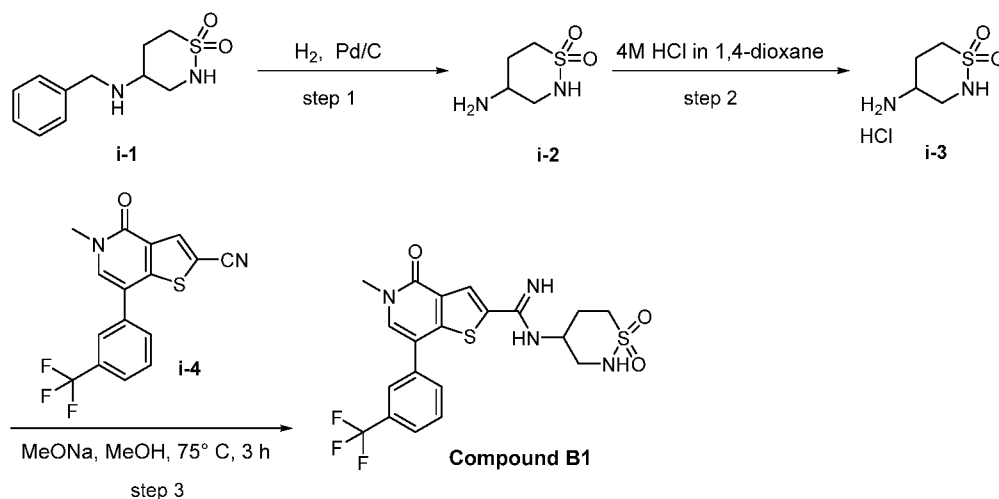
Example 6 – Composition for SS18-SSX1-BAF

The following example shows the identification of BRD9 as a component of SS18-SSX containing BAF complexes.

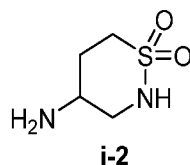
Procedure: A stable 293T cell line expressing HA-SS18SSX1 was generated using lentiviral integration. SS18-SSX1 containing BAF complexes were subject to affinity purification and subsequent mass spectrometry analysis revealed SS18-SSX1 interacting proteins.

Results: As shown in FIG. 14, BAF complexes including the SS18-SSX fusion protein also included BRD9. More than 5 unique peptides were identified for ARID1A (95 peptides), ARID1B (77 peptides), SMARCC1 (69 peptides), SMARCD1 (41 peptides), SMARCD2 (37 peptides), DPF2 (32 peptides), SMARCD3 (26 peptides), ACTL6A (25 peptides), BRD9 (22 peptides), DPF1 Isoform 2 (18 peptides), DPF3 (13 peptides), and ACTL6B (6 peptides).

Example 7 – Preparation of N-(1,1-dioxo-1λ6,2-thiazinan-4-yl)-5-methyl-4-oxo-7-[3-(trifluoromethyl)phenyl]thieno[3,2-c]pyridine-2-carboximidamide (Compound B1)



Step 1: Preparation of 4-amino-1λ6,2-thiazinane-1,1-dione (i-1)

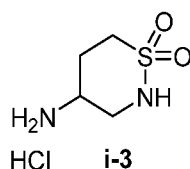


5

4-(benzylamino)-1λ6,2-thiazinane-1,1-dione (200.00 mg, 0.832 mmol, 1.00 equiv) and Pd/C (199.27 mg, 1.873 mmol, 2.25 equiv) in MeOH (10.00 mL) were stirred under an atmosphere of hydrogen at balloon and room temperature for 3 hours. The solid was filtered out, and the filtrate was concentrated under reduced pressure to afford 4-amino-1λ6,2-thiazinane-1,1-dione (120mg,96%) as a brown solid.

10 This material was used directly in the next step without further purification. LCMS (ESI) m/z: $[\text{M}+\text{H}]^+ = 151$.

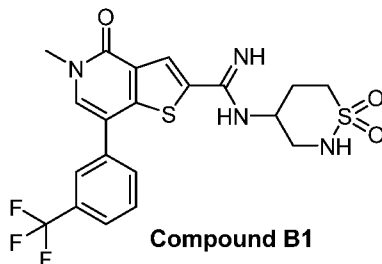
Step 2: Preparation of 4-amino-1λ6,2-thiazinane-1,1-dione hydrochloride (i-2)



15 4-amino-1λ6,2-thiazinane-1,1-dione (110.00 mg, 0.732 mmol, 1.00 equiv) was added a solution of HCl in 1,4-dioxane (4 mL, 4 M), and the resulting mixture was stirred at room temperature for 2 hours. The solvent was removed under reduced pressure to afford 4-amino-1λ6,2-thiazinane-1,1-

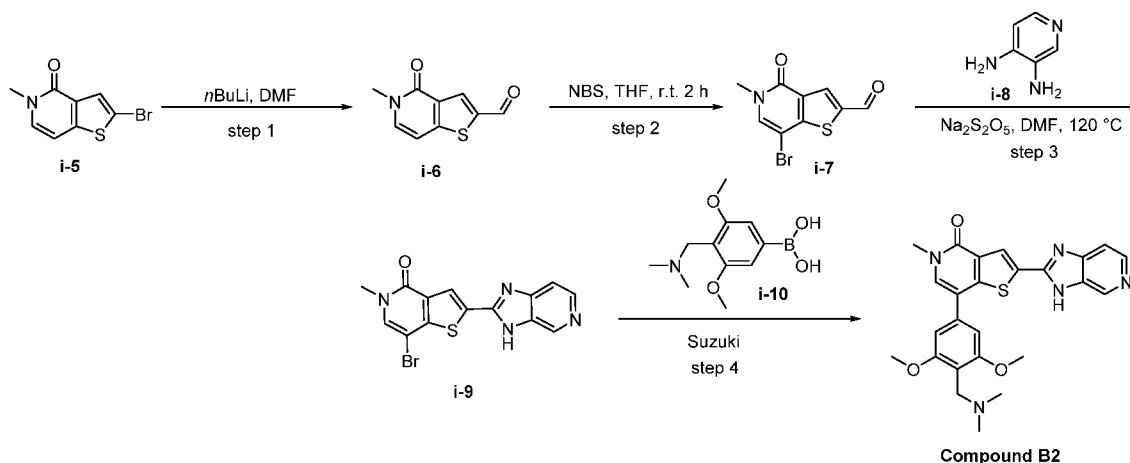
dione hydrochloride (131 mg, 96%) as a brown solid. This material was used directly in the next step without further purification. LCMS (ESI) m/z : $[M+H]^+ = 151$.

Step 3: Preparation of N-(1,1-dioxo-1 λ 6,2-thiazinan-4-yl)-5-methyl-4-oxo-7-[3-(trifluoromethyl)phenyl]thieno[3,2-c]pyridine-2-carboximidamide (Compound B1)

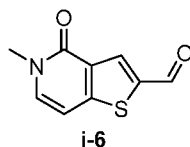


To a solution of 5-methyl-4-oxo-7-[3-(trifluoromethyl)phenyl]thieno[3,2-c]pyridine-2-carbonitrile (50.00 mg, 0.150 mmol, 1.00 equiv) in MeOH (1.00 mL) was added NaOMe (8.08 mg, 0.150 mmol, 1 equiv), and the resulting mixture was stirred at 75 °C for 3 hours. Then 4-amino-1 λ 6,2-thiazinane-1,1-dione hydrochloride (33.50 mg, 0.179 mmol, 1.2 equiv) was added to the reaction mixture. After stirring at 75 °C for 16 hours, the crude product was purified by flash C18-flash chromatography, elution gradient 0 to 50% MeCN in water (containing 0.1% NH_4HCO_3). Pure fractions were evaporated to dryness to afford crude product. The crude product was purified by preparative HPLC (conditions: XBridge Prep OBD C18 Column, 19*250 mm, 5 μm ; Mobile Phase A: Water (10 mmol/L NH_4HCO_3), Mobile Phase B: ACN; Flow rate: 25 mL/minute; Gradient: 35 B to 50 B in 12 minutes; 254/220 nm; R_T (retention time): 8.62 minutes). Fractions containing the desired compound were evaporated to dryness to afford N-(1,1-dioxo-1 λ 6,2-thiazinan-4-yl)-5-methyl-4-oxo-7-[3-(trifluoromethyl)phenyl]thieno[3,2-c]pyridine-2-carboximidamide (5.8 mg, 7.9%) as a white solid. LCMS (ESI) m/z : $[M+H]^+ = 485.20$.

Example 8 – Preparation of 7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-2-[3H-imidazo[4,5-c]pyridin-2-yl]-5-methylthieno[3,2-c]pyridin-4-one (Compound B2)

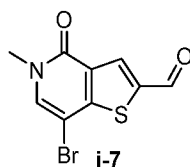


Step 1: Preparation of 5-methyl-4-oxothieno[3,2-c]pyridine-2-carbaldehyde (i-6).



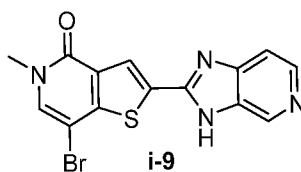
To a solution of 2-bromo-5-methylthieno[3,2-c]pyridin-4-one (2.00 g, 8.193 mmol, 1.00 equiv) in THF (20.00 mL) was added *n*-BuLi (1.05 g, 16.386 mmol, 2.00 equiv) in dropwise at -78 °C under nitrogen atmosphere, the resulting mixture was stirred at -78 °C for 30 minutes, then DMF (5.99 g, 81.930 mmol, 10.00 equiv) was added to the reaction mixture. The reaction was warmed to room temperature naturally. The reaction was quenched by the addition of sat. NH₄Cl (aq.) (30 mL) at 0 °C, and extracted with EtOAc (ethyl acetate) (50 mL x 4). The organic layer was washed with water (50 mL) and brine (50 mL), then dried over anhydrous sodium sulfate, filtered, and concentrated to give crude product that was purified by flash silica chromatography, elution gradient 0 to 60% EtOAc in petroleum ether (PE). Pure fractions were evaporated to dryness to afford 5-methyl-4-oxothieno[3,2-c]pyridine-2-carbaldehyde (658 mg, 42%) as a brown solid. LCMS (ESI) *m/z*: [M+H]⁺ = 194.

Step 2: Preparation of 7-bromo-5-methyl-4-oxothieno[3,2-c]pyridine-2-carbaldehyde (i-7)



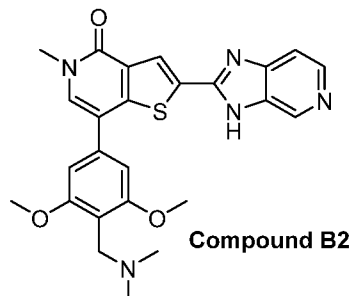
To a solution of 5-methyl-4-oxothieno[3,2-c]pyridine-2-carbaldehyde (600.00 mg, 3.105 mmol, 1.00 equiv) in THF (10.00 mL) was added NBS (663.23 mg, 3.726 mmol, 1.20 equiv), the resulting mixture was stirred at room temperature for 2 hours. The reaction mixture was diluted with EtOAc (50 mL), and washed with water (3 x 30 mL) and saturated brine (1 x 30 mL). The organic layer was dried over Na₂SO₄, filtered and evaporated to afford crude product. The crude product was purified by flash silica chromatography, elution gradient 0 to 60% EtOAc in petroleum ether. Pure fractions were evaporated to dryness to afford 7-bromo-5-methyl-4-oxothieno[3,2-c]pyridine-2-carbaldehyde (510 mg, 60%) as a brown solid. LCMS (ESI) *m/z*: [M+H]⁺ = 272.

Step 3: Preparation of 7-bromo-2-[3H-imidazo[4,5-c]pyridin-2-yl]-5-methylthieno[3,2-c]pyridin-4-one (i-9)



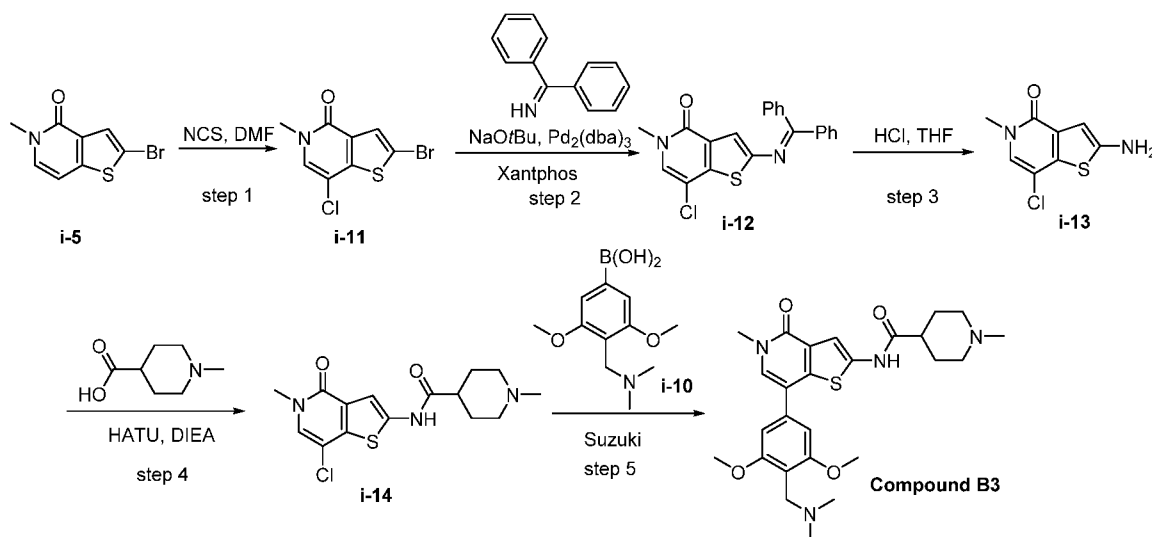
To a solution of 7-bromo-5-methyl-4-oxothieno[3,2-c]pyridine-2-carbaldehyde (300.00 mg, 1.102 mmol, 1.00 equiv) and 3,4-diaminopyridine (120.31 mg, 1.102 mmol, 1 equiv) in DMF (5.00 mL) was added Na₂S₂O₅ (628.75 mg, 3.307 mmol, 3 equiv), the resulting mixture was stirred at 120 °C for 16 hours. The solvent was removed under reduced pressure. The residue was purified by flash silica chromatography, elution gradient 0 to 10% MeOH in DCM. Pure fractions were evaporated to dryness to afford 7-bromo-2-[3H-imidazo[4,5-c]pyridin-2-yl]-5-methylthieno[3,2-c]pyridin-4-one (165 mg, 41%) as a brown solid. LCMS (ESI) *m/z*: [M+H]⁺ = 361.

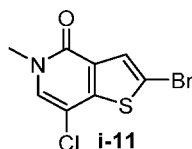
Step 4: Preparation of 7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-2-[3H-imidazo[4,5-c]pyridin-2-yl]-5-methylthieno[3,2-c]pyridin-4-one (Compound B2).



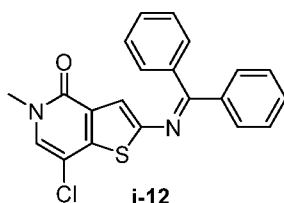
5 To a solution of 7-bromo-2-[3H-imidazo[4,5-c]pyridin-2-yl]-5-methylthieno[3,2-c]pyridin-4-one (60.00 mg, 0.166 mmol, 1.00 equiv), 4-[(dimethylamino)methyl]-3,5-dimethoxyphenylboronic acid (47.65 mg, 0.199 mmol, 1.20 equiv) and Cs_2CO_3 (108.24 mg, 0.332 mmol, 2.00 equiv) in DMF (1.00 mL) and H_2O (0.25 mL) was added $\text{Pd}(\text{dppf})\text{Cl}_2$ (12.15 mg, 0.017 mmol, 0.10 equiv), the resulting mixture was stirred at 100 °C for 1 hour under a nitrogen atmosphere. The mixture was concentrated, the crude product was purified by reverse phase flash with the following conditions to afford crude product: column, C18 silica gel; mobile phase, MeCN in water, 5% to 50% gradient in 10 min; detector, UV 254 nm. The crude product was purified by Prep-HPLC (conditions: XSelect CSH Prep C18 OBD Column, 5 μm , 19*150mm; Mobile Phase A: Water (0.05% TFA, trifluoroacetic acid); Mobile Phase B: ACN (acetonitrile); Flow rate: 25 mL/minute; Gradient: 8% B to 8% B in 2 minutes; 254/220 nm; R_T (retention time): 13.87 minutes) to afford 7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-2-[3H-imidazo[4,5-c]pyridin-2-yl]-5-methylthieno[3,2-c]pyridin-4-one (3 mg, 3.8%) as a yellow solid. ^1H NMR (400 MHz, Methanol- d_4) δ 9.19 (s, 1H), 8.55 (d, J = 6.5 Hz, 1H), 8.46 (s, 1H), 8.10 (d, J = 6.5 Hz, 1H), 7.93 (s, 1H), 7.11 (s, 2H), 4.44 (s, 2H), 4.05 (s, 6H), 3.75 (s, 3H), 2.94 (s, 6H). LCMS (ESI) m/z : $[\text{M}+\text{H}]^+ = 476.30$.

20 **Example 9 – Preparation of N-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridin-2-yl)-1-methylpiperidine-4-carboxamide (Compound B3)**

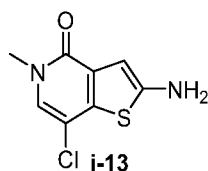


Step 1: Preparation of 2-bromo-7-chloro-5-methylthieno[3,2-c]pyridin-4-one (i-11)

To a solution of 2-bromo-5-methylthieno[3,2-c]pyridin-4-one (1.50 g, 6.145 mmol, 1.00 equiv) in DMF (5.00 mL) was added NCS (0.90 mg, 0.007 mmol, 1.1 equiv) at 25 °C. The resulting solution was stirred at 70 °C for 3 hours. The resulting mixture was concentrated. The residue was purified by chromatography on silica gel eluted with petroleum ether/EtOAc (2/1) to afford 2-bromo-7-chloro-5-methylthieno[3,2-c]pyridin-4-one (1.6 g, 94%) as a brown solid. LCMS (ESI) m/z: [M+H]⁺ = 278

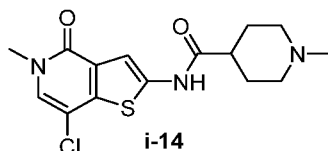
Step 2: Preparation of 7-chloro-2-[(diphenylmethylidene)amino]-5-methylthieno[3,2-c]pyridin-4-one (i-12)

To a solution of 2-bromo-7-chloro-5-methylthieno[3,2-c]pyridin-4-one (1.6 g, 5.744 mmol, 1.00 equiv) and benzophenone imine (1093.09 mg, 6.032 mmol, 1.05 equiv) in dioxane (15 mL) was added Xantphos (332.37 mg, 0.574 mmol, 0.1 equiv), sodium *tert*-butoxide (1656.09 mg, 17.232 mmol, 3 equiv), and Pd₂(dba)₃ (262.99 mg, 0.288 mmol, 0.05 equiv) at 25 °C. The resulting solution was stirred for 2 hours at 80 °C. The resulting mixture was concentrated. The residue was purified by chromatography on silica gel eluted with petroleum ether/EtOAc (5:1) to afford 7-chloro-2-[(diphenylmethylidene)amino]-5-methylthieno[3,2-c]pyridin-4-one (1.6 g, 74%) as a dark yellow solid. LCMS (ESI) m/z: [M+H]⁺ = 379.

Step 3: Preparation of 2-amino-7-chloro-5-methylthieno[3,2-c]pyridin-4-one (i-13)

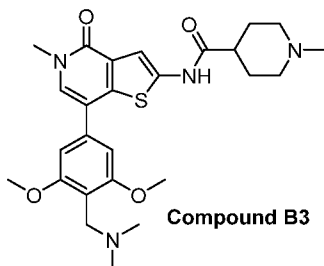
To a solution of 7-chloro-2-[(diphenylmethylidene)amino]-5-methylthieno[3,2-c]pyridin-4-one (1.60 g, 4.223 mmol, 1.00 equiv) in THF (10.00 mL) was added HCl (5.00 mL) at 25 °C. The resulting solution was stirred at 25 °C for 2 hours. The solvent was removed under reduced pressure. This resulted in 1.5 g (crude) of 2-amino-7-chloro-5-methylthieno [3,2-c]pyridin-4-one as a dark brown solid. The product was used in the next step directly without further purification. LCMS (ESI) m/z: [M+H]⁺ = 215.

Step 4: Preparation of *N*-[7-chloro-5-methyl-4-oxothieno[3,2-*c*]pyridin-2-yl]-1-methylpiperidine-4-carboxamide (*i*-14)



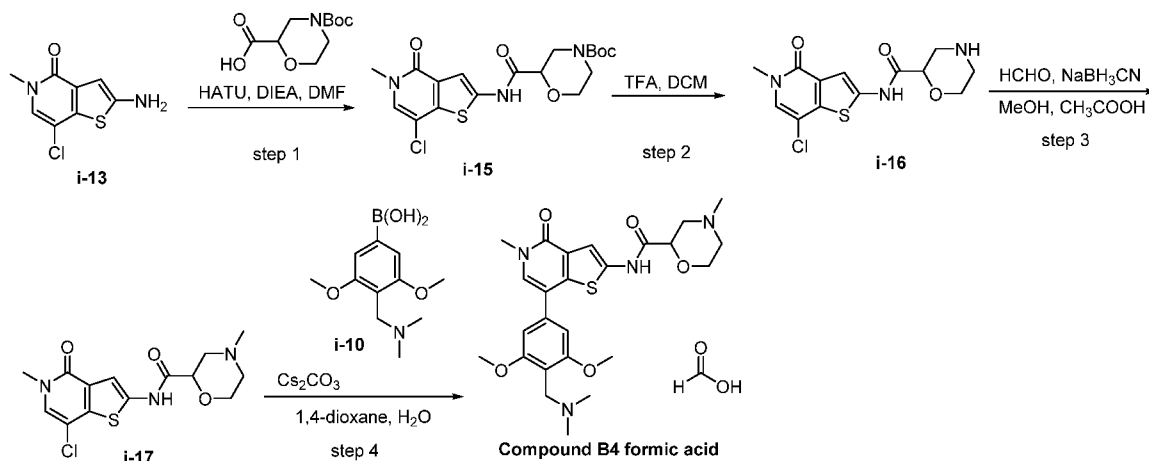
To a solution of 1-methylpiperidine-4-carboxylic acid (80.04 mg, 0.559 mmol, 1.20 equiv) and HATU (354.25 mg, 0.932 mmol, 2.00 equiv) in DMF (1.00 mL) was added 2-amino-7-chloro-5-methylthieno[3,2-*c*]pyridin-4-one (100.00 mg, 0.466 mmol, 1.00 equiv) and DIEA (180.62 mg, 1.397 mmol, 3.00 equiv), the resulting solution was stirred at 25 degree for 2 hours. The resulting mixture was concentrated. The residue was applied onto a silica gel column with CH₂Cl₂/MeOH (20:1). This resulted in (80 mg, 51%) of *N*-[7-chloro-5-methyl-4-oxothieno[3,2-*c*]pyridin-2-yl]-1-methylpiperidine-4-carboxamide as a yellow solid. LCMS (ESI) *m/z*: [M+H]⁺ = 340.10

Step 5: Preparation of *N*-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxo-4*H*,5*H*-thieno[3,2-*c*]pyridin-2-yl)-1-methylpiperidine-4-carboxamide (Compound B3)



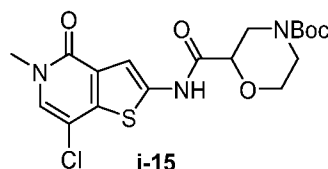
To a solution of *N*-[7-chloro-5-methyl-4-oxo-4*H*,5*H*-thieno[3,2-*c*]pyridin-2-yl]-1-methylpiperidine-4-carboxamide (60.00 mg, 0.177 mmol, 1.00 equiv) and [4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]boronic acid (50.65 mg, 0.212 mmol, 1.20 equiv) in H₂O (1.00 mL) and dioxane (3.00 mL) was added Cs₂CO₃ (172.57 mg, 0.530 mmol, 3.00 equiv) and Pd(dppf)Cl₂·CH₂Cl₂ (12.92 mg, 0.018 mmol, 0.10 equiv). The resulting solution was stirred at 80 °C for 2 hours (under N₂ atmosphere). The crude product was purified by preparative HPLC (conditions: XSelect CSH Prep C18 OBD Column, 19*150 mm; Mobile Phase A: Water (0.1% FA), Mobile Phase B: ACN; Flow rate: 25 mL/minute; Gradient: 20% B to 55% B in 8 minutes; 254 nm; R_T: 7.12 minutes). Fractions containing the desired compound were evaporated to dryness to afford *N*-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxo-4*H*,5*H*-thieno[3,2-*c*]pyridin-2-yl)-1-methylpiperidine-4-carboxamide (32 mg, 36%) as a white solid. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.68 (s, 1H), 7.23 (s, 1H), 7.06 (s, 2H), 4.42 (s, 2H), 4.02 (s, 6H), 3.75 (s, 3H), 3.64 (d, *J* = 12.6 Hz, 2H), 3.16 – 3.06 (m, 2H), 2.92 (d, *J* = 1.0 Hz, 9H), 2.82 – 2.71 (m, 1H), 2.21 (d, *J* = 14.5 Hz, 2H), 2.10 – 1.94 (m, 2H). LCMS (ESI) *m/z*: [M+H]⁺ = 499.30.

Example 10— Preparation of N-(7-[4-[(Dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridin-2-yl)-4-methylmorpholine-2-carboxamide formic acid (Compound B4 formic acid)



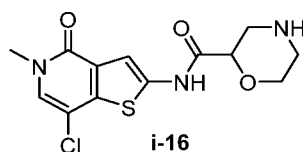
5

Step 1: Preparation of tert-butyl 2-([7-chloro-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl]carbamoyl)morpholine-4-carboxylate (i-15)



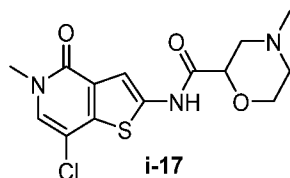
To a solution of 2-amino-7-chloro-5-methylthieno[3,2-c]pyridin-4-one (507.00 mg, 2.362 mmol, 1.00 equiv) and 4-(*tert*-butoxycarbonyl)morpholine-2-carboxylic acid (710.00 mg, 3.070 mmol, 1.3 equiv) in DMF (6 mL) was added HATU (1796.03 mg, 4.724 mmol, 2 equiv) and DIEA (1220.97 mg, 9.447 mmol, 4 equiv) at 25 °C. The resulting solution was stirred at 25 °C for 2 hours. The resulting mixture was concentrated. The residue was purified by chromatography on silica gel eluted with petroleum ether/EtOAc (2:1) to afford *tert*-butyl 2-([7-chloro-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl]carbamoyl)morpholine-4-carboxylate (820 mg, 81%) as a brown solid. LCMS (ESI) *m/z*: [M+H]⁺ = 428.

Step 2: Preparation of N-[7-chloro-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl]morpholine-2-carboxamide (i-16)



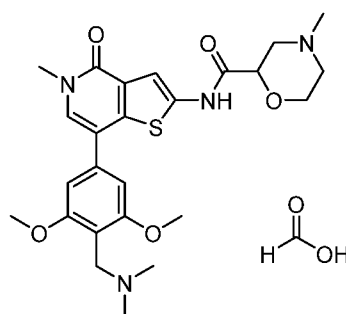
To a solution of *tert*-butyl 2-([7-chloro-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl]carbamoyl)morpholine-4-carboxylate (800.00 mg, 1.870 mmol, 1.00 equiv) in DCM (6.00 mL) was added TFA (2.00 mL) at 25 °C. The resulting solution was stirred at 25 °C for 2 hours. The solvent was removed under reduced pressure. This resulted in 1 g (crude) of *N*-[7-chloro-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl]morpholine-2-carboxamide as a dark brown solid. The product was used in the next step directly without further purification. LCMS (ESI) *m/z*: [M+H]⁺ = 328.

Step 3: Preparation of *N*-[7-chloro-5-methyl-4-oxothieno[3,2-*c*]pyridin-2-yl]-4-methylmorpholine-2-carboxamide (*i*-17)



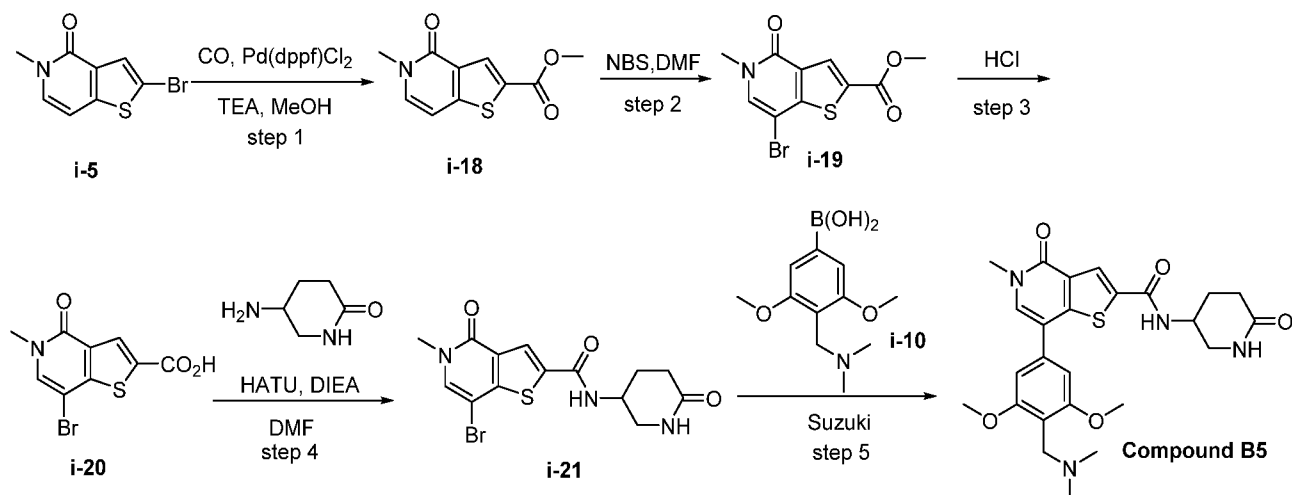
To a solution of *N*-[7-chloro-5-methyl-4-oxothieno[3,2-*c*]pyridin-2-yl]-4-methylmorpholine-2-carboxamide (1.00 g, 3.051 mmol, 1.00 equiv) in HCHO (4.00 mL) and MeOH (10.00 mL) was added NaBH₃CN (0.38 g, 0.006 mmol, 2 equiv) and CH₃COOH (0.50 mL, 8.726 mmol, 2.86 equiv) at 25 °C. The resulting solution was stirred at 25 °C for 4 hours. The resulting mixture was concentrated. The residue was purified by chromatography on silica gel eluted with petroleum ether/EtOAc (1:1) to afford *N*-[7-chloro-5-methyl-4-oxothieno[3,2-*c*]pyridin-2-yl]-4-methylmorpholine-2-carboxamide (284 mg, 27%) as a brown solid. LCMS (ESI) *m/z*: [M+H]⁺ = 342.

Step 4: Preparation of *N*-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxo-4*H*,5*H*-thieno[3,2-*c*]pyridin-2-yl)-4-methylmorpholine-2-carboxamide formic acid (Compound B4 formic acid)

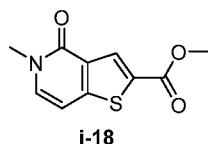


To a solution of *N*-[7-chloro-5-methyl-4-oxo-4*H*,5*H*-thieno[3,2-*c*]pyridin-2-yl]-4-methylmorpholine-2-carboxamide (100 mg, 0.293 mmol, 1.00 equiv) and [4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]boronic acid (104.92 mg, 0.439 mmol, 1.5 equiv) in H₂O (1 mL) and dioxane (4 mL) was added Cs₂CO₃ (190.64 mg, 0.585 mmol, 2 equiv) and XPhos palladium(II) biphenyl-2-amine chloride (23.02 mg, 0.029 mmol, 0.10 equiv) at 25 °C. The resulting solution was stirred at 90 °C for 12 hours. The crude product was purified by Prep-HPLC (conditions: SunFire Prep C18 OBD Column 19×150 mm 10 nm; Mobile Phase A: Water (0.1% FA), Mobile Phase B: ACN; Flow rate: 25 mL/minute; Gradient: 3% B to 3% B in 2 minutes; 254/220 nm; R_t: 7.5 minutes) to afford *N*-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxo-4*H*,5*H*-thieno[3,2-*c*]pyridin-2-yl)-4-methylmorpholine-2-carboxamide; formic acid (31.7 mg, 20%) as a light brown solid. ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.46 (s, 1H), 7.67 (s, 1H), 7.39 (d, *J* = 0.9 Hz, 1H), 7.06 (d, *J* = 1.1 Hz, 2H), 4.41 (s, 2H), 4.27 (dd, *J* = 10.3, 2.8 Hz, 1H), 4.14 – 4.01 (m, 1H), 4.02 (s, 6H), 3.79 (td, *J* = 11.4, 2.5 Hz, 1H), 3.74 (s, 3H), 3.12 (d, *J* = 11.7 Hz, 1H), 2.91 (s, 6H), 2.77 (d, *J* = 11.9 Hz, 1H), 2.38 (s, 3H), 2.28 (t, *J* = 11.6 Hz, 1H), 2.17 (t, *J* = 10.9 Hz, 1H). LCMS (ESI) *m/z*: [M+H]⁺ = 501.35.

Example 11– Preparation of 7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxo-N-(6-oxopiperidin-3-yl)-4H,5H-thieno[3,2-c]pyridine-2-carboxamide (Compound B5)

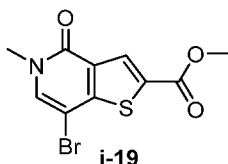


Step 1: Preparation of methyl 5-methyl-4-oxo-4,5-dihydrothieno[3,2-c]pyridine-2-carboxylate (i-18)



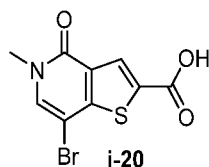
To a mixture of 2-bromo-5-methylthieno[3,2-c]pyridin-4-one (2.44 g, 9.996 mmol, 1.00 equiv) and Pd(dppf)Cl₂•CH₂Cl₂ (0.82 g, 1.00 mmol, 0.100 equiv) in MeOH (20.00 mL) was added TEA (2.78 mL, 27.460 mmol, 2.00 equiv). The resulting mixture was stirred at 100 °C for 16 hours under CO atmosphere (50 atm). Then the mixture was concentrated under reduced pressure, and the resulting residue was purified by flash silica chromatography, elution gradient 0 to 70% EtOAc in petroleum ether to give methyl 5-methyl-4-oxo-4,5-dihydrothieno[3,2-c]pyridine-2-carboxylate (1.81 g, 81%) as a yellow solid. LCMS (ESI) m/z: [M+H]⁺ = 224.

Step 2: Preparation of methyl 7-bromo-5-methyl-4-oxo-4,5-dihydrothieno[3,2-c]pyridine-2-carboxylate (i-19)



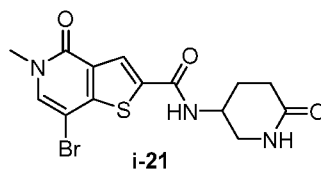
To a stirred mixture of methyl 5-methyl-4-oxothieno[3,2-c]pyridine-2-carboxylate (1.80 g, 8.063 mmol, 1.00 equiv) in DMF (30 mL) was added NBS (1.58 g, 8.869 mmol, 1.10 equiv). The resulting mixture was stirred at room temperature for 1 hour under nitrogen atmosphere. The mixture was then diluted with water (100 mL) and extracted with EtOAc (300 mL x 3). The organic layers were combined and dried over anhydrous Na₂SO₄, filtered, and concentrated to give methyl 7-bromo-5-methyl-4-oxo-4,5-dihydrothieno[3,2-c]pyridine-2-carboxylate (2.43 g, crude) as a yellow solid. This material was used directly in the next step without further purification. LCMS (ESI) m/z: [M+H]⁺ = 302.

Step 3: Preparation of 7-bromo-5-methyl-4-oxo-4,5-dihydrothieno[3,2-c]pyridine-2-carboxylic acid (i-20)



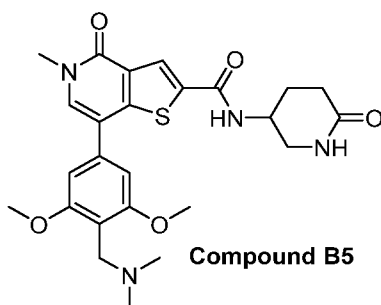
Into a sealed tube was added methyl 7-bromo-5-methyl-4-oxothieno[3,2-c]pyridine-2-carboxylate (2.43 g, 8.05 mmol, 1.00 equiv) and concentrated hydrochloric acid (40 mL). The mixture was stirred for 4 hours at 90 °C. The resulting mixture was concentrated to give 7-bromo-5-methyl-4-oxo-4,5-dihydrothieno[3,2-c]pyridine-2-carboxylic acid (2.20 g, 95%) as a brown solid. This material was used directly in the next step without further purification. LCMS (ESI) m/z : $[M+H]^+ = 288$.

Step 4: Preparation of 7-bromo-5-methyl-4-oxo-N-(6-oxopiperidin-3-yl)thieno[3,2-c]pyridine-2-carboxamide (i-21)



To a solution of 7-bromo-5-methyl-4-oxothieno[3,2-c]pyridine-2-carboxylic acid (50.00 mg, 0.174 mmol, 1.00 equiv) and HATU (131.97 mg, 0.347 mmol, 2.00 equiv) in DMF (1.00 mL) was added 5-aminopiperidin-2-one (21.79 mg, 0.191 mmol, 1.10 equiv) and DIEA (67.29 mg, 0.521 mmol, 3.00 equiv). The resulting solution was stirred at 25 °C for 2 hours. The resulting mixture was concentrated. The residue was applied onto a silica gel column with $CH_2Cl_2/MeOH$ (20:1) to afford 7-bromo-5-methyl-4-oxo-N-(6-oxopiperidin-3-yl)thieno[3,2-c]pyridine-2-carboxamide (42 mg, 63%) as a yellow solid. LCMS (ESI) m/z : $[M+H]^+ = 386.01$.

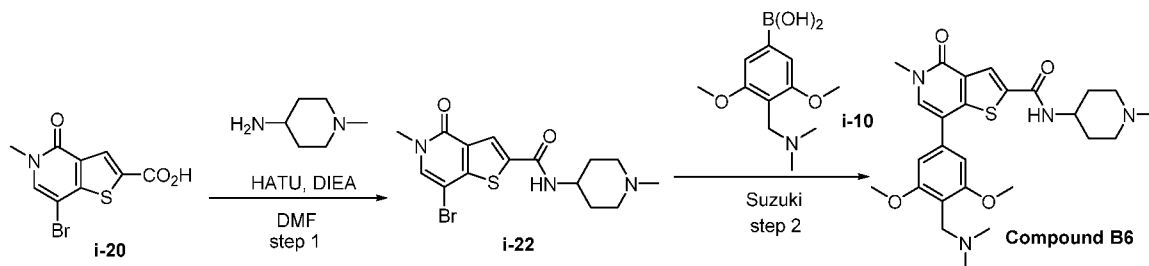
Step 5: Preparation of 7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxo-N-(6-oxopiperidin-3-yl)-4H,5H-thieno[3,2-c]pyridine-2-carboxamide (Compound B5)



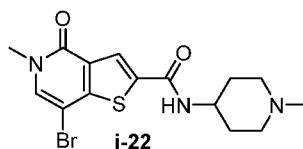
To a solution of 7-bromo-5-methyl-4-oxo-N-(6-oxopiperidin-3-yl)-4H,5H-thieno[3,2-c]pyridine-2-carboxamide (30.00 mg, 0.078 mmol, 1.00 equiv) and [4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]boronic acid (22.40 mg, 0.094 mmol, 1.20 equiv) in H_2O (1.00 mL) and dioxane (3.00 mL) was added Cs_2CO_3 (76.31 mg, 0.234 mmol, 3.00 equiv) and $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (6.38 mg, 0.008 mmol, 0.10 equiv). The resulting solution was stirred at 80 °C for 2 hours (under N_2 atmosphere). The crude product was purified by preparative HPLC (conditions: XSelect CSH Prep C18 OBD Column, 5 μm , 19*150 mm; Mobile Phase A: Water (0.1% FA), Mobile Phase B: ACN; Flow rate: 25 mL/minute; Gradient: 20% B to

55% B in 8 minutes; 254 nm; R_T : 7.12 minutes). Fractions containing the desired compound were evaporated to dryness to afford 7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxo-*N*-(6-oxopiperidin-3-yl)-4*H*,5*H*-thieno[3,2-*c*]pyridine-2-carboxamide (28 mg, 72%) as a white solid. ^1H NMR (400 MHz, Methanol-*d*4) δ 8.57 (s, 1H, FA), 8.28 (s, 1H), 7.86 (s, 1H), 7.06 (s, 2H), 4.37 (s, 2H), 4.37 – 4.30 (m, 1H), 4.02 (s, 6H), 3.75 (s, 3H), 3.58 (dd, J = 12.0, 4.9 Hz, 1H), 3.30 – 3.26 (m, 1H), 2.88 (s, 6H), 2.55 – 2.47 (m, 2H), 2.19 – 2.01 (m, 2H). LCMS (ESI) m/z : $[\text{M}+\text{H}]^+ = 499.35$.

Example 12 – Preparation of 7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-*N*-(1-methylpiperidin-4-yl)-4-oxo-4*H*,5*H*-thieno[3,2-*c*]pyridine-2-carboxamide (Compound B6)

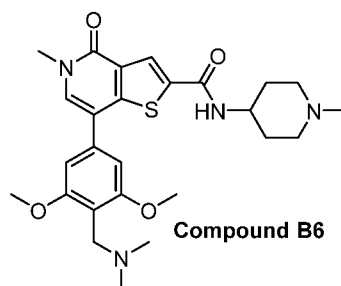


*Step 1: Preparation of 7-bromo-5-methyl-*N*-(1-methylpiperidin-4-yl)-4-oxo-4*H*,5*H*-thieno[3,2-*c*]pyridine-2-carboxamide (i-22)*



To a solution of 7-bromo-5-methyl-4-oxo-4*H*,5*H*-thieno[3,2-*c*]pyridine-2-carboxylic acid (50.00 mg, 0.174 mmol, 1.00 equiv) and HATU (131.97 mg, 0.347 mmol, 2.00 equiv) in DMF (1.00 mL) was added 1-methylpiperidin-4-amine (21.80 mg, 0.191 mmol, 1.10 equiv) and DIEA (67.29 mg, 0.521 mmol, 3.00 equiv). The resulting solution was stirred at 25 °C for 2 hours. The resulting mixture was concentrated. The residue was applied onto a silica gel column with $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (20:1). This resulted in (45 mg, 68%) of 7-bromo-5-methyl-*N*-(1-methylpiperidin-4-yl)-4-oxo-4*H*,5*H*-thieno[3,2-*c*]pyridine-2-carboxamide as a yellow solid. LCMS (ESI) m/z : $[\text{M}+\text{H}]^+ = 384.01$.

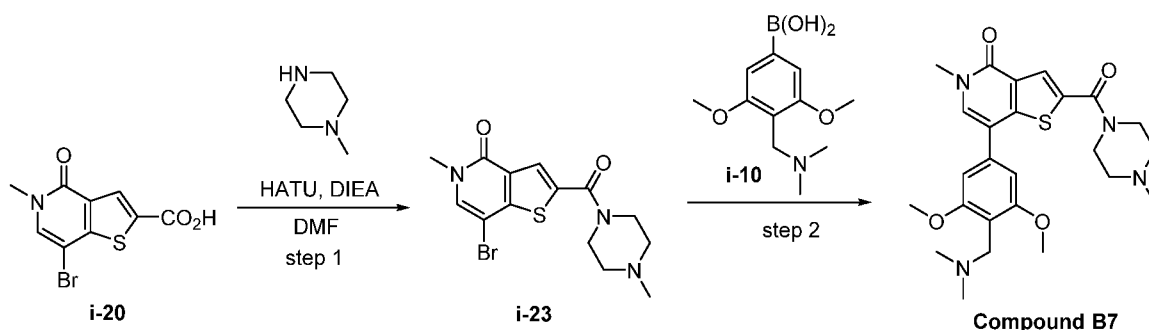
*Step 2: Preparation of 7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-*N*-(1-methylpiperidin-4-yl)-4-oxo-4*H*,5*H*-thieno[3,2-*c*]pyridine-2-carboxamide (Compound B6)*



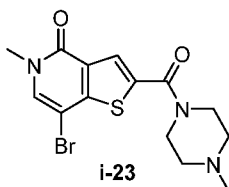
To a solution of 7-bromo-5-methyl-*N*-(1-methylpiperidin-4-yl)-4-oxo-4*H*,5*H*-thieno[3,2-*c*]pyridine-2-carboxamide (30.00 mg, 0.078 mmol, 1.00 equiv) and [4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]boronic acid (22.40 mg, 0.094 mmol, 1.20 equiv) in H_2O (1.00 mL) and dioxane (3.00 mL) was added Cs_2CO_3 (76.31 mg, 0.234 mmol, 3.00 equiv) and $\text{Pd}(\text{dppf})\text{Cl}_2 \cdot \text{CH}_2\text{Cl}_2$ (6.38 mg, 0.008

mmol, 0.10 equiv). The resulting solution was stirred at 80 °C for 2 hours (under N₂ atmosphere). The crude product was purified by preparative HPLC (conditions: XSelect CSH Prep C18 OBD Column, 5 µm, 19*150 mm; Mobile Phase A: Water (0.1% FA), Mobile Phase B: ACN; Flow rate: 25 mL/minute; Gradient: 20% B to 55% B in 8 minutes; 254 nm; R_t: 7.12 minutes). Fractions containing the desired compound were evaporated to dryness to afford 7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-*N*-(1-methylpiperidin-4-yl)-4-oxo-4*H*,5*H*-thieno[3,2-*c*]pyridine-2-carboxamide (21 mg, 54%) as a white solid. ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.52 (s, 1H, FA), 8.26 (s, 1H), 7.86 (s, 1H), 7.07 (s, 2H), 4.40 (s, 2H), 4.02 (s, 7H), 3.75 (s, 3H), 3.27 (d, *J*=11.2 Hz, 2H), 2.90 (s, 6H), 2.79 – 2.67 (m, 2H), 2.62 (s, 3H), 2.12 (d, *J*=13.4 Hz, 2H), 1.94 – 1.79 (m, 2H). LCMS (ESI) *m/z*: [M+H]⁺ = 499.25.

Example 13 - Preparation of 7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-2-(4-methylpiperazine-1-carbonyl)-4*H*,5*H*-thieno[3,2-*c*]pyridin-4-one (Compound B7)

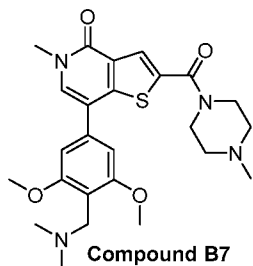


*Step 1: Preparation of 7-bromo-5-methyl-2-(4-methylpiperazine-1-carbonyl)thieno[3,2-*c*]pyridin-4-one (i-23)*



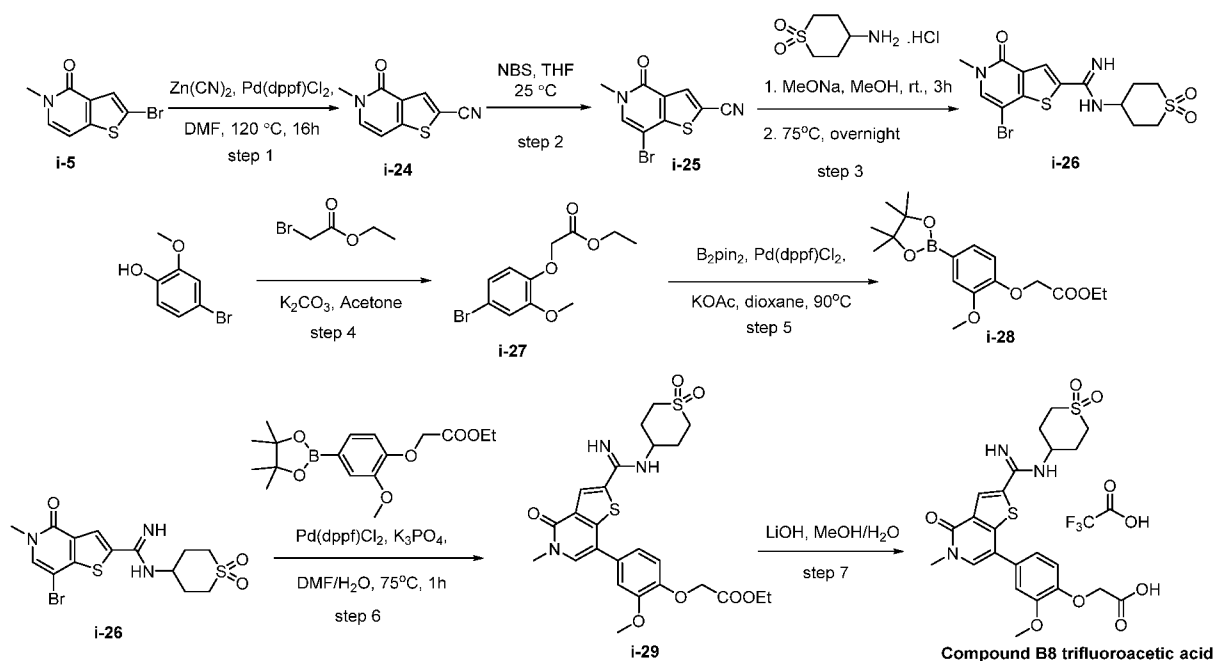
To a solution of 7-bromo-5-methyl-4-oxothieno[3,2-*c*]pyridine-2-carboxylic acid (150.00 mg, 0.521 mmol, 1.00 equiv), HATU (296.93 mg, 0.781 mmol, 1.50 equiv) and DIEA (134.57 mg, 1.041 mmol, 2.00 equiv) in DMF (10.00 mL). The resulting mixture was stirred for 10 minutes at 25 °C. Then 1-methylpiperazine (62.58 mg, 0.625 mmol, 1.20 equiv) was added to the reaction mixture. The resulting solution was stirred for 2 hours at 25 °C. The resulting mixture was concentrated. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:1). This resulted in 80 mg (42%) of 7-bromo-5-methyl-2-(4-methylpiperazine-1-carbonyl)thieno[3,2-*c*]pyridin-4-one as a yellow solid.

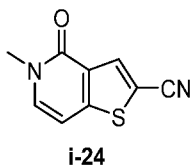
Step 2: Preparation of 7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-2-(4-methylpiperazine-1-carbonyl)-4H,5H-thieno[3,2-c]pyridin-4-one (Compound B7)



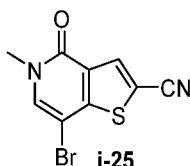
To a solution of 7-bromo-5-methyl-2-(4-methylpiperazine-1-carbonyl)-4H,5H-thieno[3,2-c]pyridin-4-one (100.00 mg, 0.270 mmol, 1.00 equiv) and Cs_2CO_3 (263.99 mg, 0.810 mmol, 3.00 equiv) in 1,4-dioxane (5.00 mL) was added [4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]boronic acid (64.57 mg, 0.270 mmol, 1.00 equiv), $\text{Pd}(\text{dppf})\text{Cl}_2 \cdot \text{CH}_2\text{Cl}_2$ (22.06 mg, 0.027 mmol, 0.10 equiv), and H_2O (1.00 mL). The resulting solution was stirred for 2 hours at 80 °C. The resulting solution was diluted with 10 mL of water. The resulting solution was extracted with ethyl acetate (3 x 10 mL) and the organic layers combined and dried over anhydrous sodium sulfate and concentrated. The crude product was purified by Prep-HPLC (conditions: 2#SHIMADZU (HPLC-01); SunFire C18 OBD Prep Column, 19 mm X 250 mm; mobile phase: Water (0.1% FA, formic acid) and ACN (hold 5% PhaseB in 2 minutes, up to 12% in 10 minutes); UV Detector). This resulted in 5.3 mg (4.1%) of 7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-2-(4-methylpiperazine-1-carbonyl)-4H,5H-thieno[3,2-c]pyridin-4-one as a brown semi-solid. ^1H NMR (400 MHz, Methanol- d_4) δ 8.45 (s, 2H, FA), 7.93 (s, 1H), 7.87 (s, 1H), 7.06 (s, 2H), 4.41 (s, 2H), 4.01 (s, 6H), 3.97 – 3.85 (m, 4H), 3.75 (s, 3H), 2.91 (s, 6H), 2.75 – 2.64 (m, 4H), 2.45 (s, 3H); LCMS (ESI) m/z : $[\text{M}+\text{H}]^+ = 485.20$.

Example 14 – Preparation of 2-[4-[2-[N-(1,1-dioxo-1 λ 6-thian-4-yl)carbamimidoyl]-5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridin-7-yl]-2-methoxyphenoxy]acetic acid trifluoroacetic acid (Compound B8 trifluoroacetic acid)

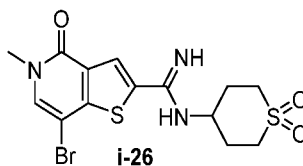


Step 1 Preparation of 5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridine-2-carbonitrile (i-24)

To a solution of 2-bromo-5-methyl-4H,5H-thieno[3,2-c]pyridin-4-one (500.00 mg, 2.048 mmol, 1.00 equiv) and $\text{Zn}(\text{CN})_2$ (529.22 mg, 4.506 mmol, 2.20 equiv) in DMF (20.00 mL) was added $\text{Pd}(\text{dppf})\text{Cl}_2$ (149.87 mg, 0.205 mmol, 0.10 equiv). The resulting mixture was stirred at 120 °C for 16 hours under N_2 atmosphere. Fifteen identical reactions were set up in 15 sealed tubes in parallel. The reaction mixtures were combined and diluted with EA (500 mL). The resulting mixture was washed with water (3 x 300 mL) and saturated brine (300 mL). The organic layer was dried over Na_2SO_4 , filtered, and evaporated to afford crude product. The crude product was purified by flash silica chromatography, elution gradient 0 to 100% EtOAc in petroleum ether. Pure fractions were evaporated to dryness to afford 5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridine-2-carbonitrile (4.4 g, 75%) as a black solid.

Step 2: Preparation of 7-bromo-5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridine-2-carbonitrile (i-25)

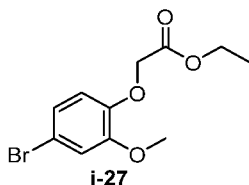
To a solution of 5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridine-2-carbonitrile (4.40 g, 23.131 mmol, 1.00 equiv) in THF (50.00 mL) was added NBS (6.18 g, 34.697 mmol, 1.50 equiv). The resulting mixture was stirred at room temperature for 16 hours. The reaction mixture was diluted with EA (400 mL). The resulting mixture was washed with water (3 x 200 mL) and saturated brine (300 mL). The organic layer was dried over Na_2SO_4 , filtered, and evaporated to afford crude product. The crude product was purified by flash silica chromatography, elution gradient 0 to 100% EtOAc in petroleum ether. Pure fractions were evaporated to dryness to afford 7-bromo-5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridine-2-carbonitrile (3.5 g, 56%) as a brown solid.

Step 3: Preparation of 7-bromo-N-(1,1-dioxo-1λ6-thian-4-yl)-5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridine-2-carboximidamide (i-26)

To a solution of 7-bromo-5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridine-2-carbonitrile (3 g, 11.147 mmol, 1.00 equiv) in MeOH (45.00 mL, 11.451 mmol, 99.70 equiv) was added MeONa (2.00 g, 11.147 mmol, 1 equiv) solution in MeOH (30% by weight). The reaction mixture was heated to 75 °C for 3 hours. Then 4-amino-1λ6-thiane-1,1-dione hydrochloride (2.48 g, 0.013 mmol, 1.2 equiv) was added at 75 °C, and the reaction mixture was stirred for a further 16 hours. The volatile components were removed in vacuo, and the resulting solid was suspended in MeOH (50 mL), filtered under reduced

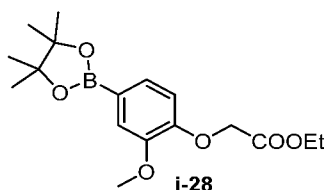
pressure, and washed with MeOH (20 mL) to afford 7-bromo-N-(1,1-dioxo-1λ6-thian-4-yl)-5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridine-2-carboximidamide (3.0 g, 64%) as a brown solid.

Step 4: Preparation of ethyl 2-(4-bromo-2-methoxyphenoxy)acetate (i-27)



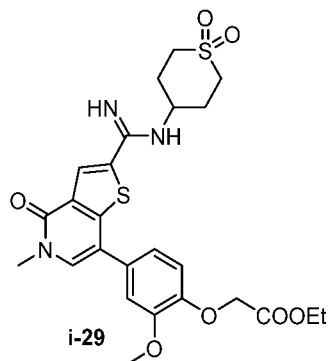
To a solution of 4-bromo-2-methoxyphenol (5 g, 24.626 mmol, 1 equiv) and K_2CO_3 (6.81 g, 49.253 mmol, 2 equiv) in acetone (50 mL) was added ethyl 2-bromoacetate (4.94 g, 29.580 mmol, 1.20 equiv). The resulting mixture was stirred at room temperature for 16 hours. The reaction mixture was diluted with EA (500 mL), The resulting mixture was washed with water (3 x 300 mL) and saturated brine (300 mL). The organic layer was dried over Na_2SO_4 , filtered, and evaporated to afford crude product. The crude product was purified by flash silica chromatography, elution gradient 0 to 8% EtOAc in petroleum ether. Pure fractions were evaporated to dryness to afford ethyl 2-(4-bromo-2-methoxyphenoxy)acetate (4 g, 56%) as a yellow oil.

Step 5: Preparation of ethyl 2-[2-methoxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]acetate (i-28)



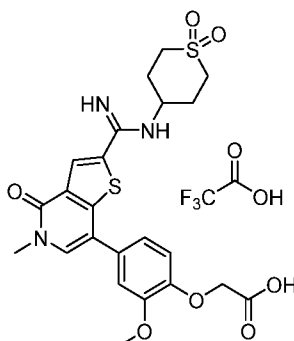
To a solution of ethyl 2-(4-bromo-2-methoxyphenoxy)acetate (6 g, 20.752 mmol, 1 equiv) and 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (6.32 g, 24.903 mmol, 1.2 equiv) in solvent dioxane (120 mL) was added KOAc (4.07 g, 41.505 mmol, 2 equiv) and $Pd(dppf)Cl_2$ (1.52 g, 2.075 mmol, 0.1 equiv). The resulting solution was stirred at 90 °C for 1 hour (under N_2 atmosphere). The resulting mixture was washed with water (3 x 300 mL). The organic phase was concentrated under reduced pressure. The residue was purified by flash silica chromatography, elution gradient 0 to 60% EtOAc in petroleum ether. Pure fractions were evaporated to dryness to afford ethyl 2-[2-methoxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]acetate (6.9 g, 98%) as a yellow oil.

Step 6: Preparation of ethyl 2-(4-[2-[N-(1,1-dioxo-1 λ 6-thian-4-yl)carbamimidoyl]-5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridin-7-yl]-2-methoxyphenoxy)acetate (i-29)



To a solution of 7-bromo-N-(1,1-dioxo-1 λ 6-thian-4-yl)-5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridine-2-carboximidamide (1.00 g, 2.391 mmol, 1.00 equiv), ethyl 2-[2-methoxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy]acetate (0.88 g, 2.630 mmol, 1.10 equiv), and K₃PO₄ (1.01 g, 4.781 mmol, 2.00 equiv) in water (2.00 mL) and DMF (20.00 mL) was added Pd(dppf)Cl₂ (0.17 g, 0.239 mmol, 0.10 equiv). The resulting mixture was stirred at 75 °C for 1 hour. The reaction mixture was diluted with EA (500 mL). The resulting mixture was washed with water (3 x 300 mL) and saturated brine (300 mL). The organic layer was dried over Na₂SO₄, filtered, and evaporated to afford crude product. The crude product was purified by flash silica chromatography, elution gradient 0 to 15% MeOH in DCM. Pure fractions were evaporated to dryness to afford ethyl 2-(4-[2-[N-(1,1-dioxo-1 λ 6-thian-4-yl)carbamimidoyl]-5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridin-7-yl]-2-methoxyphenoxy)acetate (860 mg, 66%) as a brown solid.

Step 7: Preparation of 2-(4-[2-[N-(1,1-dioxo-1 λ 6-thian-4-yl)carbamimidoyl]-5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridin-7-yl]-2-methoxyphenoxy)acetic acid trifluoroacetic acid (Compound B8 trifluoroacetic acid)



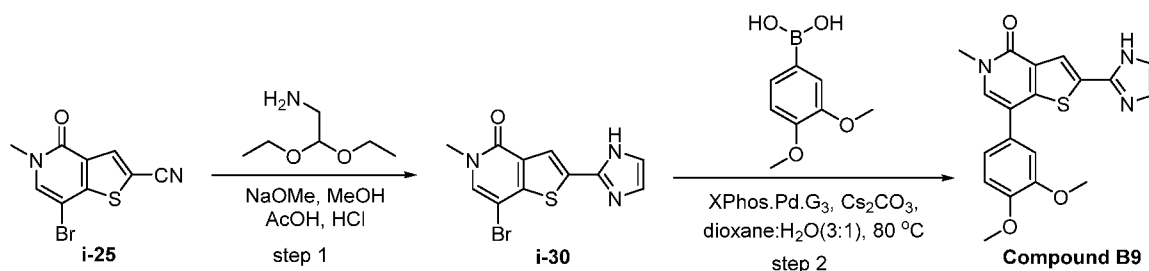
Compound B8 trifluoroacetic acid

To a solution of ethyl 2-(4-[2-[N-(1,1-dioxo-1 λ 6-thian-4-yl)carbamimidoyl]-5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridin-7-yl]-2-methoxyphenoxy)acetate (560 mg, 1.023 mmol, 1.00 equiv) in MeOH (25.00 mL) and H₂O (2.50 mL) was added LiOH·H₂O (429.48 mg, 10.226 mmol, 10.00 equiv). The resulting mixture was stirred at room temperature for 5 hours. The mixture was acidified to pH 2 with 1 N HCl (aq.). The crude product was purified by HPLC (conditions: XSelect CSH Prep C18 OBD Column, 5 μ m, 19*150mm; Mobile Phase A: Water (0.05% TFA), Mobile Phase B: ACN; Flow rate: 25 mL/minute; Gradient: 5% B to 22% B in 8 minutes; 254 nm; R_t: 5.68 minutes). Fractions containing the desired compound were evaporated to dryness to afford 2-(4-[2-[N-(1,1-dioxo-1 λ 6-thian-4-yl)carbamimidoyl]-5-

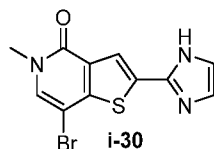
methyl-4-oxo-4H,5H-thieno[3,2-c]pyridin-7-yl]-2-methoxyphenoxy)acetic acid trifluoroacetic acid (330 mg, 49%) as a yellow solid. LCMS (ES, m/z): 520.20. ^1H NMR (400 MHz, DMSO- d_6) δ 9.73 (d, $J=8.1$ Hz, 1H), 9.65 (s, 1H), 9.34 (s, 1H), 8.55 (s, 1H), 7.99 (s, 1H), 7.25 – 7.12 (m, 2H), 7.02 (d, $J=8.4$ Hz, 1H), 4.76 (s, 2H), 4.01 (d, $J=8.9$ Hz, 1H), 3.87 (s, 3H), 3.63 (s, 3H), 3.30 – 3.15 (m, 4H). 2.28–2.15 (m, 4H).

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Example 15 – Preparation of 7-(3,4-dimethoxyphenyl)-2-(1H-imidazol-2-yl)-5-methyl-4H,5H-thieno[3,2-c]pyridine-4-one (Compound B9)



Step 1: Preparation of 7-bromo-2-(1H-imidazol-2-yl)-5-methyl-4H,5H-thieno[3,2-c]pyridine-4-one (i-30)

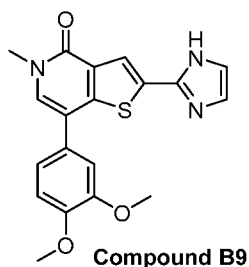


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To a solution of 7-bromo-5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridine-2-carbonitrile (50.00 mg, 0.186 mmol, 1.00 equiv) and NaOMe (100.37 mg, 1.858 mmol, 10.00 equiv) in MeOH (1.00 mL) was stirred for 3 hours at room temperature. To the above mixture was added AcOH (446.28 mg, 7.432 mmol, 40.00 equiv) and HCl (1.50 mL, 49.368 mmol, 265.72 equiv) at room temperature. The resulting mixture was stirred for additional 16 hours at 75 °C. The residue was dissolved in EtOAc (100 mL). The resulting mixture was washed with water (3 x 30 mL). The resulting mixture was concentrated under reduced pressure. The residue was purified by Prep-TLC (PE/EtOAc 5:1) to afford 7-bromo-2-(1H-imidazol-2-yl)-5-methyl-4H,5H-thieno[3,2-c]pyridine-4-one (30 mg, 52%) as a white solid. LCMS (ES, m/z): 310.0.

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Step 2: Preparation of 7-(3,4-dimethoxyphenyl)-2-(1H-imidazol-2-yl)-5-methyl-4H,5H-thieno[3,2-c]pyridine-4-one (Compound B9)



To a solution of 7-bromo-2-(1H-imidazol-2-yl)-5-methyl-4H,5H-thieno[3,2-c]pyridine-4-one (30.00 mg, 0.097 mmol, 1.00 equiv) and (3,4-dimethoxyphenyl)boronic acid (17.60 mg, 0.097 mmol, 1 equiv) in dioxane (1.50 mL) and H₂O (0.50 mL) was added Cs₂CO₃ (63.03 mg, 0.193 mmol, 2.00 equiv) and XPhos-Pd-G3 (16.37 mg, 0.019 mmol, 0.2 equiv). The resulting solution was stirred at 80 °C for 1 hour (under N₂ atmosphere). The crude product was purified by preparative HPLC (conditions: XBridge Shield

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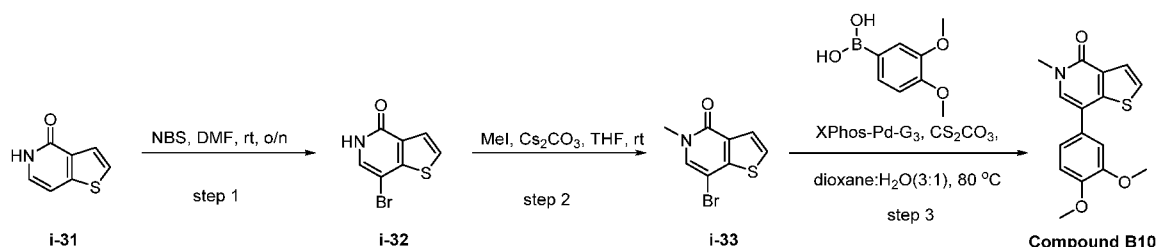
RP18 OBD Column, 5 μ m, 19*150mm; Mobile Phase A: Water (10 mmol/L NH_4HCO_3), Mobile Phase B: ACN; Flow rate: 25 mL/minute; Gradient: 25% B to 33% B in 8 minutes; 254 nm; R_T : 6.77 minutes).

Fractions containing the desired compound were evaporated to dryness to afford 7-(3,4-

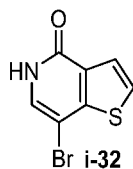
dimethoxyphenyl)-2-(1*H*-imidazol-2-yl)-5-methyl-4*H*,5*H*-thieno[3,2-*c*]pyridin-4-one (10.8 mg, 30%) as a

white solid. LCMS (ES, m/z): 368.1. $^1\text{H-NMR}$ (400 MHz, CD_3OD) δ 7.96 (s, 1H), 7.62 (s, 1H), 7.26 (m, J = 2.1 Hz, 1H), 7.24 (m, J = 8.1, 2.2 Hz, 1H), 7.17 (s, 2H), 7.11 (m, J = 8.1 Hz, 1H), 3.94 (s, 3H), 3.92 (s, 3H), 3.74 (s, 3H).

Example 16 – Preparation of 7-(3,4-dimethoxyphenyl)-5-methyl-4*H*,5*H*-thieno[3,2-*c*]pyridin-4-one (Compound B10)

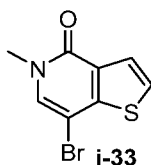


*Step 1: Preparation of 7-bromothieno[3,2-*c*]pyridin-4(5*H*)-one (i-32)*



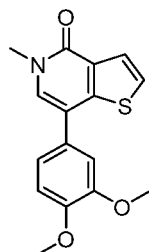
A solution of 4*H*,5*H*-thieno[3,2-*c*]pyridin-4-one (1 g, 6.615 mmol, 1 equiv) and NBS (1.41 g, 7.938 mmol, 1.2 equiv) in DMF (10 mL) was stirred for 16 hours at room temperature. The resulting solution was diluted with EtOAc. The resulting mixture was washed with water (3 x 50 mL). The resulting mixture was concentrated. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (30/70). Fractions containing the desired compound were evaporated to dryness to afford 7-bromo-4*H*,5*H*-thieno[3,2-*c*]pyridin-4-one (440.0 mg, 29%) as a purple solid. LCMS (ES, m/z): 230.0.

*Step 2: Preparation of 7-bromo-5-methyl-4H,5H-thieno[3,2-*c*]pyridin-4-one (i-33)*



To a solution of 7-bromo-4*H*,5*H*-thieno[3,2-*c*]pyridin-4-one (200.00 mg, 0.869 mmol, 1.00 equiv) and Cs_2CO_3 (849.67 mg, 2.608 mmol, 3 equiv) in THF (10.00 mL) was added MeI (246.76 mg, 1.739 mmol, 2 equiv) at room temperature. The resulting mixture was stirred for 2 hours at room temperature. The resulting mixture was concentrated under reduced pressure. The residue was purified by Prep-TLC (hexane/ EtOAc 5:1) to afford 7-bromo-5-methyl-4*H*,5*H*-thieno[3,2-*c*]pyridin-4-one (200mg, 94%) as a brown solid. LCMS (ES, m/z): 244.0.

Step 3: Preparation of 7-(3,4-dimethoxyphenyl)-5-methyl-4H,5H-thieno[3,2-c]pyridin-4-one (Compound B10)

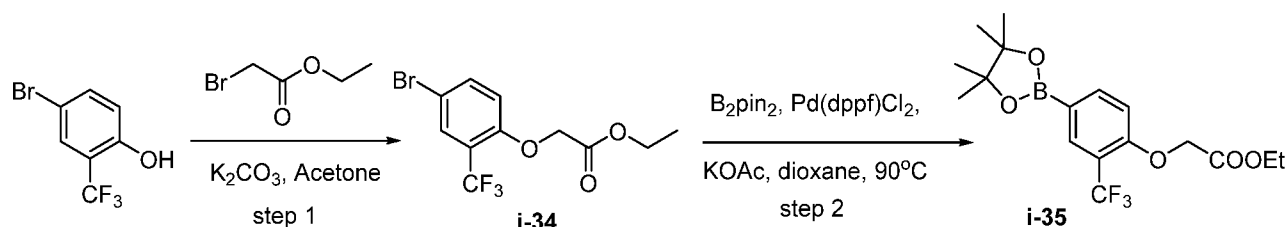


Compound B10

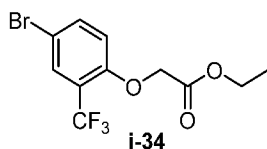
To a solution of 7-bromo-5-methyl-4H,5H-thieno[3,2-c]pyridin-4-one (100.00 mg, 0.410 mmol, 1.00 equiv) and (3,4-dimethoxyphenyl)boronic acid (74.55 mg, 0.410 mmol, 1 equiv) in solvent H₂O (1.00 mL) and dioxane (3.00 mL) was added Cs₂CO₃ (266.95 mg, 0.819 mmol, 2 equiv) and XPhos-Pd-G3 (69.35 mg, 0.082 mmol, 0.2 equiv). The resulting solution was stirred at 80 °C for 1 hour (under N₂ atmosphere). The crude product was purified by preparative HPLC (conditions: XSelect CSH Prep C18 OBD Column, 5 µm, 19*150mm; Mobile Phase A: Water (0.1% FA), Mobile Phase B: ACN; Flow rate: 25 mL/minute; Gradient: 20% B to 55% B in 8 minutes; 254 nm; R_T: 7.12 minutes). Fractions containing the desired compound were evaporated to dryness to afford 7-(3,4-dimethoxyphenyl)-5-methyl-4H,5H-thieno[3,2-c]pyridin-4-one (60.1 mg, 48%) as a white solid. LCMS (ES, *m/z*): 302. ¹H NMR (400 MHz, DMSO) δ 7.72 (s, 1H), 7.66 (d, *J* = 5.4 Hz, 1H), 7.58 (d, *J* = 5.4 Hz, 1H), 7.22-7.15 (m, 2H), 7.09 (d, *J* = 8.1 Hz, 1H), 3.83 (d, *J* = 6.4 Hz, 6H), 3.60 (s, 3H).

Example 17 – Preparation of Intermediates

Preparation of Ethyl 2-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)phenoxy]acetate (i-35)

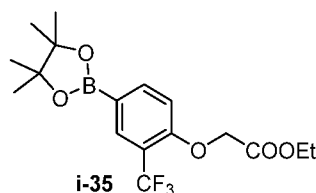


Step 1: Preparation of Ethyl 2-[4-bromo-2-(trifluoromethyl)phenoxy]acetate (i-34)



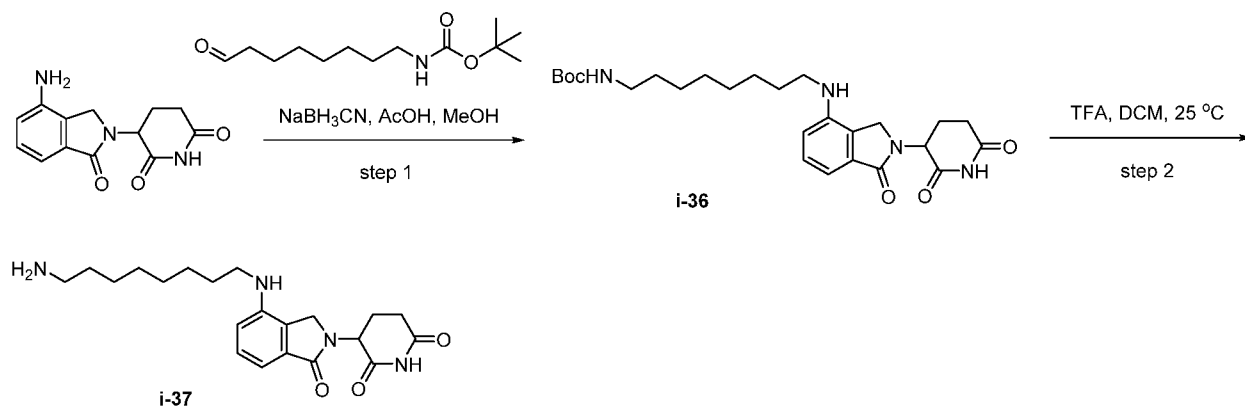
To a solution of 4-bromo-2-(trifluoromethyl)phenol (5 g, 20.746 mmol, 1 equiv) and K₂CO₃ (5.73 g, 41.493 mmol, 2 equiv) in acetone (50 mL) was added ethyl 2-bromoacetate (5.20 g, 31.119 mmol, 1.5 equiv) at room temperature. The resulting mixture was stirred for 1 hour at room temperature. The solid was then filtered off, the filtrate was concentrated, and the residue was purified by silica gel column chromatography, eluted with PE / EtOAc (5:1) to afford ethyl 2-[4-bromo-2-(trifluoromethyl)phenoxy]acetate (6.5 g, 96%) as a white solid. LCMS (ESI) *m/z*: [M+H]⁺ = 327.

Step 2: Preparation of Ethyl 2-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)phenoxy]acetate (i-35)

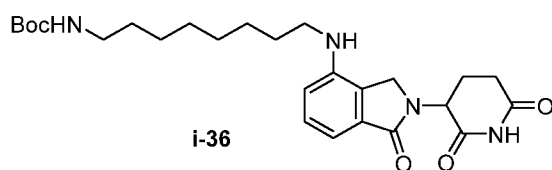


To a solution of ethyl 2-[4-bromo-2-(trifluoromethyl)phenoxy]acetate (1 g, 3.057 mmol, 1 equiv) and 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (931.6 mg, 3.669 mmol, 1.2 equiv) in dioxane (10 mL) was added KOAc (0.60 g, 6.114 mmol, 2.00 equiv) and Pd(dppf)Cl₂ (223.7 mg, 0.306 mmol, 0.1 equiv). The resulting mixture was stirred for 1 h at 90 °C under a nitrogen atmosphere. The mixture was concentrated and the residue was purified by silica gel column chromatography, eluted with PE / EtOAc (5 : 1) to afford ethyl 2-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)phenoxy]acetate (800 mg, 70%) as a yellow oil. LCMS (ESI) m/z: [M+H]⁺ = 375.

Preparation of tert-butyl N-(8-[[2-(2,6-dioxopiperidin-3-yl)-1-oxo-2,3-dihydro-1H-isoindol-4-yl]amino]octyl)carbamate (i-37)

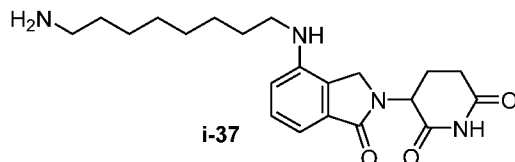


Step 1: Preparation of tert-butyl (8-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindolin-4-yl)amino)octyl)carbamate (i-36)



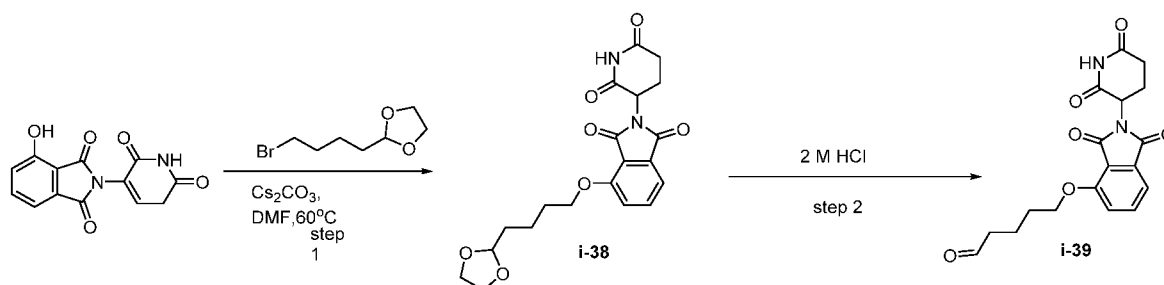
To a solution of 3-(4-amino-1-oxo-2,3-dihydro-1H-isoindol-2-yl)piperidine-2,6-dione (200 mg, 0.773 mmol, 1 equiv) and tert-butyl N-(8-oxooctyl)carbamate (225.31 mg, 0.927 mmol, 1.2 equiv) in MeOH (10 mL) was added NaBH₃CN (145.41 mg, 2.319 mmol, 3 equiv) and AcOH (0.5 mL). The resulting solution was stirred at 25 °C for 1 hour. The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (5:1) to afford tert-butyl N-(8-[[2-(2,6-dioxopiperidin-3-yl)-1-oxo-2,3-dihydro-1H-isoindol-4-yl]amino]octyl)carbamate (202 mg, 62%) as an off-white solid. LCMS (ESI) m/z: [M+H]⁺ = 487.

Step 2: Preparation of *tert*-butyl *N*-(8-[[2-(2,6-dioxopiperidin-3-yl)-1-oxo-2,3-dihydro-1*H*-isoindol-4-yl]amino]octyl)carbamate (*i*-37)

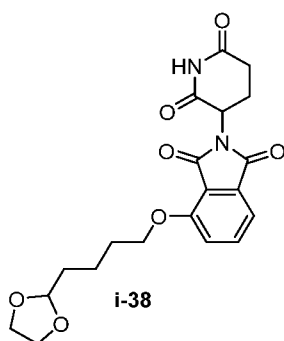


5 To a solution of *tert*-butyl *N*-(8-[[2-(2,6-dioxopiperidin-3-yl)-1-oxo-2,3-dihydro-1*H*-isoindol-4-yl]amino]octyl)carbamate (100 mg, 0.310 mmol, 1 equiv) in DCM (5.0 ml) was added TFA (2.0 ml). The resulting solution was stirred at 25 °C for 1 hour. The resulting mixture was concentrated under reduced pressure. The residue was purified by reverse flash chromatography (conditions: column, C18 silica gel; mobile phase, MeCN in water, 10% to 50% gradient in 10 minutes; detector, UV 254 nm). This resulted
10 in 3-[4-[(8-amino)octyl]amino]-1-oxo-2,3-dihydro-1*H*-isoindol-2-yl]piperidine-2,6-dione (103 mg, 87%) as a yellow solid. LCMS (ESI) *m/z*: [M+H]⁺ = 387.

Preparation of 5-((2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindolin-4-yl)oxy)pentanal (*i*-39)

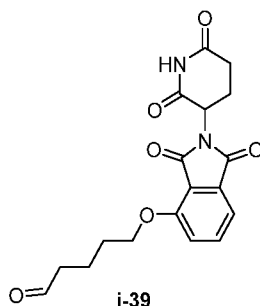


15 **Step 1: Preparation of 4-(4-(1,3-dioxolan-2-yl)butoxy)-2-(2,6-dioxopiperidin-3-yl)isoindoline-1,3-dione (*i*-38)**



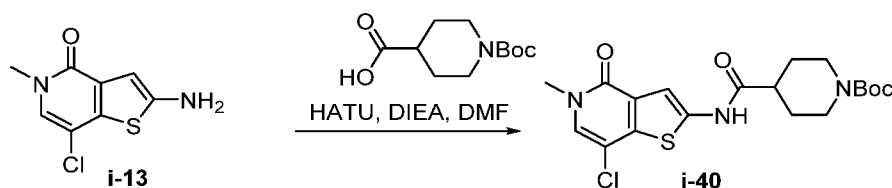
To a stirred mixture of 2-(2,6-dioxopiperidin-3-yl)-4-hydroxyisoindole-1,3-dione (400 mg, 1.459 mmol, 1.00 equiv) and 2-(4-bromobutyl)-1,3-dioxolane (274.5 mg, 1.313 mmol, 0.90 equiv) in DMF (4.00 mL) was added Cs₂CO₃ (950.5 mg, 2.917 mmol, 2.00 equiv) at 60 °C under nitrogen atmosphere. The
20 resulting mixture was stirred for 5 hours. The resulting mixture was filtered with acetonitrile (200 mL), concentrated, and purified by Prep-TLC (PE/EtOAc (1:1)) to afford 4-[4-(1,3-dioxolan-2-yl)butoxy]-2-(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione (81 mg, 13%) as a colorless oil. LCMS (ESI) *m/z*: [M+H]⁺ = 403.

Step 2: Preparation of 5-((2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindolin-4-yl)oxy)pentanal (i-39)



To a stirred mixture of 4-[4-(1,3-dioxolan-2-yl)butoxy]-2-(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione (46.0 mg, 0.114 mmol, 1.00 equiv) in H₂O (3.0 mL) was added 4 M HCl in dioxane (3 mL) dropwise at room temperature under nitrogen atmosphere. After 3 hours, saturated NaHCO₃ solution (50 mL) was added to the mixture. The mixture was then extracted with EtOAc (100 mL x 3), and the combined organic layers were concentrated to give 5-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]oxy]pentanal (35mg, 70%) as a light yellow semi-solid. LCMS (ESI) m/z: [M+H]⁺ = 359.

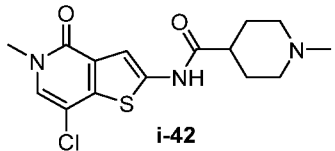
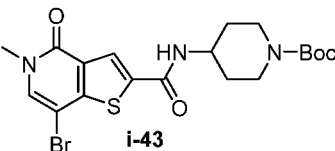
Preparation of tert-butyl 4-([7-chloro-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl]carbamoyl)piperidine-1-carboxylate (i-40)



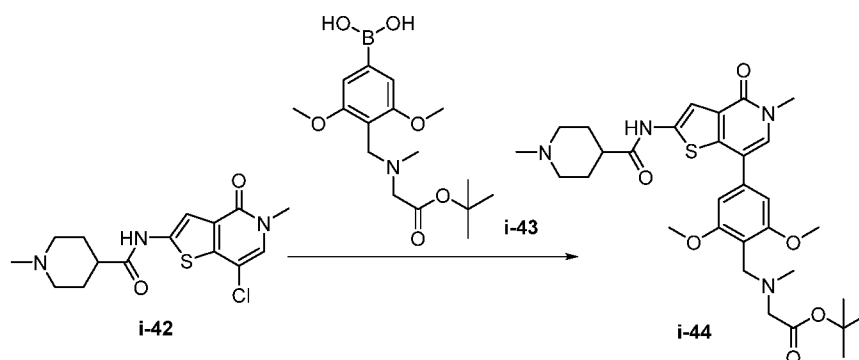
To a solution of 2-amino-7-chloro-5-methylthieno[3,2-c]pyridin-4-one (300.0 mg, 1.397 mmol, 1.00 equiv) and 1-(*tert*-butoxycarbonyl)piperidine-4-carboxylic acid (416.5 mg, 1.817 mmol, 1.3 equiv) in solvent DMF (4 mL) was added DIEA (722.5 mg, 5.590 mmol, 4 equiv) and HATU (1062.7 mg, 2.795 mmol, 2 equiv). The resulting solution was stirred at 25 °C for 2 hours. The mixture was diluted with EtOAc (30 mL) and washed with water (30 mL x 3). The organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated to give a crude product. The crude product was purified by chromatography on silica gel eluted with DCM/MeOH (from 20:1 to 10:1) to give *tert*-butyl 4-([7-chloro-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl]carbamoyl)piperidine-1-carboxylate (360 mg, 61%) as a brown solid. LCMS (ESI) m/z: [M+H]⁺ = 426.

The following compounds (intermediates i-41, i-42, and i-43) were prepared in a similar manner as described in the preparation of intermediate i-40.

Compound (Intermediate No.)	Structure	Analytical Data
<i>tert</i> -butyl 3-([7-chloro-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl]carbamoyl)piperidine-1-carboxylate (i-41)	 i-41	340 mg (57%) as a yellow oil; LCMS (ESI) m/z: [M+H] ⁺ = 426.12

7-chloro-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl]-1-methylpiperidine-4-carboxamide (i-42)	 i-42	80 mg (51%) as a yellow solid; LCMS (ESI) m/z: [M+H] ⁺ = 340
<i>tert</i> -butyl 4-(7-bromo-5-methyl-4-oxo-4,5-dihydrothieno[3,2-c]pyridine-2-carboxamido)piperidine-1-carboxylate (i-42)	 i-43	154 mg (31%) as a yellow solid; LCMS (ESI) m/z: [M+H] ⁺ = 470

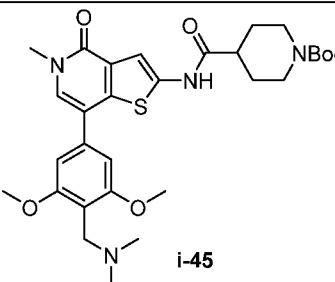
Preparation of *tert*-butyl 2-[[[2,6-dimethoxy-4-[5-methyl-2-(1-methylpiperidine-4-amido)-4-oxothieno[3,2-c]pyridin-7-yl]phenyl]methyl](methyl)amino]acetate (i-44)

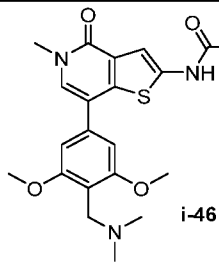
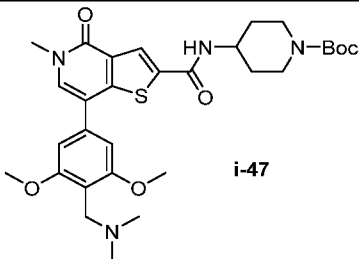


5 To a solution of *N*-[7-chloro-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl]-1-methylpiperidine-4-carboxamide (50.0 mg, 0.147 mmol, 1.00 equiv) and 4-[[[2-(*tert*-butoxy)-2-oxoethyl](methyl)amino]methyl]-3,5-dimethoxyphenylboronic acid (59.9 mg, 0.177 mmol, 1.20 equiv) in solvent dioxane (1.50 mL) and H₂O (0.50 mL) was added Pd(dppf)Cl₂·CH₂Cl₂ (8.5 mg, 0.015 mmol, 0.10 equiv) and Cs₂CO₃ (95.9 mg, 0.294 mmol, 2.00 equiv), and the resulting solution was stirred at 90 °C

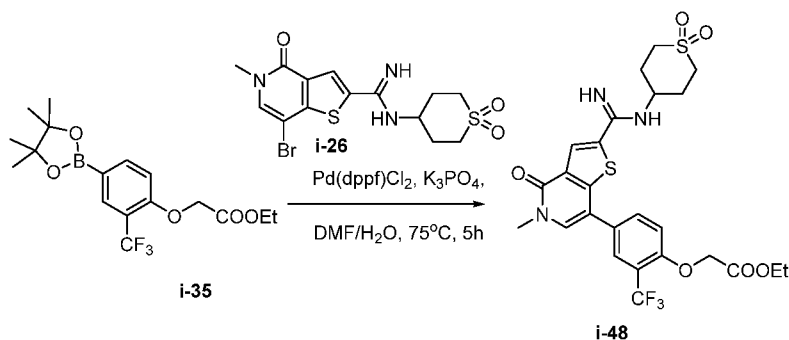
10 for 3 hours. The reaction mixture was then diluted with 10 mL of water and extracted ethyl acetate (2 x 20 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated. The residue was applied onto a silica gel column with CH₂Cl₂/MeOH (20:1). This resulted in *tert*-butyl 2-[[[2,6-dimethoxy-4-[5-methyl-2-(1-methylpiperidine-4-amido)-4-oxothieno[3,2-c]pyridin-7-yl]phenyl]methyl](methyl)amino]acetate (40 mg, 45%) as a yellow solid. LCMS (ESI) m/z: [M+H]⁺ = 599.

15 The following compounds (intermediates i-45, i-46, and i-47) were prepared in a similar manner as described in the preparation of intermediate i-44.

Compound (Intermediate No.)	Structure	Analytical Data
<i>tert</i> -butyl 4-[(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl)carbamoyl]piperidine-1-carboxylate (i-45)	 i-45	168 mg (34%) as a brown solid; LCMS (ESI) m/z: [M+H] ⁺ = 585

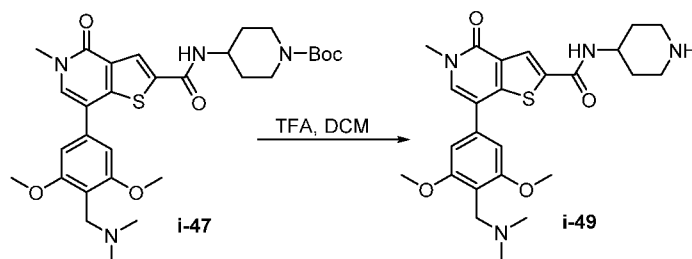
Compound (Intermediate No.)	Structure	Analytical Data
<i>tert</i> -butyl 3-[(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl)carbamoyl]piperidine-1-carboxylate (i-46)		260 mg (63%) as a red oil; LCMS (ESI) m/z: [M+H] ⁺ = 585.27
<i>tert</i> -butyl 4-(7-(4-((dimethylamino)methyl)-3,5-dimethoxyphenyl)-5-methyl-4-oxo-4,5-dihydrothieno[3,2-c]pyridine-2-carboxamido)piperidine-1-carboxylate (i-47)		122 mg (62%) as a brown solid; LCMS (ESI) m/z: [M+H] ⁺ = 585

Preparation of ethyl 2-(4-[2-[*N*-(1,1-dioxo-1λ6-thian-4-yl)carbamimidoyl]-5-methyl-4-oxo-4*H*,5*H*-thieno[3,2-*c*]pyridin-7-yl]-2-(trifluoromethyl)phenoxy)acetate (i-48)



- 5 To a solution of ethyl 2-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trifluoromethyl)phenoxy]acetate (100 mg, 0.267 mmol, 1 equiv) and 7-bromo-*N*-(1,1-dioxo-1λ6-thian-4-yl)-5-methyl-4-oxo-4*H*,5*H*-thieno[3,2-*c*]pyridine-2-carboximidamide (111.8 mg, 0.267 mmol, 1 equiv) in DMF (3 mL) and H₂O (0.3 mL) was added K₃PO₄ (113.46 mg, 0.535 mmol, 2 equiv) and Pd(dppf)Cl₂ (39.1 mg, 0.053 mmol, 0.2 equiv) at room temperature. The resulting mixture was stirred for 1 hour at 75 °C under
- 10 nitrogen atmosphere. The mixture was concentrated and the residue was purified by silica gel column chromatography, eluted with CH₂Cl₂ / MeOH (5:1) to afford ethyl 2-(4-[2-[*N*-(1,1-dioxo-1λ6-thian-4-yl)carbamimidoyl]-5-methyl-4-oxo-4*H*,5*H*-thieno[3,2-*c*]pyridin-7-yl]-2-(trifluoromethyl)phenoxy) acetate (97 mg, 62%) as an off-white solid. LCMS (ESI) m/z: [M+H]⁺ = 586.

Preparation of *N*-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-*c*]pyridin-2-yl)piperidine-4-carboxamide (i-49)

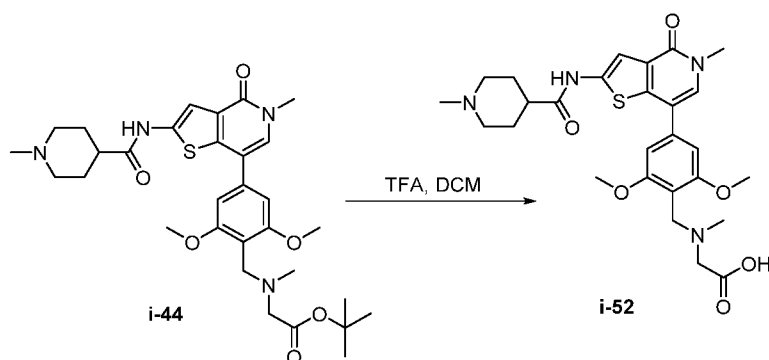


To a solution of *tert*-butyl 4-[(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-*c*]pyridin-2-yl)carbamoyl]piperidine-1-carboxylate (168.0 mg, 0.287 mmol, 1.00 equiv) in DCM (9.00 mL) was added TFA (3.00 mL, 13.463 mmol, 262.41 equiv), and the resulting solution was stirred at 25 °C for 2 hours. The solvent was removed to afford *N*-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-*c*]pyridin-2-yl)piperidine-4-carboxamide (180 mg, crude) as a brown solid that was used directly without further purification. LCMS (ESI) *m/z*: [M+H]⁺ = 485.

The following compounds (intermediates i-50 and i-51) were prepared in a similar manner as described in the preparation of intermediate i-49.

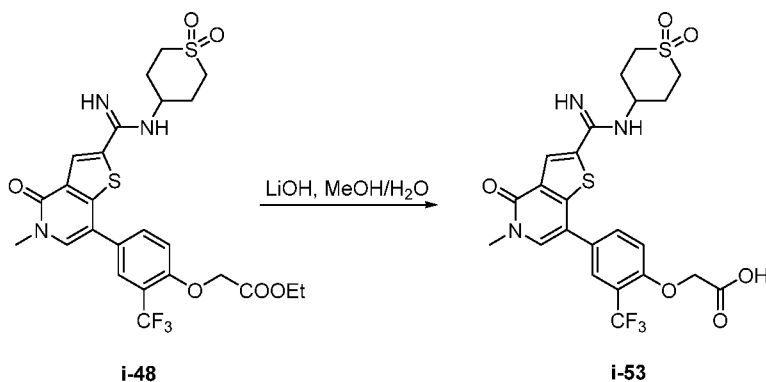
Compound (Intermediate No.)	Structure	Analytical Data
<i>N</i> -(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2- <i>c</i>]pyridin-2-yl)piperidine-3-carboxamide (i-50)		160 mg (88%) as a red oil; LCMS (ESI) <i>m/z</i> : [M+H] ⁺ = 485.21
<i>N</i> -(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2- <i>c</i>]pyridin-2-yl)piperidine-4-carboxamide (i-51)		180 mg (crude) as a brown solid (used directly without further purification); LCMS(ESI) <i>m/z</i> : [M+H] ⁺ = 485

Preparation of [(2,6-dimethoxy-4-[5-methyl-2-(1-methylpiperidine-4-amido)-4-oxothieno[3,2-*c*]pyridin-7-yl]phenyl)methyl](methyl)amino]acetic acid (i-52)



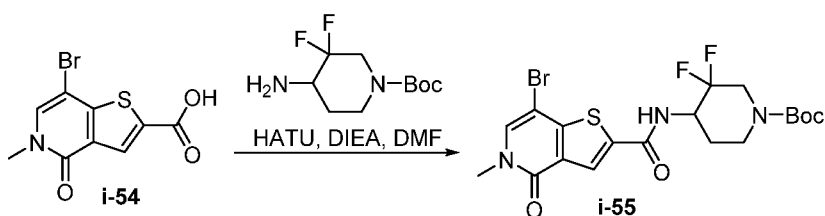
To a solution of *tert*-butyl 2-[(2,6-dimethoxy-4-[5-methyl-2-(1-methylpiperidine-4-amido)-4-oxothieno[3,2-c]pyridin-7-yl]phenyl)methyl](methyl)amino]acetate (40.0 mg, 0.067 mmol, 1.00 equiv) in DCM (2.00 mL) was added TFA (2.00 mL), and the resulting solution was stirred at 25 °C for 1 hour. The resulting mixture was concentrated to afford [(2,6-dimethoxy-4-[5-methyl-2-(1-methylpiperidine-4-amido)-4-oxothieno[3,2-c]pyridin-7-yl]phenyl)methyl](methyl)amino]acetic acid (50 mg, crude) as a yellow solid that was used directly without further purification.

Preparation of 2-(4-[2-[*N*-(1,1-dioxo-1 λ 6-thian-4-yl)carbamimidoyl]-5-methyl-4-oxo-4*H*,5*H*-thieno[3,2-c]pyridin-7-yl]-2-(trifluoromethyl)phenoxy)acetic acid (*i*-53)



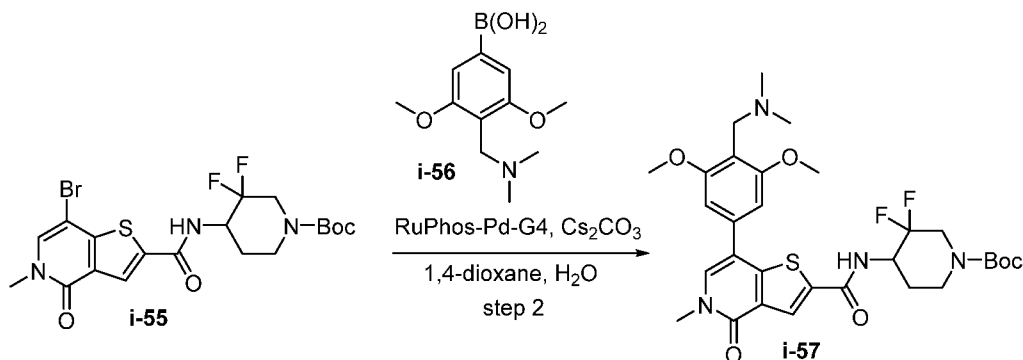
A solution of ethyl 2-(4-[2-[*N*-(1,1-dioxo-1 λ 6-thian-4-yl)carbamimidoyl]-5-methyl-4-oxo-4*H*,5*H*-thieno[3,2-c]pyridin-7-yl]-2-(trifluoromethyl)phenoxy)acetate (90 mg, 0.154 mmol, 1 equiv) and LiOH·H₂O (64.49 mg, 1.537 mmol, 10 equiv) in MeOH (2 mL) and H₂O (0.5 mL) was stirred for 1 hour at room temperature. The resulting mixture was concentrated under vacuum and afforded 2-(4-[2-[*N*-(1,1-dioxo-1 λ 6-thian-4-yl)carbamimidoyl]-5-methyl-4-oxo-4*H*,5*H*-thieno[3,2-c]pyridin-7-yl]-2-(trifluoromethyl)phenoxy)acetic acid (80 mg, 93%) as a yellow solid. LCMS (ESI) *m/z*: [M+H]⁺ = 558.

Preparation of *tert*-butyl 4-[7-bromo-5-methyl-4-oxothieno[3,2-c]pyridine-2-amido]-3,3-difluoropiperidine-1-carboxylate (*i*-55)



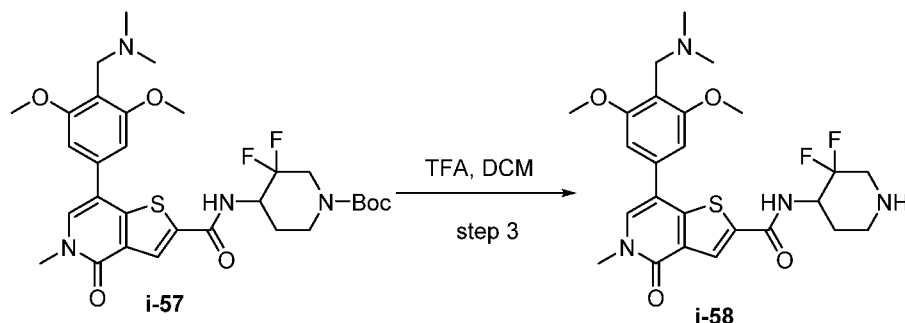
To a solution of 7-bromo-5-methyl-4-oxothieno[3,2-c]pyridine-2-carboxylic acid (200.0 mg, 0.694 mmol, 1.00 equiv) and *tert*-butyl 4-amino-3,3-difluoropiperidine-1-carboxylate (213.2 mg, 0.902 mmol, 1.3 equiv) in DMF (4 mL) was added DIEA (448.57 mg, 3.471 mmol, 5 equiv) and HATU (527.8 mg, 1.388 mmol, 2 equiv), and the resulting solution was stirred at room temperature for 4 hours. The mixture was diluted with EtOAc (20 mL) and washed with water (30 mL x 3). The organic layers were combined and dried over anhydrous sodium sulfate, filtered, and concentrated to give a crude product. The crude product was purified by chromatography on silica gel eluted with DCM/MeOH (from 30:1 to 20:1) to give *tert*-butyl 4-[7-bromo-5-methyl-4-oxothieno[3,2-c]pyridine-2-amido]-3,3-difluoropiperidine-1-carboxylate (100 mg, 28.45%) as a brown yellow solid. LCMS (ESI) *m/z*: [M+H]⁺ = 506.

Preparation of *tert*-butyl 4-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-c]pyridine-2-amido)-3,3-difluoropiperidine-1-carboxylate (i-57)



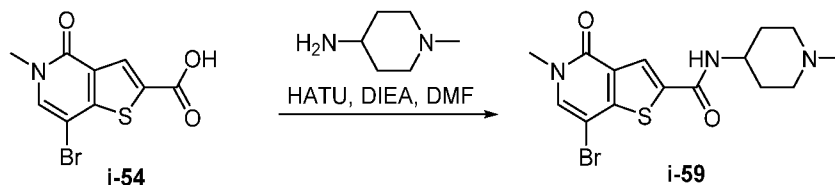
- 5 To a solution of *tert*-butyl 4-[7-bromo-5-methyl-4-oxothieno[3,2-c]pyridine-2-amido]-3,3-difluoropiperidine-1-carboxylate (90.0 mg, 0.178 mmol, 1.00 equiv) and 4-[(dimethylamino)methyl]-3,5-dimethoxyphenylboronic acid (63.7 mg, 0.267 mmol, 1.5 equiv) in dioxane (4 mL) and H₂O (0.4 mL) was added Cs₂CO₃ (115.8 mg, 0.355 mmol, 2 equiv) and RuPhos Palladacycle Gen.4 (15.1 mg, 0.018 mmol, 0.1 equiv). The resulting solution was stirred at room temperature for 2 hours (under N₂ atmosphere).
- 10 The mixture was diluted with EtOAc (20 mL) and washed with water (30 mL x 3). The organic layers were combined and dried over anhydrous sodium sulfate, filtered, and concentrated to give a crude product. The crude product was purified by chromatography on silica gel eluted with DCM/MeOH (from 20:1 to 10:1) to give *tert*-butyl 4-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-c]pyridine-2-amido)-3,3-difluoropiperidine-1-carboxylate (66 mg, 59.82%) as an off-white solid. LCMS (ESI) *m/z*: [M+H]⁺ = 621.
- 15

Preparation of *N*-(3,3-difluoropiperidin-4-yl)-7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-c]pyridine-2-carboxamide (i-58)



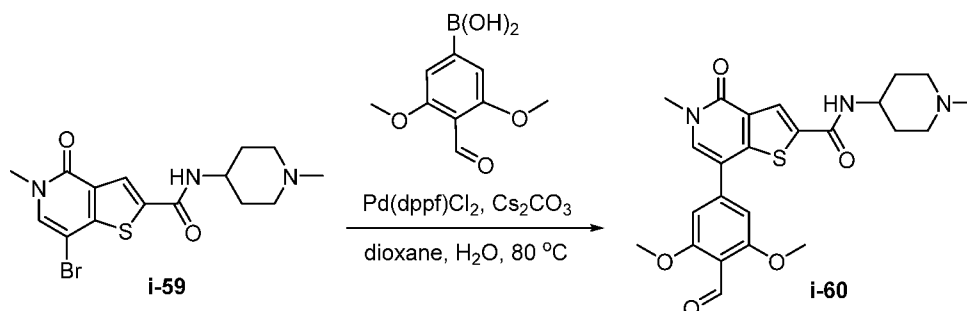
- 20 To a solution of *tert*-butyl 4-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-c]pyridine-2-amido)-3,3-difluoropiperidine-1-carboxylate (66.0 mg, 0.106 mmol, 1.00 equiv) in DCM (9.00 mL) was added TFA (3 mL, 40.389 mmol, 379.85 equiv). The resulting solution was stirred at room temperature for 2 hours. The reaction mixture was concentrated under reduced pressure to afford *N*-(3,3-difluoropiperidin-4-yl)-7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-c]pyridine-2-carboxamide (66mg, crude) as a yellow solid that was used directly without further purification. LCMS (ESI) *m/z*: [M+H]⁺ = 521.
- 25

Preparation of 7-bromo-5-methyl-*N*-(1-methylpiperidin-4-yl)-4-oxo-4,5-dihydrothieno[3,2-*c*]pyridine-2-carboxamide (i-59)



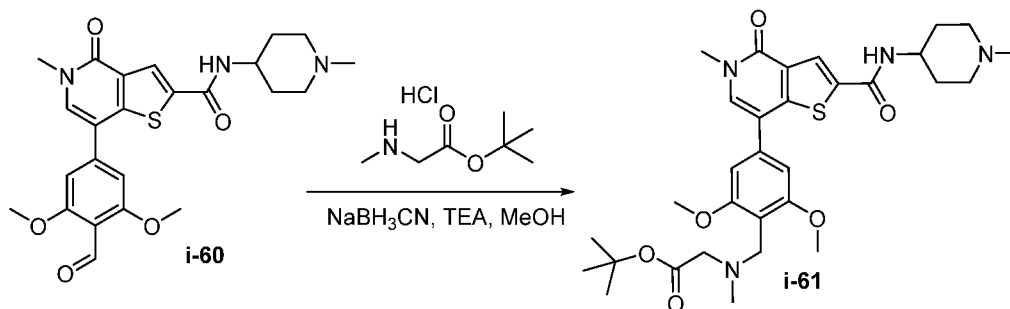
To a stirred mixture of 7-bromo-5-methyl-4-oxothieno[3,2-*c*]pyridine-2-carboxylic acid (200.00 mg, 0.694 mmol, 1.00 equiv) and 1-methylpiperidin-4-amine (118.90 mg, 1.041 mmol, 1.50 equiv) in DMF (2.00 mL) was added HATU (527.88 mg, 1.388 mmol, 2 equiv) at 0 °C. After 10 minutes, DIEA (358.86 mg, 2.777 mmol, 4.00 equiv) was added, and the reaction mixture was stirred for 10 minutes at 0 °C. The mixture was allowed to stirred one hour at room temperature. The resulting mixture was extracted with the mixture of DCM and isopropanol (3:1; 3 x 100 mL), concentrated, and purified by silica gel column chromatography, eluted with DCM / MeOH (10:1) to afford 7-bromo-5-methyl-*N*-(1-methylpiperidin-4-yl)-4-oxothieno[3,2-*c*]pyridine-2-carboxamide (232 mg, 82.10%) as a yellow solid. LCMS (ESI) *m/z*: [M+H]⁺ = 384.

Preparation of 7-(4-formyl-3,5-dimethoxyphenyl)-5-methyl-*N*-(1-methylpiperidin-4-yl)-4-oxo-4,5-dihydrothieno[3,2-*c*]pyridine-2-carboxamide (i-60)



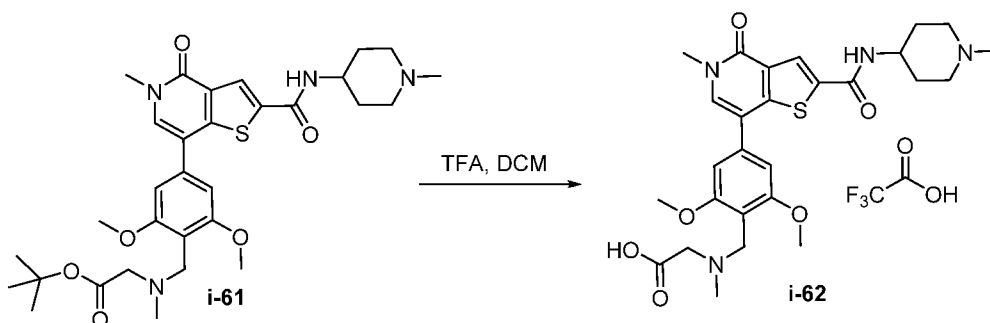
To a stirred mixture of 7-bromo-5-methyl-*N*-(1-methylpiperidin-4-yl)-4-oxothieno[3,2-*c*]pyridine-2-carboxamide (232.00 mg, 0.604 mmol, 1.00 equiv) and 4-formyl-3,5-dimethoxyphenylboronic acid (190.16 mg, 0.906 mmol, 1.50 equiv) in dioxane (4.00 mL) and H₂O (0.80 mL) was added Pd(dppf)Cl₂·CH₂Cl₂ (49.30 mg, 0.060 mmol, 0.10 equiv) and Cs₂CO₃ (590.10 mg, 1.811 mmol, 3.00 equiv). The mixture was allowed to stir at 80 °C under nitrogen atmosphere for 3 hours. The resulting mixture was filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with DCM/MeOH (10:1) to afford 7-(4-formyl-3,5-dimethoxyphenyl)-5-methyl-*N*-(1-methylpiperidin-4-yl)-4-oxothieno[3,2-*c*]pyridine-2-carboxamide (131 mg, 43.67%) as a yellow solid. LCMS (ESI) *m/z*: [M+H]⁺ = 470.

Preparation of *tert*-butyl 2-[[[(2,6-dimethoxy-4-[5-methyl-2-[(1-methylpiperidin-4-yl)carbamoyl]-4-oxothieno[3,2-c]pyridin-7-yl]phenyl)methyl](methyl)amino]acetate (i-61)



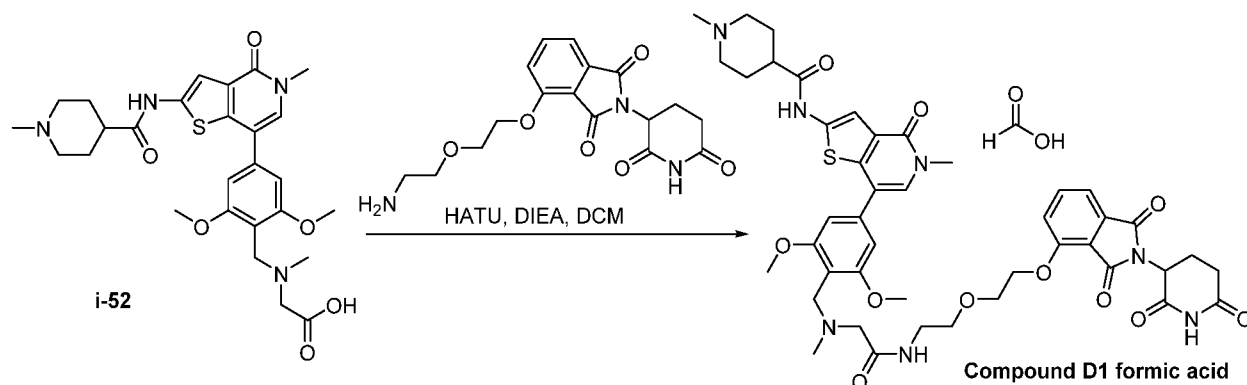
To a stirred mixture of 7-(4-formyl-3,5-dimethoxyphenyl)-5-methyl-N-(1-methylpiperidin-4-yl)-4-oxothieno[3,2-c]pyridine-2-carboxamide (131.00 mg, 0.279 mmol, 1.00 equiv) and *tert*-butyl 2-(methylamino)acetate hydrochloride (60.82 mg, 0.335 mmol, 1.20 equiv) in MeOH (1.50 mL) was added TEA (84.69 mg, 0.837 mmol, 3.00 equiv) at room temperature. After 30 minutes, NaBH₃CN (52.60 mg, 0.837 mmol, 3.00 equiv) was added at room temperature. After 3 hours, the reaction mixture was purified by silica gel column chromatography, eluted with DCM/MeOH (20:1) to afford *tert*-butyl 2-[[[(2,6-dimethoxy-4-[5-methyl-2-[(1-methylpiperidin-4-yl)carbamoyl]-4-oxothieno[3,2-c]pyridin-7-yl]phenyl)methyl](methyl)amino]acetate (84 mg, 50.28%) as a yellow solid. LCMS (ESI) *m/z*: [M+H]⁺ = 599.

Preparation of [[[(2,6-dimethoxy-4-[5-methyl-2-[(1-methylpiperidin-4-yl)carbamoyl]-4-oxothieno[3,2-c]pyridin-7-yl]phenyl)methyl](methyl)amino] trifluoroacetic acid (i-62)



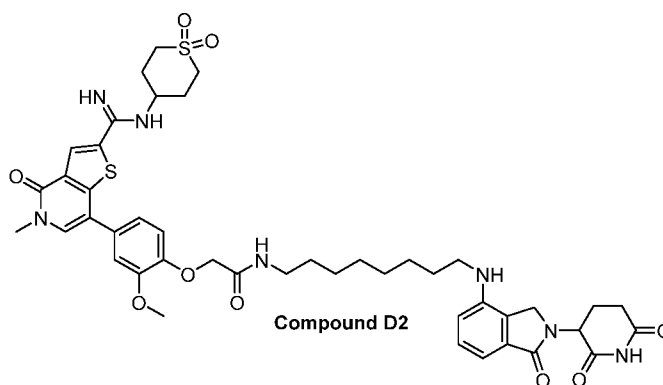
To a stirred mixture of *tert*-butyl 2-[[[(2,6-dimethoxy-4-[5-methyl-2-[(1-methylpiperidin-4-yl)carbamoyl]-4-oxothieno[3,2-c]pyridin-7-yl]phenyl)methyl](methyl)amino]acetate (84.00 mg, 0.140 mmol, 1.00 equiv) in DCM (4.00 mL) was added TFA (1.00 mL) dropwise at room temperature and stirred for one hour at room temperature. The resulting mixture was concentrated under vacuum. This resulted in [[[(2,6-dimethoxy-4-[5-methyl-2-[(1-methylpiperidin-4-yl)carbamoyl]-4-oxothieno[3,2-c]pyridin-7-yl]phenyl)methyl](methyl)amino] trifluoroacetic acid (101 mg, 96.48%) as a yellow crude solid. LCMS (ESI) *m/z*: [M+H]⁺ = 543.

Example 18 – Preparation of N-[7-(4-[[[2-(2-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]oxy]ethoxy)ethyl]carbamoyl]methyl)(methyl)amino]methyl]-3,5-dimethoxyphenyl)-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl]-1-methylpiperidine-4-carboxamide formic acid (Compound D1 formic acid)



To a solution of [[2,6-dimethoxy-4-[5-methyl-2-(1-methylpiperidine-4-amido)-4-oxothieno[3,2-c]pyridin-7-yl]phenyl]methyl)(methyl)amino]acetic acid (50.0 mg, 0.092 mmol, 1.00 equiv) and HATU (70.1 mg, 0.184 mmol, 2.00 equiv) in DMF (2.00 mL) was added 4-[2-(2-aminoethoxy)ethoxy]-2-(2,6-dioxopiperidin-3-yl)isindole-1,3-dione (33.3 mg, 0.092 mmol, 1.00 equiv) and DIEA (35.7 mg, 0.276 mmol, 3.00 equiv). The resulting solution was stirred at 25 °C for 2 hours. The crude product was purified by preparative HPLC (conditions: XSelect CSH Prep C18 OBD Column, 5 µm, 19*150mm; Mobile Phase A: Water (0.1% FA), Mobile Phase B: ACN; Flow rate: 25 mL/minute; Gradient: 20% B to 55% B in 8 minutes; 254 nm; R_T: 7.12 minutes) to afford *N*-[7-(4-[[[2-(2-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]oxy]ethoxy)ethyl]carbamoyl]methyl)(methyl)amino]methyl]-3,5-dimethoxyphenyl)-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl]-1-methylpiperidine-4-carboxamide formic acid (7 mg, 8.6%) of as a yellow solid. ¹H NMR (300 MHz, Methanol-*d*₄) δ 8.40 (br s, 0.4H, FA), 7.64 – 7.53 (m, 2H), 7.25 (d, *J*=7.2 Hz, 1H), 7.20 – 7.09 (m, 2H), 6.97 (s, 2H), 5.07 (dd, *J*=12.9, 5.3 Hz, 1H), 4.29 (s, 2H), 4.07 – 3.90 (m, 8H), 3.73 (s, 4H), 3.63 – 3.48 (m, 7H), 3.46 – 3.38 (m, 2H), 3.18 – 3.02 (m, 2H), 2.91 – 2.72 (m, 9H), 2.64 – 2.47 (m, 1H), 2.25 – 1.98 (m, 5H). LCMS (ESI) *m/z*: [M+H]⁺ = 886.80.

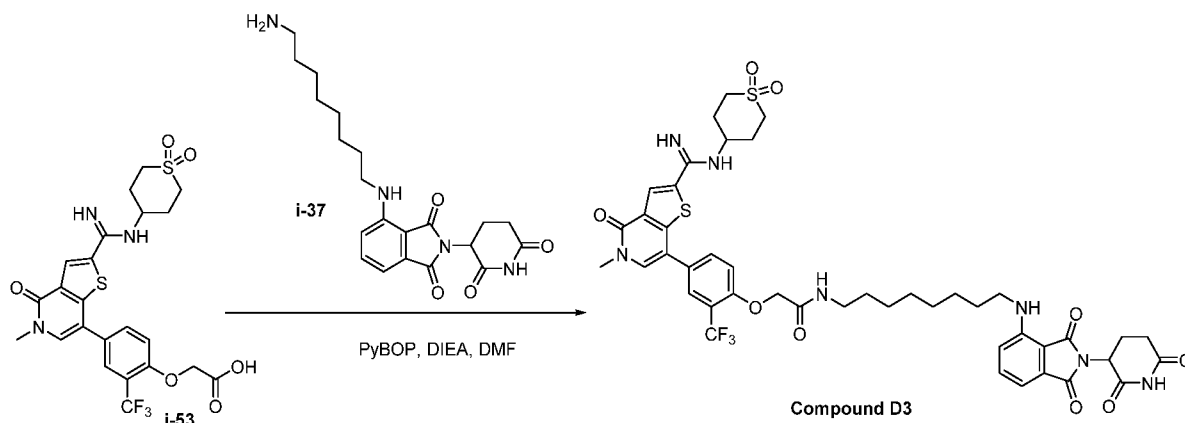
The following compound (compound D2) was prepared in a similar manner as described for compound D1.



2-(4-[2-[*N*-(1,1-dioxo-λ⁶-thian-4-yl) carbamimidoyl]-5-methyl-4-oxo-4*H*,5*H*-thieno[3,2-c]pyridin-7-yl]-2-methoxyphenoxy)-*N*-(8-[[2-(2,6-dioxopiperidin-3-yl)-1-oxo-2,3-dihydro-1*H*-isindol-4-yl]amino]octyl)acetamide (14 mg, 16%) as a yellow solid. ¹H NMR (300 MHz, Methanol-*d*₄) δ 8.54 (s, 0.4H, FA), 8.21 (s, 1H), 7.74 (s, 1H), 7.34 – 7.16 (m, 3H), 7.13 (d, *J*=8.3 Hz, 1H), 7.02 (d, *J*=7.5 Hz, 1H),

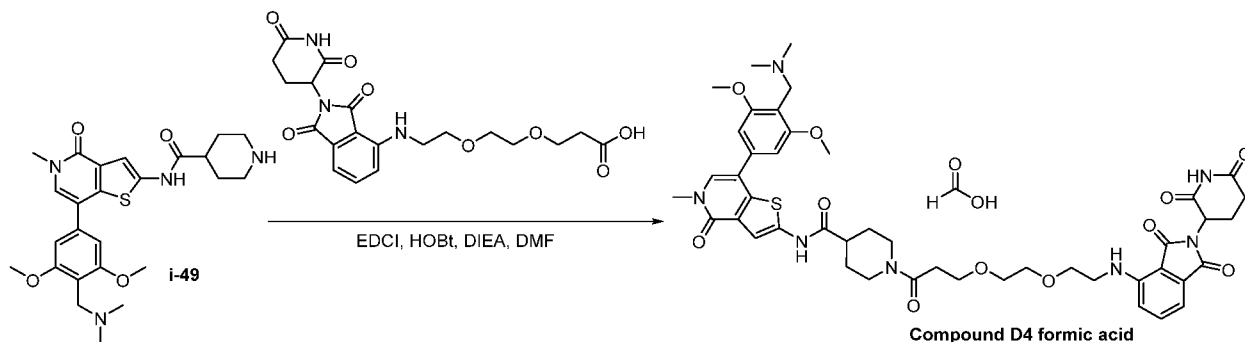
6.75 (d, J = 8.0 Hz, 1H), 5.16 (dd, J = 13.3, 5.1 Hz, 1H), 4.59 (d, J = 5.2 Hz, 3H), 4.28 (d, J = 3.0 Hz, 2H), 3.96 (s, 3H), 3.73 (s, 3H), 3.29 – 3.10 (m, 4H), 3.03 – 2.79 (m, 3H), 2.51 (td, J = 13.2, 5.0 Hz, 1H), 2.32 – 2.15 (m, 5H), 1.61 (dd, J = 15.5, 7.3 Hz, 4H), 1.36 (s, 8H). LCMS (ESI) m/z : $[M+H]^+$ = 888.30.

5 Example 19 – Preparation of 2-(4-[2-[N-(1,1-dioxo-1 λ 6-thian-4-yl)carbamimidoyl]-5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridin-7-yl]-2-(trifluoromethyl)phenoxy)-N-(8-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxo-2,3-dihydro-1H-isoindol-4-yl]amino]octyl)acetamide (Compound D3)



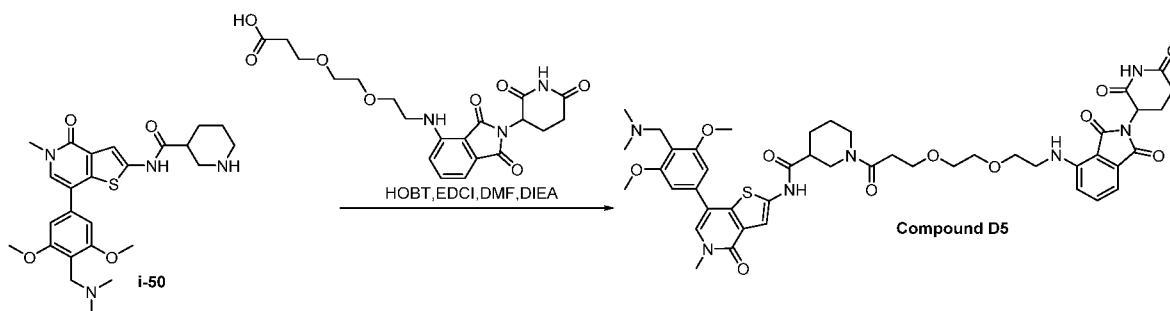
To a solution of 2-(4-[2-[N-(1,1-dioxo-1 λ 6-thian-4-yl)carbamimidoyl]-5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridin-7-yl]-2-(trifluoromethyl)phenoxy)acetic acid (69 mg, 0.124 mmol, 1 equiv) and DIEA (N,N-diisopropylamine) (48 mg, 0.371 mmol, 3 equiv) in DMF (1 mL) was added PyBOP (96.6 mg, 0.186 mmol, 1.5 equiv) and 4-[[8-aminooctyl]amino]-2-(2,6-dioxopiperidin-3-yl)-1,3-dioxo-2,3-dihydro-1H-isoindole-1,3-dione (49.6 mg, 0.124 mmol, 1 equiv). The resulting solution was stirred at room temperature for overnight. Without workup, the crude product (69 mg) was purified by Prep-HPLC (conditions: SunFire Prep C18 OBD Column 19 $\times$ 150mm 5 μ m 10 nm; Mobile Phase A: Water (0.1% FA), Mobile Phase B: ACN; Flow rate: 25 mL/minute; Gradient: 25% B to 55% B in 8 minutes; 254 nm; R_T : 7.35 minutes) to afford 2-(4-[2-[N-(1,1-dioxo-1 λ 6-thian-4-yl)carbamimidoyl]-5-methyl-4-oxo-4H,5H-thieno[3,2-c]pyridin-7-yl]-2-(trifluoromethyl)phenoxy)-N-(8-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxo-2,3-dihydro-1H-isoindol-4-yl]amino]octyl)acetamide (30 mg, 25%) as a yellow solid. ^1H NMR (300 MHz, DMSO- d_6) δ 11.10 (s, 1H), 8.23 (s, 1H), 8.14 (s, 0.26H, FA), 7.94-7.78 (m, 4H), 7.62-7.50 (m, 1H), 7.30 (d, J = 8.8 Hz, 1H), 7.03 (dd, J = 13.8, 7.8 Hz, 2H), 6.51 (t, J = 5.9 Hz, 1H), 5.05 (dd, J = 12.8, 5.3 Hz, 1H), 4.74 (s, 2H), 3.69 (s, 1H), 3.58 (s, 3H), 3.26 (d, J = 6.6 Hz, 2H), 3.20-3.09 (m, 5H), 3.12-2.96 (m, 1H), 2.98-2.79 (m, 1H), 2.61 (s, 1H), 2.03 (s, 4H), 1.79-1.68 (m, 1H), 1.55-1.45 (m, 4H), 1.30 (s, 8H). LCMS (ESI) m/z : $[M+H]^+$ = 940.50.

Example 20 – Preparation of N-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl)-1-[3-[2-(2-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]amino]ethoxy)ethoxy]propanoyl]piperidine-4-carboxamide formic acid (Compound D4)



To a solution of 3-[2-(2-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]amino]ethoxy)ethoxy]propanoic acid (39.4 mg, 0.091 mmol, 1.1 equiv), HOBT (22.3 mg, 0.165 mmol, 2 equiv), and EDCI (31.7 mg, 0.165 mmol, 2 equiv) in DMF (1 mL) was added *N*-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl)piperidine-4-carboxamide (40.0 mg, 0.083 mmol, 1.00 equiv) and DIEA (53.4 mg, 0.413 mmol, 5 equiv), and the resulting solution was stirred at 25 °C for 2 hours. Without any additional work-up, the mixture was purified by Prep-HPLC (conditions: SunFire C18 OBD Prep Column, 100Å, 5 µm, 19 mm X 250 mm; Mobile Phase A: Water (0.1% FA), Mobile Phase B: ACN; Flow rate: 25 mL/minute; Gradient: 11 B to 26 B in 13 minutes; 254 nm) to give *N*-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl)-1-[3-[2-(2-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]amino]ethoxy)ethoxy]propanoyl]piperidine-4-carboxamide formic acid (22.3 mg, 29%). ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.56 (br s, 0.8H, FA), 7.64 (s, 1H), 7.47 – 7.41 (m, 1H), 7.15 (d, *J* = 2.2 Hz, 1H), 7.03 – 6.98 (m, 3H), 6.95 (d, *J* = 7.2 Hz, 1H), 5.02 (dd, *J* = 12.7, 5.4 Hz, 1H), 4.59 (d, *J* = 13.3 Hz, 1H), 4.28 (s, 2H), 4.13 (d, *J* = 13.9 Hz, 1H), 3.99 (s, 6H), 3.81 – 3.66 (m, 9H), 3.65 – 3.61 (m, 2H), 3.52 – 3.44 (m, 2H), 3.23 – 3.14 (m, 1H), 2.88 – 2.79 (m, 8H), 2.77 – 2.60 (m, 4H), 2.55 – 2.46 (m, 1H), 2.11 – 2.01 (m, 1H), 1.95 – 1.74 (m, 3H), 1.73 – 1.60 (m, 1H). LCMS (ESI) *m/z*: [M+H]⁺ = 900.50.

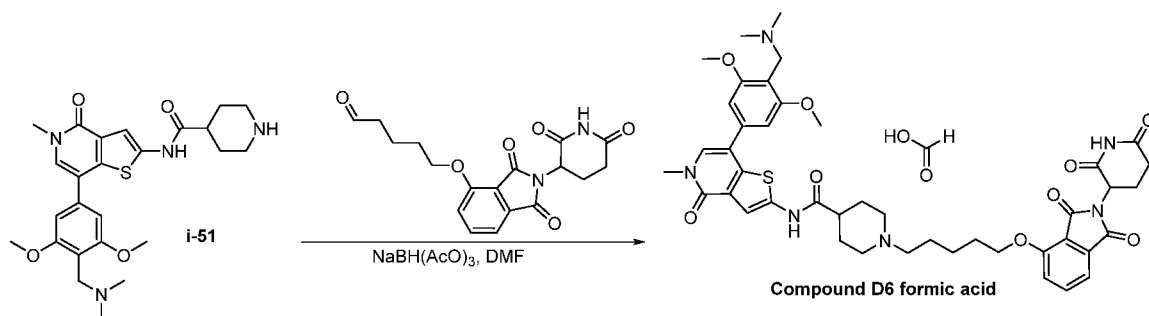
Example 21 – Preparation of N-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl)-1-[3-[2-(2-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]amino]ethoxy)ethoxy]propanoyl]piperidine-3-carboxamide (Compound D5)



To a stirred solution of 3-[2-(2-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]amino]ethoxy)ethoxy]propanoic acid (53.66 mg, 0.124 mmol, 1.20 equiv) in DMF (1.00 mL) was added HOBT (27.88 mg, 0.206 mmol, 2.00 equiv) and EDCI (39.56 mg, 0.206 mmol, 2.00 equiv) at 25 °C. The

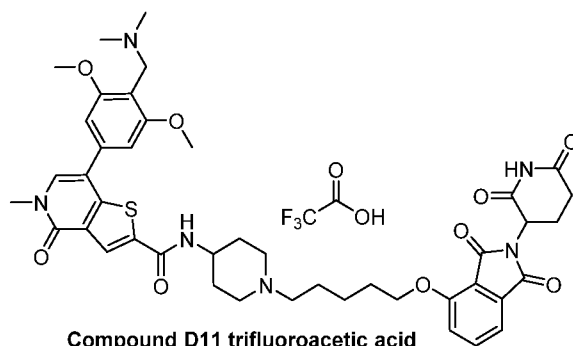
resulting mixture was stirred for 20 minutes at 25 °C. Then *N*-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-*c*]pyridin-2-yl)piperidine-3-carboxamide (50.00 mg, 0.103 mmol, 1.00 equiv) and DIEA (40.00 mg, 0.310 mmol, 3.00 equiv) was added to the reaction mixture. The resulting mixture was stirred for 2 hours at room temperature. The crude product was purified by Prep-HPLC (conditions: SunFire C18 OBD Prep Column, 100Å, 5 µm, 19 mm X 250 mm; mobile phase, Water (0.1% FA) and ACN (11% Phase B up to 23% in 18 minutes); Detector, UV) to afford *N*-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-*c*]pyridin-2-yl)-1-[3-[2-(2-[(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]amino)ethoxy]ethoxy]propanoyl)piperidine-3-carboxamide (12 mg, 13%) as a green solid. ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.57 (brs, 0.8H, FA), 7.66 – 7.58 (m, 1H), 7.57 – 7.25 (m, 1H), 7.19 – 7.06 (m, 1H), 7.05 – 6.95 (m, 3H), 6.86 – 6.76 (m, 1H), 5.04 (dd, *J*=12.5, 5.4 Hz, 1H), 4.53 – 4.40 (m, 1H), 4.37 – 4.24 (m, 0.5H), 4.20 (d, *J*=7.0 Hz, 2H), 4.03 – 3.98 (m, 6H), 3.95 – 3.88 (m, 0.5H), 3.81 – 3.62 (m, 11H), 3.52 – 3.48 (m, 1H), 3.45 – 3.36 (m, 1.5H), 3.21 – 3.12 (m, 0.5H), 3.06 – 2.92 (m, 1H), 2.87 – 2.63 (m, 11H), 2.61 – 2.53 (m, 1H), 2.25 – 1.98 (m, 2H), 1.86 – 1.73 (m, 2H), 1.69 – 1.46 (m, 1H). LCMS (ESI) *m/z*: [M+H]⁺ = 900.50.

Example 22 – Preparation of *N*-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-*c*]pyridin-2-yl)-1-(5-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]oxy]pentyl)piperidine-4-carboxamide formic acid (Compound D6 formic acid)



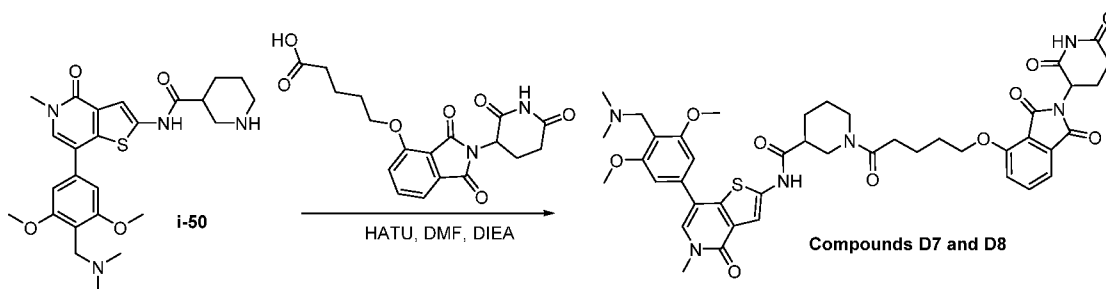
To a solution of *N*-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-*c*]pyridin-2-yl)piperidine-4-carboxamide (30.0 mg, 0.062 mmol, 1.00 equiv) and 5-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]oxy]pentanal (24.4 mg, 0.068 mmol, 1.10 equiv) in DMF (1.00 mL) was added sodium triacetoxyborohydride (26.2 mg, 0.124 mmol, 2.00 equiv), and the resulting solution was stirred at room temperature for 2 hours. Without any additional work-up, the mixture was purified by Prep-HPLC (conditions: Xselect CSH F-Phenyl OBD column, 19*250, 5 µm; Mobile Phase A: Water (0.1% FA), Mobile Phase B: ACN; Flow rate: 25 mL/minute; Gradient: 7 B to 19 B in 12 minutes; 254/220 nm) to give *N*-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-*c*]pyridin-2-yl)-1-(5-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]oxy]pentyl)piperidine-4-carboxamide; formic acid (4.7 mg, 8.7%). ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.55 (br s, 1.1H, FA), 7.67 (s, 1H), 7.63 – 7.57 (m, 1H), 7.29 (d, *J*=7.1 Hz, 1H), 7.21 (s, 1H), 7.16 (d, *J*=8.4 Hz, 1H), 7.05 (s, 2H), 5.13 (dd, *J*=12.9, 5.5 Hz, 1H), 4.38 (s, 2H), 4.02 (s, 6H), 3.85 (t, *J*=7.0 Hz, 2H), 3.74 (s, 3H), 3.39 – 3.35 (m, 2H), 2.93 – 2.87 (m, 8H), 2.78 (s, 2H), 2.71 – 2.56 (m, 4H), 2.15 – 2.08 (m, 1H), 2.05 – 1.92 (m, 4H), 1.77 – 1.60 (m, 4H), 1.44 – 1.34 (m, 2H). LCMS (ESI) *m/z*: [M+H]⁺ = 827.50.

Compound D11 was prepared in a similar manner as described for compound D6.

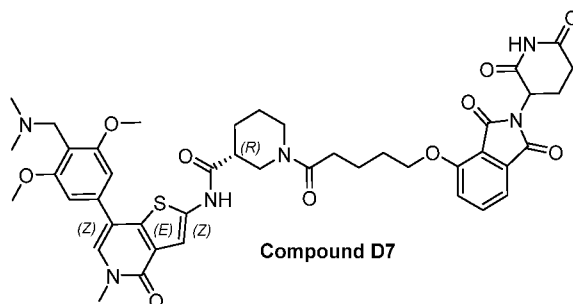


7-(4-((dimethylamino)methyl)-3,5-dimethoxyphenyl)-*N*-(1-(5-((2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindolin-4-yl)oxy)pentyl)piperidin-4-yl)-5-methyl-4-oxo-4,5-dihydrothieno[3,2-c]pyridine-2-carboxamide trifluoroacetic acid (12.8 mg, 26%) as a white solid. ¹H NMR (300 MHz, Methanol-*d*₄) δ 8.25 (s, 1H), 7.87 (s, 1H), 7.67 (t, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 7.2 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 1H), 7.06 (s, 2H), 5.16 (dd, *J* = 12.8, 5.4 Hz, 1H), 4.42 (s, 2H), 4.24 – 4.10 (m, 1H), 4.02 (s, 6H), 3.88 (t, *J* = 6.8 Hz, 2H), 3.75 (s, 3H), 3.69 (s, 2H), 3.25 – 3.06 (m, 4H), 2.96 – 2.87 (m, 8H), 2.77 – 2.60 (m, 1H), 2.31 – 2.14 (m, 3H), 2.01 – 1.88 (m, 2H), 1.86 – 1.62 (m, 4H), 1.51 – 1.39 (m, 2H). LCMS (ESI) *m/z*: [M+H]⁺ = 827.40.

Example 23 – Preparation of (3R) and (3S) *N*-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxo thieno[3,2-c]pyridin-2-yl)-1-(5-[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]oxy]pent anoyl)piperidine-3-carboxamide (Compounds D7 and D8)



To a stirred solution of *N*-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl)piperidine-3-carboxamide (50.00 mg, 0.103 mmol, 1.00 equiv) and 5-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]oxy]pentanoic acid (46.35 mg, 0.124 mmol, 1.20 equiv) in DMF (1 mL) was added DIEA (26.67 mg, 0.206 mmol, 2.00 equiv) dropwise at room temperature. The resulting mixture was stirred for 15 minutes at room temperature. Then HATU (58.84 mg, 0.155 mmol, 1.50 equiv) was added to the reaction mixture. The resulting mixture was stirred for 1 hour at room temperature. The crude products were purified by Prep-HPLC (conditions: SunFire C18 OBD Prep Column, 100Å, 5 μm, 19 mm X 250 mm; mobile phase, Water (0.1% FA) and ACN (7% Phase B up to 21% in 12 minutes); Detector, UV).



5



15

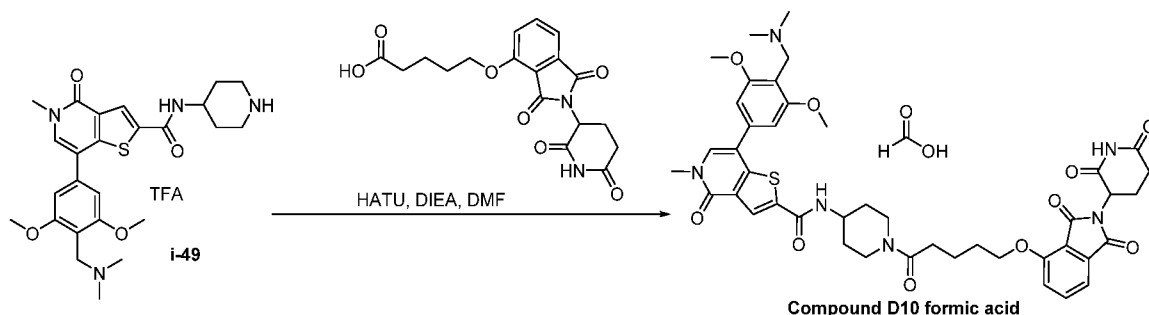
20



25

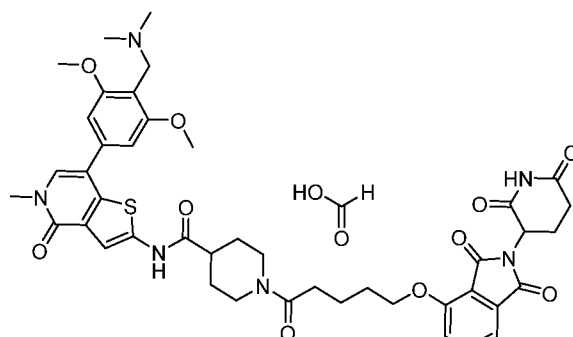
reaction mixture. The resulting mixture was stirred for 2 hours at room temperature. The crude product was purified by Prep-HPLC (conditions: SunFire C18 OBD Prep Column, 100Å, 5 µm, 19 mm X 250 mm; mobile phase, Water (0.1% FA) and ACN (7% Phase B up to 21% in 12 minutes); Detector, UV). This resulted in *N*-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-*c*]pyridin-2-yl)-1-(5-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]oxy]pentyl) piperidine-3-carboxamide (5.2 mg, 10%) as a red semi-solid. ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.45 (br s, 0.2H, FA), 7.66 (d, *J*=5.8 Hz, 1H), 7.62 – 7.55 (m, 1H), 7.33 – 7.12 (m, 3H), 7.04 (d, *J*=2.0 Hz, 2H), 5.14 – 5.04 (m, 1H), 4.41 (s, 2H), 4.01 (d, *J*=5.8 Hz, 6H), 3.86 (d, *J*=7.5 Hz, 2H), 3.74 (s, 3H), 3.31 – 3.12 (m, 3H), 3.04 – 2.95 (m, 3H), 2.91 (s, 6H), 2.89 – 2.82 (m, 2H), 2.73 – 2.60 (m, 1H), 2.10 – 1.93 (m, 3H), 1.90 – 1.73 (m, 4H), 1.66 (t, *J*=7.1 Hz, 2H), 1.48 – 1.38 (m, 2H). LCMS (ESI) *m/z*: [M+H]⁺ = 827.80.

Example 25 – Preparation of 7-(4-((dimethylamino)methyl)-3,5-dimethoxyphenyl)-*N*-(1-(5-((2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindolin-4-yl)oxy)pentanoyl)piperidin-4-yl)-5-methyl-4-oxo-4,5-dihydrothieno[3,2-*c*]pyridine-2-carboxamide formic acid (Compound D10 formic acid)



Into a stirred mixture of 7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxo-*N*-(piperidin-4-yl)thieno[3,2-*c*]pyridine-2-carboxamide (25.0 mg, 0.052 mmol, 1.00 equiv) and 5-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]oxy]pentanoic acid (19.3 mg, 0.052 mmol, 1.00 equiv) in DMF (0.50 mL) was added HATU (49.0 mg, 0.129 mmol, 2.50 equiv) at 0 °C under nitrogen atmosphere. After 10 minutes, to the above mixture was added DIEA (33.3 mg, 0.258 mmol, 5.00 equiv) at 0 °C under nitrogen atmosphere and stirred for 10 minutes. Then the mixture was allowed to stir at room temperature for 2 hours. The crude product was purified by Prep-HPLC (conditions: Sunfire C18 OBD Prep Column, 100A, 5 µm, 19mm*250mm; Mobile Phase A: Water (0.1% FA), Mobile Phase B: ACN; Flow rate: 25 mL/minute; Gradient: 12% B to 35% B in 15 minutes; 254/220 nm; R_t: 11.34 minutes). This resulted in 7-(4-((dimethylamino)methyl)-3,5-dimethoxyphenyl)-*N*-(1-(5-((2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindolin-4-yl)oxy)pentanoyl)piperidin-4-yl)-5-methyl-4-oxo-4,5-dihydrothieno[3,2-*c*]pyridine-2-carboxamide; formic acid (7.8 mg, 17%) as a white solid. ¹H NMR (300 MHz, Methanol-*d*₄) δ 8.56 (br s, 0.9H, FA), 8.23 (s, 1H), 7.84 (s, 1H), 7.83 – 7.76 (m, 1H), 7.47 (d, *J*=8.8 Hz, 2H), 7.06 (s, 2H), 5.14 – 5.05 (m, 1H), 4.61 – 4.52 (m, 1H), 4.36 – 4.27 (m, 4H), 4.16 – 4.05 (m, 2H), 4.01 (s, 6H), 3.74 (s, 3H), 2.85 (s, 7H), 2.81 – 2.73 (m, 3H), 2.69 – 2.59 (m, 3H), 2.14 – 2.06 (m, 1H), 2.04 – 1.87 (m, 6H), 1.66 – 1.47 (m, 2H). LCMS (ESI) *m/z*: [M+H]⁺ = 841.50.

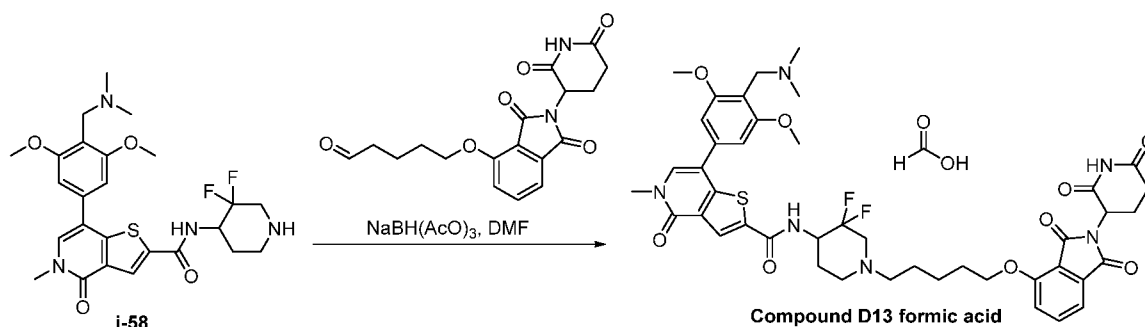
Compound D12 was prepared in a similar manner as described in compound D10.



Compound D12 formic acid

N-(7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-c]pyridin-2-yl)-1-(5-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]oxy]pentanoyl)piperidine-4-carboxamide formic acid (8.2 mg, 15%) as a light yellow solid. ¹H NMR (400 MHz, Methanol-*d*4) δ 8.57 (brs, 0.7H, FA), 7.79 (dd, *J* = 8.6, 7.3 Hz, 1H), 7.64 (s, 1H), 7.45 (dd, *J* = 7.6, 3.3 Hz, 2H), 7.20 (d, *J* = 3.1 Hz, 1H), 7.03 (s, 2H), 5.10 – 5.04 (m, 1H), 4.62 – 4.56 (m, 1H), 4.32 – 4.23 (m, 4H), 4.16 – 4.08 (m, 1H), 4.00 (s, 6H), 3.74 (s, 3H), 3.23 – 3.15 (m, 1H), 2.79 (s, 6H), 2.76 – 2.59 (m, 6H), 2.15 – 2.07 (m, 1H), 1.99 – 1.84 (m, 7H), 1.81 – 1.58 (m, 2H). LCMS (ESI) *m/z*: [M+H]⁺ = 841.35.

Example 26 – Preparation of 7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-*N*-[1-(5-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]oxy]pentyl)-3,3-difluoropiperidin-4-yl]-5-methyl-4-oxothieno[3,2-c]pyridine-2-carboxamide formic acid (Compound D13 formic acid)

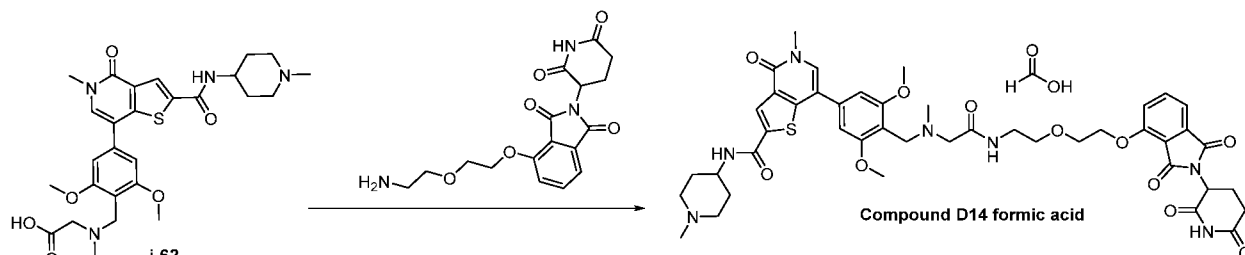


To a solution of *N*-(3,3-difluoropiperidin-4-yl)-7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-c]pyridine-2-carboxamide (40.0 mg, 0.077 mmol, 1.00 equiv) and 5-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]oxy]pentanal (30.29 mg, 0.085 mmol, 1.1 equiv) in DMF (1 mL) was added NaBH(AcO)₃ (32.6 mg, 0.154 mmol, 2 equiv). The resulting solution was stirred at room temperature for 2 hours. Without any additional work-up, the mixture was purified by Prep-HPLC (conditions: SunFire C18 OBD Prep Column, 100Å, 5 μm, 19 mm X 250 mm; Mobile Phase A: Water (0.05% FA), Mobile Phase B: ACN; Flow rate: 25 mL/minute; Gradient: 13 B to 25 B in 10 minutes; 254 nm) to afford 7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-*N*-[1-(5-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]oxy]pentyl)-3,3-difluoropiperidin-4-yl]-5-methyl-4-oxothieno[3,2-c]pyridine-2-carboxamide formic acid (20.9 mg, 29.78%) as a white solid. ¹H NMR (400 MHz, DMSO-*d*6) δ 11.11 (s, 1H), 8.87 (d, *J* = 8.8 Hz, 1H), 8.59 (s, 1H), 8.15 (s, 0.3H, FA), 7.97 (s, 1H), 7.82 (t, *J* = 7.9 Hz, 1H), 7.54 (d, *J* = 8.6 Hz, 1H), 7.45 (d, *J* = 7.3 Hz, 1H), 6.96 (s, 2H), 5.09 (dd, *J* = 12.9, 5.4 Hz, 1H), 4.38 – 4.20 (m, 3H), 3.88 (s, 6H), 3.79 (s, 2H), 3.63 (s, 3H), 3.15 (s, 1H), 2.96 – 2.83 (m, 2H), 2.70 – 2.56 (m, 3H), 2.41 (s,

8H), 2.19 (t, $J=11.4$ Hz, 1H), 2.08 – 2.00 (m, 1H), 1.92 – 1.73 (m, 4H), 1.58 – 1.43 (m, 4H). LCMS (ESI) m/z : $[M+H]^+ = 863.35$.

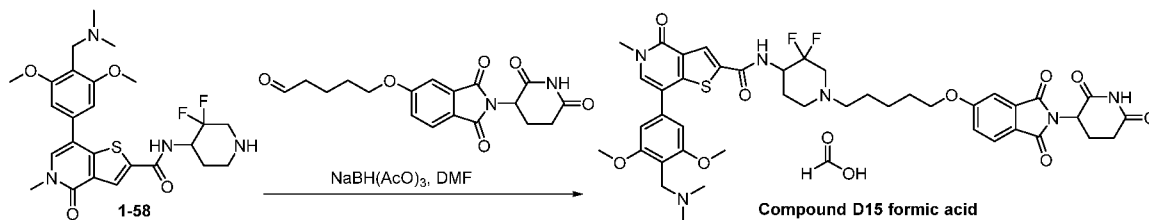
Example 27 – Preparation of 7-(4-[[[2-(2-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-

yl]oxy]ethoxy)ethyl] carbamoyl]methyl)(methyl)amino]methyl]-3,5-dimethoxyphenyl)-5-methyl-N-(1-methylpiperidin-4-yl)-4-oxothieno[3,2-c]pyridine-2-carboxamide formic acid (Compound D14 formic acid)



To a stirred mixture of [[(2,6-dimethoxy-4-[5-methyl-2-[(1-methylpiperidin-4-yl)carbamoyl]-4-oxothieno[3,2-c]pyridin-7-yl]phenyl)methyl](methyl)amino]acetic acid (50.00 mg, 0.076 mmol, 1.00 equiv) and 4-[2-(2-aminoethoxy)ethoxy]-2-(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione trifluoroacetic acid (36.20 mg, 0.076 mmol, 1.00 equiv) in DMF (1.00 mL) was added HATU (72.38 mg, 0.190 mmol, 2.50 equiv) at 0 °C under atmosphere. After 10 minutes, DIEA (49.20 mg, 0.381 mmol, 5.00 equiv) was added at 0 °C under nitrogen atmosphere, and the reaction mixture was then stirred for 10 minutes. Then the mixture was allowed to stir at room temperature for 3 hours. The crude product (0.1% TA) was concentrated, purified by Prep-TLC (DCM/MeOH = 10:1) to afford crude product. Then the crude product was purified by Prep-HPLC (conditions: Sunfire C18 OBD Prep Column, 100Å, 5 µm, 19 mm*250 mm; Mobile Phase A: Water (0.05% FA), Mobile Phase B: ACN; Flow rate: 25 mL/minute; Gradient: 12 B to 35 B in 12 minutes; 254 nm; R_T : 11.68 minutes). This resulted in 7-(4-[[[2-(2-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-4-yl]oxy]ethoxy)ethyl]carbamoyl]methyl)(methyl)amino]methyl]-3,5-dimethoxyphenyl)-5-methyl-N-(1-methylpiperidin-4-yl)-4-oxothieno[3,2-c]pyridine-2-carboxamide formic acid (3.0 mg, 7.96%) as a white solid. ^1H NMR (400 MHz, Methanol- d_4) δ 8.45 (s, 1.0H, FA), 8.21 (s, 1H), 7.78 (s, 1H), 7.64 (dd, $J=8.6, 7.2$ Hz, 1H), 7.33 (dd, $J=7.8, 2.1$ Hz, 2H), 6.88 (s, 2H), 5.07 (dd, $J=12.7, 5.5$ Hz, 1H), 4.32 – 4.26 (m, 2H), 4.17 – 4.08 (m, 1H), 4.02 (s, 2H), 3.92 (s, 6H), 3.90 – 3.86 (m, 2H), 3.73 (s, 3H), 3.69 (t, $J=5.2$ Hz, 2H), 3.54 – 3.43 (m, 6H), 3.09 (t, $J=12.2$ Hz, 2H), 2.91 – 2.80 (m, 4H), 2.78 – 2.61 (m, 2H), 2.56 (s, 3H), 2.27 – 2.18 (m, 2H), 2.14 – 2.06 (m, 1H), 2.02 – 1.89 (m, 2H). LCMS (ESI) m/z : $[M+H]^+ = 886.20$.

Example 28 – Preparation of 7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-N-[1-(5-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-5-yl]oxy]pentyl)-3,3-difluoropiperidin-4-yl]-5-methyl-4-oxothieno[3,2-c]pyridine-2-carboxamide formic acid (Compound D15 formic acid)



To a solution of *N*-(3,3-difluoropiperidin-4-yl)-7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-5-methyl-4-oxothieno[3,2-c]pyridine-2-carboxamide (40.0 mg, 0.077 mmol, 1.00 equiv) and 5-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-5-yl]oxy]pentanal (30.3 mg, 0.085 mmol, 1.1 equiv) in DMF (1 mL) was added NaBH(AcO)₃ (32.6 mg, 0.154 mmol, 2 equiv). The resulting solution was stirred at room temperature for 2 hours. Without any additional work-up, the mixture was purified by Prep-HPLC (conditions: SunFire C18 OBD Prep Column, 100Å, 5 µm, 19 mm X 250 mm; Mobile Phase A: Water (0.05% FA), Mobile Phase B: ACN; Flow rate: 25 mL/minute; Gradient: 15 B to 25 B in 12 minutes; 254 nm) to afford 7-[4-[(dimethylamino)methyl]-3,5-dimethoxyphenyl]-*N*-[1-(5-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisindol-5-yl]oxy]pentyl)-3,3-difluoropiperidin-4-yl]-5-methyl-4-oxothieno[3,2-c]pyridine-2-carboxamide formic acid (14 mg, 19.81%) as a white solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.12 (s, 1H), 8.88 (d, *J* = 8.8 Hz, 1H), 8.60 (s, 1H), 8.15 (s, 0.3H, FA), 7.98 (s, 1H), 7.84 (d, *J* = 8.3 Hz, 1H), 7.44 (d, *J* = 2.3 Hz, 1H), 7.36 (dd, *J* = 8.3, 2.3 Hz, 1H), 6.97 (s, 2H), 6.53 (s, 0.3H, FA salt), 5.13 (dd, *J* = 12.9, 5.3 Hz, 1H), 4.35 (s, 1H), 4.20 (t, *J* = 6.5 Hz, 2H), 3.88 (s, 6H), 3.82 (s, 2H), 3.63 (s, 3H), 3.15 (s, 1H), 2.95 – 2.84 (m, 2H), 2.65 – 2.55 (m, 3H), 2.44 (s, 8H), 2.18 (t, *J* = 11.3 Hz, 1H), 2.10 – 2.01 (m, 1H), 1.91 – 1.74 (m, 4H), 1.57 – 1.41 (m, 4H). LCMS (ESI) *m/z*: [M+H]⁺ = 863.35.

Example 29 – Preparation of Compounds D16-D90

In analogy to the procedures described in the examples above, compounds D16-D90 were prepared using the appropriate starting materials

Compound No.	LCMS	¹ H NMR
D16	LCMS (ESI) <i>m/z</i> : [M+H] ⁺ = 863.35	¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 11.11 (s, 1H), 8.87 (d, <i>J</i> = 8.8 Hz, 1H), 8.59 (s, 1H), 8.15 (s, 0.3H, FA), 7.97 (s, 1H), 7.82 (t, <i>J</i> = 7.9 Hz, 1H), 7.54 (d, <i>J</i> = 8.6 Hz, 1H), 7.45 (d, <i>J</i> = 7.3 Hz, 1H), 6.96 (s, 2H), 5.09 (dd, <i>J</i> = 12.9, 5.4 Hz, 1H), 4.38 – 4.20 (m, 3H), 3.88 (s, 6H), 3.79 (s, 2H), 3.63 (s, 3H), 3.15 (s, 1H), 2.96 – 2.83 (m, 2H), 2.70 – 2.56 (m, 3H), 2.41 (s, 8H), 2.19 (t, <i>J</i> = 11.4 Hz, 1H), 2.08 – 2.00 (m, 1H), 1.92 – 1.73 (m, 4H), 1.58 – 1.43 (m, 4H).

Compound No.	LCMS	¹ H NMR
D17	879.15	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.96 (s, 1H), 8.89 (d, J = 8.8 Hz, 1H), 8.60 (s, 1H), 8.17 (s, 2H, FA), 8.01 (s, 1H), 7.53 (d, J = 8.8 Hz, 1H), 7.34 (d, J = 1.6 Hz, 1H), 7.25 (d, J = 1.7 Hz, 1H), 7.07 (d, J = 7.6 Hz, 2H), 5.15 – 4.95 (m, 1H), 4.47 – 4.14 (m, 3H), 3.89 (s, 3H), 3.62 (s, 3H), 3.59 – 3.52 (m, 2H), 3.33 – 3.14 (m, 4H), 3.03 – 2.79 (m, 3H), 2.69 – 2.54 (m, 8H), 2.46 – 2.26 (m, 3H), 2.25 – 2.16 (m, 7H), 2.05 – 1.90 (m, 1H), 1.90 – 1.69 (m, 2H).
D18	929.25	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.95 (s, 1H), 8.95 (d, J = 9.0 Hz, 1H), 8.62 (d, J = 13.0 Hz, 1H), 8.14 (s, 0.47H, FA), 8.00 (s, 1H), 7.50 (d, J = 8.2 Hz, 1H), 7.00 (s, 2H), 6.56 – 6.45 (m, 2H), 5.04 (dd, J = 13.2, 5.1 Hz, 1H), 4.62 (s, 2H), 4.31 (d, J = 16.9 Hz, 1H), 4.18 (d, J = 17.0 Hz, 2H), 4.00 (s, 2H), 3.90 (s, 6H), 3.65 (d, J = 9.8 Hz, 7H), 3.22 (dd, J = 15.8, 3.3 Hz, 2H), 3.01 – 2.84 (m, 3H), 2.64 – 2.53 (m, 6H), 2.44 – 2.31 (m, 5H), 2.02 – 1.88 (m, 3H), 1.88 – 1.66 (m, 4H).
D19	915.25	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.96 (s, 1H), 8.98 (s, 1H, TFA salt), 8.92 (d, J = 8.8 Hz, 1H), 8.61 (s, 1H), 8.02 (s, 1H), 7.53 (d, J = 8.2 Hz, 1H), 7.03 (s, 2H), 6.56 – 6.48 (m, 2H), 5.05 (dd, J = 13.1, 5.0 Hz, 1H), 4.50 – 4.10 (m, 7H), 3.93 (s, 6H), 3.74 (s, 4H), 3.64 (s, 3H), 3.04 – 2.84 (m, 4H), 2.81 – 2.76 (m, 8H), 2.69 – 2.55 (m, 5H), 2.40 – 2.30 (m, 2H), 2.12 – 1.94 (m, 5H), 1.91 – 1.75 (m, 2H).
D20	752.2	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.97 (s, 1H), 9.63 (s, 1H), 8.23 (s, 2H, FA), 8.14 (s, 1H), 7.37 (d, J = 8.1 Hz, 1H), 7.14 (s, 2H), 6.72 – 6.64 (m, 2H), 5.13 – 5.04 (m, 1H), 4.31 (d, J = 16.6 Hz, 1H), 4.18 (d, J = 16.6 Hz, 1H), 3.86 (s, 6H), 3.81 (s, 2H), 3.68 (s, 3H), 3.56 (s, 6H), 3.17 (s, 2H), 2.91 (m, J = 17.7, 13.4, 5.4 Hz, 1H), 2.59 (d, J = 17.0 Hz, 2H), 2.45 (d, J = 6.9 Hz, 2H), 2.40 – 2.22 (m, 5H), 2.04 – 1.93 (m, 1H), 1.72 (t, J = 5.4 Hz, 4H).
D21	734.34	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.99 (s, 1H), 9.87 (d, J = 53.7 Hz, 2H, TFA), 8.26 (d, J = 2.0 Hz, 1H), 7.90 (s, 1H), 7.41 (d, J = 8.8 Hz, 1H), 7.14 (d, J = 2.1 Hz, 1H), 6.91 (d, J = 2.2 Hz, 2H), 6.70 (dd, J = 4.8, 2.4 Hz, 2H), 5.07 (dd, J = 13.3, 5.1 Hz, 1H), 4.50 – 4.28 (m, 3H), 4.20 (d, J = 17.0 Hz, 2H), 3.95 (s, 6H), 3.73 (s, 2H), 3.65 (s, 5H), 2.96 (s, 3H), 2.78 (d, J = 4.7 Hz, 2H), 2.63 (s, 2H), 2.43 – 2.31 (m, 1H), 2.12 (d, J = 13.6 Hz, 2H), 2.03 – 1.79 (m, 3H).

Compound No.	LCMS	¹ H NMR
D22	818.15	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.97 (s, 1H), 9.51 (s, 1H, TFA), 9.05 (s, 1H, TFA), 8.61 (s, 1H), 8.03 (s, 1H), 7.60 (d, J = 8.4 Hz, 1H), 7.19 – 7.10 (m, 2H), 7.06 (s, 2H), 5.07 (dd, J = 13.3, 5.1 Hz, 1H), 4.64 (s, 1H), 4.44 – 4.30 (m, 3H), 4.24 (d, J = 17.0 Hz, 1H), 3.99 (d, J = 12.7 Hz, 2H), 3.96 (s, 6H), 3.76 (s, 1H), 3.65 (s, 3H), 3.50 (m, 1H), 3.40 (m, 1H), 3.25 (m, 1H), 3.21 (m, 2H), 3.00 – 2.70 (m, 5H), 2.69 – 2.55 (m, 2H), 2.45 – 2.29 (m, 2H), 2.09 (s, 2H), 2.03 – 1.93 (m, 1H).
D23	854.35	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.36 (s, 1H), 8.30 (s, 0.3H, FA), 7.85 (s, 1H), 7.76 (d, J = 8.5 Hz, 1H), 7.46 (d, J = 2.3 Hz, 1H), 7.33 (dd, J = 8.6, 2.3 Hz, 1H), 7.05 (s, 2H), 5.11 (dd, J = 12.5, 5.5 Hz, 1H), 4.50 – 4.37 (m, 1H), 4.31 (s, 2H), 4.02 (s, 6H), 3.75 (s, 3H), 3.69 (s, 4H), 3.40 – 3.35 (m, 2H), 3.31 – 3.21 (m, 2H), 3.19 (t, J = 9.9 Hz, 1H), 2.97 (d, J = 12.0 Hz, 1H), 2.89 (ddd, J = 18.3, 14.2, 5.1 Hz, 1H), 2.78 (d, J = 3.2 Hz, 1H), 2.73 (d, J = 9.9 Hz, 1H), 2.47 (dd, J = 28.7, 12.4 Hz, 1H), 2.40 (s, 3H), 2.31 (t, J = 11.7 Hz, 1H), 2.19 – 2.04 (m, 1H), 2.01 (dd, J = 11.9, 4.4 Hz, 1H), 1.96 (d, J = 7.4 Hz, 1H).
D24	LCMS (ESI) m/z: [M+H] ⁺ = 846.25	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.37 (d, J = 1.8 Hz, 1H), 7.89 (s, 1H), 7.49 (d, J = 8.2 Hz, 1H), 7.37 (d, J = 11.8 Hz, 2H), 7.08 (s, 2H), 5.16 (dd, J = 13.3, 5.0 Hz, 1H), 4.74 (m, 1H), 4.43 (d, J = 6.3 Hz, 4H), 4.10 (d, J = 12.5 Hz, 1H), 4.02 (s, 6H), 3.95 (d, J = 12.6 Hz, 2H), 3.87 (s, 1H), 3.76 (s, 3H), 3.53 (d, 2H), 3.22 (s, 1H), 2.92 (s, 8H), 2.89 – 2.74 (m, 2H), 2.60 – 2.42 (m, 1H), 2.21 (s, 5H), 1.90 (t, J = 11.8 Hz, 2H).
D25	LCMS (ESI) m/z: [M+H] ⁺ = 846.25.	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.36 (s, 1H), 7.88 (s, 1H), 7.67 (d, J = 9.2 Hz, 1H), 7.13-7.03 (t, 4H), 5.12 (dd, J = 13.2, 5.1 Hz, 1H), 4.75 (s, 1H), 4.52 – 4.33 (m, 4H), 4.12 (d, J = 12.9 Hz, 2H), 4.02 (s, 6H), 3.93 (s, 1H), 3.75 (s, 3H), 3.65 - 3.46 (m, 3H), 3.25 (s, 1H), 2.99 (d, J = 12.6 Hz, 2H), 2.92 – 2.73 (m, 7H), 2.57 – 2.40 (m, 1H), 2.27 (s, 1H), 2.21 (s, 5H), 1.90 (q, J = 12.2, 11.6 Hz, 2H).
D26	LCMS (ESI) m/z: [M+H] ⁺ = 943.45.	¹ H NMR (300 MHz, DMSO-d ₆ , D ₂ O) δ 8.45 (s, 1H), 7.90 (s, 1H), 7.75 (d, J = 8.5 Hz, 1H), 7.40 (d, J = 2.0 Hz, 1H), 7.31 (dd, J = 8.6, 2.3 Hz, 1H), 6.99 – 6.95 (m, 2H), 5.02 (dd, J = 12.8, 5.6 Hz, 1H), 4.76 – 4.58 (m, 1H), 4.35 – 4.12 (m, 4H), 3.96 – 3.83 (m, 7H), 3.72 – 3.48 (m, 7H), 3.39 (d, J = 11.5 Hz, 2H), 3.31 – 3.07 (m, 7H), 2.97 (t, J = 12.3 Hz, 2H), 2.86 (s, 3H), 2.83 – 2.72 (m, 1H), 2.69 – 2.55 (m, 2H), 2.19 – 2.00 (m, 3H), 1.87 – 1.56 (m, 5H), 1.49 – 1.32 (m, 2H).

Compound No.	LCMS	¹ H NMR
D27	LCMS (ESI) m / z: [M+H] ⁺ = 935.55.	¹ H NMR (300 MHz, DMSO-d ₆ , D ₂ O) δ 8.45 (s, 1H), 7.90 (s, 1H), 7.75 (d, <i>J</i> = 8.5 Hz, 1H), 7.40 (d, <i>J</i> = 2.0 Hz, 1H), 7.31 (dd, <i>J</i> = 8.6, 2.3 Hz, 1H), 6.99 – 6.95 (m, 2H), 5.02 (dd, <i>J</i> = 12.8, 5.6 Hz, 1H), 4.76 – 4.58 (m, 1H), 4.35 – 4.12 (m, 4H), 3.96 – 3.83 (m, 7H), 3.72 – 3.48 (m, 7H), 3.39 (d, <i>J</i> = 11.5 Hz, 2H), 3.31 – 3.07 (m, 7H), 2.97 (t, <i>J</i> = 12.3 Hz, 2H), 2.86 (s, 3H), 2.83 – 2.72 (m, 1H), 2.69 – 2.55 (m, 2H), 2.19 – 2.00 (m, 3H), 1.87 – 1.56 (m, 5H), 1.49 – 1.32 (m, 2H).
D28	LCMS (ESI) m/z: [M+H] ⁺ = 875.50.	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.58 (s, 1H, FA), 8.35 (s, 1H), 7.85 – 7.78 (m, 2H), 7.42 (d, <i>J</i> = 2.2 Hz, 1H), 7.33 (dd, <i>J</i> = 8.3, 2.3 Hz, 1H), 7.02 (s, 2H), 5.12 (dd, <i>J</i> = 12.2, 5.4 Hz, 1H), 4.52 – 4.39 (m, 1H), 4.36 (s, 2H), 4.20 (t, <i>J</i> = 6.3 Hz, 2H), 4.06 (t, <i>J</i> = 8.0 Hz, 4H), 4.00 (s, 6H), 3.74 (s, 3H), 3.26 – 3.18 (m, 1H), 3.07 – 2.97 (m, 1H), 2.89 – 2.69 (m, 3H), 2.59 – 2.36 (m, 5H), 2.34 – 2.23 (m, 1H), 2.20 – 2.07 (m, 1H), 2.02 – 1.85 (m, 4H), 1.69 – 1.54 (m, 4H).
D29	LCMS (ESI) m/z: [M+H] ⁺ = 853.45.	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.52 (s, 2H, FA), 8.22 (s, 1H), 7.86 – 7.76 (m, 2H), 7.46 (dd, <i>J</i> = 8.3, 2.4 Hz, 2H), 7.05 (s, 2H), 5.09 (dd, <i>J</i> = 12.5, 5.2 Hz, 1H), 4.55 (d, <i>J</i> = 13.7 Hz, 1H), 4.48 (s, 2H), 4.34 – 4.26 (m, 2H), 4.20 (t, <i>J</i> = 8.2 Hz, 4H), 4.14 – 4.05 (m, 2H), 4.02 (s, 6H), 3.74 (s, 3H), 3.29 – 3.18 (m, 1H), 2.86 – 2.60 (m, 6H), 2.58 – 2.46 (m, 2H), 2.14 – 1.87 (m, 7H), 1.69 – 1.44 (m, 2H).
D30	LCMS (ESI) m/z: [M+H] ⁺ = 922.35	¹ H NMR (400 MHz, DMSO-d ₆ with a drop of D ₂ O) δ 9.07 (d, <i>J</i> = 8.5 Hz, 1H, FA salt), 8.49 (s, 1H), 7.91 (s, 1H), 7.76 (dd, <i>J</i> = 8.5, 7.3 Hz, 1H), 7.42 (dd, <i>J</i> = 11.9, 7.9 Hz, 2H), 6.92 (s, 2H), 5.01 (dd, <i>J</i> = 12.8, 5.5 Hz, 1H), 4.53 (br s, 1H), 4.28 (s, 4H), 3.85 – 3.31 (m, 6H), 3.78 (s, 4H), 3.60 (s, 3H), 3.55 (d, <i>J</i> = 5.6 Hz, 2H), 3.35 – 3.21 (m, 3H), 2.87 – 2.55 (m, 10H), 2.48 – 2.40 (m, 2H), 2.09 – 1.93 (m, 3H).
D31	LCMS (ESI) m/z: [M+H] ⁺ = 925.15.	¹ H NMR (400 MHz, DMSO-d ₆) δ 11.10 (s, 1H), 8.27 (s, 1H), 8.14 (s, 0.4H, FA), 7.98 (dd, <i>J</i> = 5.3, 3.5 Hz, 2H), 7.96 – 7.86 (m, 2H), 7.79 (d, <i>J</i> = 7.0 Hz, 2H), 7.56 (dd, <i>J</i> = 8.6, 7.1 Hz, 1H), 7.03 (dd, <i>J</i> = 13.0, 7.8 Hz, 2H), 6.86 (s, 1H), 6.48 (t, <i>J</i> = 5.9 Hz, 1H), 5.05 (dd, <i>J</i> = 12.7, 5.4 Hz, 1H), 3.85 (s, 2H), 3.71 (d, <i>J</i> = 16.7 Hz, 1H), 3.60 (s, 3H), 3.52 – 3.37 (m, 2H), 3.23 (q, <i>J</i> = 6.5 Hz, 3H), 2.99 (d, <i>J</i> = 6.6 Hz, 2H), 2.88 (ddd, <i>J</i> = 16.7, 13.7, 5.2 Hz, 1H), 2.59 (d, <i>J</i> = 18.0 Hz, 2H), 2.49 – 2.41 (m, 1H), 2.22 (s, 1H), 2.06 – 1.94 (m, 1H), 1.66 – 1.45 (m, 2H), 1.42 – 1.00 (m, 11H).

Compound No.	LCMS	¹ H NMR
D32	LCMS (ESI) m/z: [M+H] ⁺ = 886.20	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.45 (s, 1.0H, FA), 8.21 (s, 1H), 7.78 (s, 1H), 7.64 (dd, <i>J</i> = 8.6, 7.2 Hz, 1H), 7.33 (dd, <i>J</i> = 7.8, 2.1 Hz, 2H), 6.88 (s, 2H), 5.07 (dd, <i>J</i> = 12.7, 5.5 Hz, 1H), 4.32 – 4.26 (m, 2H), 4.17 – 4.08 (m, 1H), 4.02 (s, 2H), 3.92 (s, 6H), 3.90 – 3.86 (m, 2H), 3.73 (s, 3H), 3.69 (t, <i>J</i> = 5.2 Hz, 2H), 3.54 – 3.43 (m, 6H), 3.09 (t, <i>J</i> = 12.2 Hz, 2H), 2.91 – 2.80 (m, 4H), 2.78 – 2.61 (m, 2H), 2.56 (s, 3H), 2.27 – 2.18 (m, 2H), 2.14 – 2.06 (m, 1H), 2.02 – 1.89 (m, 2H).
D33	LCMS (ESI) m/z: [M+H] ⁺ = 921.65	
D34	LCMS (ESI) m/z: [M+H] ⁺ = 921.45	
D35	LCMS (ESI) m/z: [M+H] ⁺ = 935.6	
D36	LCMS (ESI) m/z: [M+H] ⁺ = 907.4	
D37	LCMS (ESI) m/z: [M+H] ⁺ = 893.45	
D38	LCMS (ESI) m/z: [M+H] ⁺ = 879.25	
D39	LCMS (ESI) m/z: [M+H] ⁺ = 893.5	
D40	LCMS (ESI) m/z: [M+H] ⁺ = 921.75	
D41	LCMS (ESI) m/z: [M+H] ⁺ = 893.15	
D42	LCMS (ESI) m/z: [M+H] ⁺ = 907.65	
D43	LCMS (ESI) m/z: [M+H] ⁺ = 893.3	¹ H NMR (400 MHz, DMSO-d ₆) δ 11.07 (s, 1H), 8.82 – 8.73 (m, 1H), 8.36 (d, <i>J</i> = 4.1 Hz, 1H), 8.22 (s, 2H, FA), 7.92 (d, <i>J</i> = 4.3 Hz, 1H), 7.65 (dd, <i>J</i> = 8.5, 6.6 Hz, 1H), 7.32 (d, <i>J</i> = 2.3 Hz, 1H), 7.26 – 7.18 (m, 1H), 6.91 (s, 2H), 5.11 – 5.00 (m, 1H), 3.85 (d, <i>J</i> = 2.3 Hz, 6H), 3.61 (d, <i>J</i> = 3.9 Hz, 6H), 3.45 – 3.38 (m, 4H), 3.25 (t, <i>J</i> = 5.8 Hz, 1H), 3.19 (t, <i>J</i> = 6.5 Hz, 1H), 2.93 – 2.83 (m, 1H), 2.72 – 2.66 (m, 1H), 2.65 – 2.60 (m, 2H), 2.59 – 2.53 (m, 7H), 2.48 – 2.44 (m, 3H), 2.26 (d, <i>J</i> = 2.3 Hz, 8H), 2.05 – 1.94 (m, 3H), 1.55 (dd, <i>J</i> = 12.5, 6.1 Hz, 1H), 1.46 – 1.36 (m, 1H), 1.08 – 0.97 (m, 1H).

Compound No.	LCMS	¹ H NMR
D44	LCMS (ESI) m/z: [M+H] ⁺ = 893.3	
D45	929.45	
D46	943.45	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.07 (s, 1H), 8.92 (d, J = 8.6 Hz, 1H), 8.59 (d, J = 8.7 Hz, 1H), 8.22 (s, 1H, FA), 7.96 (s, 1H), 7.66 (d, J = 8.4 Hz, 1H), 6.92 (s, 2H), 6.81 (s, 1H), 6.73 – 6.63 (m, 1H), 5.06 (dd, J = 12.6, 5.4 Hz, 1H), 4.75 – 4.07 (m, 4H), 4.04 – 3.93 (m, 4H), 3.85 (s, 6H), 3.63 (s, 4H), 3.54 – 3.51 (m, 4H), 2.93 – 2.55 (m, 8H), 2.20 (s, 7H), 2.12 – 2.00 (m, 3H), 1.93 – 1.82 (m, 2H).
D47	LCMS (ESI) m/z: [M+H] ⁺ = 461.45	
D48	LCMS (ESI) m/z: [M+H] ⁺ = 951.4	
D49	LCMS (ESI) m/z: [M+H] ⁺ = 937.4	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.09 (s, 1H), 8.97 (t, J = 5.8 Hz, 1H), 8.40 (s, 1H), 8.16 (s, 1H FA), 7.99 (s, 1H), 7.69 (d, J = 8.5 Hz, 1H), 7.35 (d, J = 2.2 Hz, 1H), 7.27 (dd, J = 8.6, 2.2 Hz, 1H), 6.99 (s, 2H), 5.08 (dd, J = 12.7, 5.4 Hz, 1H), 4.09 (t, J = 6.5 Hz, 1H), 4.00 (s, 2H), 3.90 (s, 6H), 3.62 (s, 3H), 3.60 – 3.49 (m, 4H), 3.46 – 3.42 (m, 6H), 3.02 – 2.60 (m, 9H), 2.59 – 2.55 (m, 7H), 2.37 (t, J = 7.0 Hz, 2H), 2.07 – 1.87 (m, 3H), 1.78 – 1.68 (m, 2H), 1.67 – 1.57 (m, 4H), 1.49 – 1.39 (m, 1H).
D50	LCMS (ESI) m/z: [M+H] ⁺ = 923.4	
D51	LCMS (ESI) m/z: [M+H] ⁺ = 907.4	
D52	LCMS (ESI) m/z: [M+H] ⁺ = 893.4	
D53	LCMS (ESI) m/z: [M+H] ⁺ = 879.	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.09 (s, 1H), 8.80 (t, J = 5.7 Hz, 1H), 8.36 (s, 1H), 7.92 (s, 1H), 7.66 (d, J = 8.5 Hz, 1H), 7.32 (d, J = 2.2 Hz, 1H), 7.23 (dd, J = 8.7, 2.3 Hz, 1H), 6.90 (s, 2H), 5.07 (dd, J = 12.8, 5.4 Hz, 1H), 3.58 (d, J = 12.5 Hz, 5H), 3.37 (d, J = 13.7 Hz, 8H), 3.24 (t, J = 6.2 Hz, 2H), 2.89 (td, J = 17.8, 15.7, 5.3 Hz, 1H), 2.69 (s, 3H), 2.55 (s, 3H), 2.34 (d, J = 6.2 Hz, 3H), 2.22 (s, 6H), 2.17 (d, J = 8.5 Hz, 1H), 2.01 (s, 1H), 1.89 (dd, J = 12.1, 6.6 Hz, 2H).
D54	LCMS (ESI) m/z: [M+H] ⁺ = 921.25	

Compound No.	LCMS	¹ H NMR
D55	LCMS (ESI) m/z: [M+H] ⁺ = 907.35	
D56	LCMS (ESI) m/z: [M+H] ⁺ = 454.5	
D57	LCMS (ESI) m/z: [M+H] ⁺ = 893.35	
D58	LCMS (ESI) m/z: [M+H] ⁺ = 907.35	
D59	LCMS (ESI) m/z: [M+H] ⁺ = 863.50.	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.56 (s, 1H, FA), 7.83 – 7.74 (m, 1H), 7.67 (s, 1H), 7.45 (d, <i>J</i> = 7.8 Hz, 2H), 7.25 (d, <i>J</i> = 1.9 Hz, 1H), 7.06 (s, 2H), 5.10 (dd, <i>J</i> = 12.2, 5.4 Hz, 1H), 4.36 (s, 2H), 4.27 (t, <i>J</i> = 6.1 Hz, 2H), 4.02 (s, 6H), 3.74 (s, 3H), 3.24 – 3.17 (m, 1H), 3.03 – 2.93 (m, 2H), 2.88 (s, 6H), 2.83 – 2.67 (m, 3H), 2.57 – 2.42 (m, 3H), 2.27 (t, <i>J</i> = 11.1 Hz, 1H), 2.19 – 2.09 (m, 2H), 1.99 – 1.88 (m, 3H), 1.71 – 1.57 (m, 4H).
D60		
D61	LCMS (ESI) m/z: [M+H] ⁺ = 469.3	
D62	LCMS (ESI) m/z: [M+H] ⁺ = 909.2	
D63	LCMS (ESI) m/z: [M+H] ⁺ = 893.25	¹ H NMR (400 MHz, DMSO-d ₆) δ 11.10 (d, <i>J</i> = 3.2 Hz, 1H), 8.86 (dd, <i>J</i> = 26.1, 5.8 Hz, 1H), 8.55 (d, <i>J</i> = 38.1 Hz, 1H), 8.15 (s, 1H, FA), 8.04 – 7.87 (m, 1H), 7.66 (dd, <i>J</i> = 25.8, 8.5 Hz, 1H), 7.38 – 7.24 (m, 1H), 7.20 – 7.07 (m, 1H), 7.03 – 6.90 (m, 2H), 5.08 (dd, <i>J</i> = 12.7, 6.4 Hz, 1H), 4.37 – 4.25 (m, 1H), 4.04 (s, 2H), 3.89 (d, <i>J</i> = 15.0 Hz, 6H), 3.77 – 3.53 (m, 7H), 3.45 – 3.41 (m, 3H), 3.24 (s, 3H), 3.16 – 3.04 (m, 2H), 3.03 – 2.73 (m, 4H), 2.64 – 2.55 (m, 10H), 2.41 – 2.36 (m, 2H), 2.05 – 1.85 (m, 2H).
D64	LCMS (ESI) m/z: [M+H] ⁺ = 865.25	
D65	LCMS (ESI) m/z: [M+H] ⁺ = 879.35	
D66	LCMS (ESI) m/z: [M+H] ⁺ = 879.3	
D67	921.5	

Compound No.	LCMS	¹ H NMR
D68	LCMS (ESI) m/z: [M+H] ⁺ = 893.5	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.08 (s, 1H), 8.80 (dd, <i>J</i> = 11.0, 5.8 Hz, 1H), 8.54 (s, 1H), 8.14 (s, 1H FA), 8.01 – 7.92 (m, 1H), 7.65 (dd, <i>J</i> = 18.7, 8.5 Hz, 1H), 7.37 – 7.15 (m, 2H), 6.99 (d, <i>J</i> = 11.3 Hz, 2H), 5.11 – 5.01 (m, 1H), 4.48 – 4.20 (m, 2H), 4.13 (s, 2H), 3.92 (s, 6H), 3.62 (d, <i>J</i> = 9.3 Hz, 3H), 3.48 – 3.36 (m, 10H), 2.98 – 2.72 (m, 4H), 2.70 – 2.59 (m, 9H), 2.42 – 2.34 (m, 1H), 2.14 – 1.92 (m, 2H), 1.78 – 1.56 (m, 3H).
D69	LCMS (ESI) m/z: [M+H] ⁺ = 879.4	
D70	LCMS (ESI) m/z: [M+H] ⁺ = 865.25	
D71	LCMS (ESI) m/z: [M+H] ⁺ = 813.25.	¹ H NMR (300 MHz, Methanol-d ₄) δ 7.81 (d, <i>J</i> = 8.3 Hz, 1H), 7.46 (s, 1H), 7.42 (d, <i>J</i> = 2.2 Hz, 1H), 7.33 (dd, <i>J</i> = 8.4, 2.3 Hz, 1H), 6.95 (s, 2H), 6.41 (s, 1H), 5.11 (dd, <i>J</i> = 12.4, 5.4 Hz, 1H), 4.37 (d, <i>J</i> = 13.5 Hz, 1H), 4.22 (t, <i>J</i> = 5.8 Hz, 2H), 4.06 (s, 2H), 3.99 – 3.92 (m, 7H), 3.71 (s, 3H), 3.59 – 3.51 (m, 1H), 3.06 – 2.93 (m, 1H), 2.91 – 2.68 (m, 4H), 2.66 – 2.51 (m, 8H), 2.23 – 2.05 (m, 3H), 1.96 – 1.82 (m, 4H), 1.54 – 1.35 (m, 2H).
D72	LCMS (ESI) m/z: [M+H] ⁺ = 907.45	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.09 (s, 1H), 9.04 – 8.96 (m, 1H), 8.39 (s, 1H), 8.29 (s, 2H, FA), 7.94 (s, 1H), 7.68 (dd, <i>J</i> = 8.5, 3.4 Hz, 1H), 7.35 (d, <i>J</i> = 2.7 Hz, 1H), 7.27 (d, <i>J</i> = 7.3 Hz, 1H), 6.91 – 6.86 (m, 2H), 5.07 (dd, <i>J</i> = 12.7, 5.3 Hz, 1H), 4.44 – 4.34 (m, 1H), 3.84 (s, 6H), 3.62 (s, 4H), 3.53 – 3.48 (m, 10H), 2.93 – 2.82 (m, 2H), 2.63 – 2.55 (m, 6H), 2.33 – 2.23 (m, 3H), 2.21 – 2.07 (m, 9H), 2.00 – 1.80 (m, 3H).
D73	LCMS (ESI) m/z: [M+H] ⁺ = 893.3	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.09 (s, 1H), 9.01 – 8.92 (m, 1H), 8.39 (s, 1H), 8.23 (s, 3H, FA), 7.95 (s, 1H), 7.68 (d, <i>J</i> = 8.5 Hz, 1H), 7.35 (d, <i>J</i> = 2.2 Hz, 1H), 7.27 (d, <i>J</i> = 8.8 Hz, 1H), 6.91 (s, 2H), 5.08 (dd, <i>J</i> = 12.7, 5.3 Hz, 1H), 4.33 – 4.24 (m, 1H), 3.85 (s, 6H), 3.62 (s, 5H), 3.44 (s, 5H), 2.97 – 2.81 (m, 2H), 2.77 – 2.69 (m, 3H), 2.64 – 2.53 (m, 5H), 2.39 – 2.33 (m, 3H), 2.27 (s, 6H), 2.17 – 2.09 (m, 2H), 2.04 – 1.84 (m, 4H), 1.68 (s, 2H).
D74	LCMS (ESI) m/z: [M+H] ⁺ = 893.3	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.09 (s, 1H), 9.00 – 8.93 (m, 1H), 8.37 (s, 1H), 8.20 (s, 1H, FA), 7.95 (s, 1H), 7.68 (d, <i>J</i> = 8.5 Hz, 1H), 7.35 (d, <i>J</i> = 2.2 Hz, 1H), 7.30 – 7.23 (m, 1H), 6.91 (s, 2H), 5.08 (dd, <i>J</i> = 12.8, 5.3 Hz, 1H), 4.31 – 4.19 (m, 2H), 4.12 (s, 1H), 3.92 (s, 1H), 3.87 – 3.80 (m, 7H), 3.63 – 3.56 (m, 6H), 3.45 – 3.40 (m, 8H), 2.91 – 2.83 (m, 1H), 2.64 – 2.55 (m, 5H), 2.32 – 2.20 (m, 10H), 2.08 – 1.96 (m, 1H).

Compound No.	LCMS	¹ H NMR
D75	LCMS (ESI) m/z: [M+H] ⁺ = 879.45	
D76	LCMS (ESI) m/z: [M+H] ⁺ = 907.35	
D77	LCMS (ESI) m/z: [M+H] ⁺ = 867.50.	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.24 (s, 1H), 7.87 (s, 1H), 7.80 (d, <i>J</i> = 8.4 Hz, 1H), 7.52 (d, <i>J</i> = 2.3 Hz, 1H), 7.39 (dd, <i>J</i> = 8.6, 2.3 Hz, 1H), 7.07 (s, 2H), 5.12 (dd, <i>J</i> = 12.3, 5.4 Hz, 1H), 4.60 (d, <i>J</i> = 14.2 Hz, 1H), 4.42 (s, 2H), 4.40 – 4.29 (m, 2H), 4.20 – 4.12 (m, 1H), 4.02 (s, 7H), 3.87 – 3.78 (m, 2H), 3.75 (s, 4H), 3.66 – 3.45 (m, 4H), 3.21 – 3.12 (m, 1H), 2.99 – 2.89 (m, 8H), 2.86 – 2.70 (m, 3H), 2.19 – 2.07 (m, 3H), 1.72 – 1.57 (m, 2H).
D78	LCMS (ESI) m/z: [M+H] ⁺ = 881.50.	¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 11.09 (s, 1H), 8.66 (d, <i>J</i> = 7.6 Hz, 1H), 8.41 (s, 1H), 8.23 (s, 1H, FA), 7.95 (s, 1H), 7.68 (d, <i>J</i> = 8.5 Hz, 1H), 7.36 (d, <i>J</i> = 2.3 Hz, 1H), 7.27 (dd, <i>J</i> = 8.7, 2.3 Hz, 1H), 6.91 (s, 2H), 5.08 (dd, <i>J</i> = 12.9, 5.4 Hz, 1H), 4.35 (d, <i>J</i> = 13.1 Hz, 1H), 4.05 – 3.92 (m, 3H), 3.85 (s, 6H), 3.62 (s, 3H), 3.57 (s, 2H), 3.47 – 3.41 (m, 6H), 3.17 – 3.11 (m, 1H), 2.94 – 2.83 (m, 1H), 2.76 – 2.66 (m, 1H), 2.61 – 2.55 (m, 7H), 2.22 (s, 6H), 2.06 – 1.98 (m, 1H), 1.92 – 1.79 (m, 2H), 1.55 – 1.32 (m, 2H).
D79	LCMS (ESI) m/z: [M+H] ⁺ = 889.25	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.35 (d, <i>J</i> = 1.6 Hz, 1H), 7.88 (s, 1H), 7.81 (d, <i>J</i> = 8.4 Hz, 1H), 7.51 (d, <i>J</i> = 2.2 Hz, 1H), 7.40 (d, <i>J</i> = 8.4 Hz, 1H), 7.08 (s, 2H), 5.13 (dd, <i>J</i> = 12.1, 5.3 Hz, 1H), 4.58 – 4.45 (m, 1H), 4.42 (s, 2H), 4.02 (s, 6H), 3.87 – 3.77 (m, 4H), 3.76 (s, 3H), 3.69 – 3.57 (m, 4H), 3.49 – 3.38 (m, 3H), 3.16 (d, <i>J</i> = 11.8 Hz, 1H), 3.03 – 2.97 (m, 2H), 2.92 (s, 6H), 2.90 – 2.70 (m, 3H), 2.70 – 2.41 (m, 2H), 2.19 – 1.94 (m, 3H).
D80	LCMS (ESI) m/z: [M+H] ⁺ = 841.35	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.53 (s, 2H, FA), 8.32 (s, 1H), 7.87 (s, 1H), 7.80 (dd, <i>J</i> = 8.6, 7.3 Hz, 1H), 7.47 (dd, <i>J</i> = 7.9, 4.8 Hz, 2H), 7.06 (s, 2H), 5.09 (dd, <i>J</i> = 12.7, 5.5 Hz, 1H), 4.41 – 4.31 (m, 4H), 4.23 – 4.17 (m, 1H), 4.02 (s, 6H), 3.99 – 3.82 (m, 1H), 3.75 (s, 3H), 3.49 – 3.38 (m, 2H), 2.89 (s, 6H), 2.88 – 2.82 (m, 4H), 2.78 – 2.65 (m, 2H), 2.23 – 2.12 (m, 3H), 2.06 – 1.93 (m, 8H), 1.86 – 1.75 (m, 2H).

Compound No.	LCMS	¹ H NMR
D81	LCMS (ESI) m/z: [M+H] ⁺ = 828.30 .	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.09 (s, 1H), 8.79 (s, 1H), 8.37 (s, 1H), 8.23 (s, 2H FA), 7.94 (s, 1H), 7.81 (dd, <i>J</i> = 8.5, 7.2 Hz, 1H), 7.53 (d, <i>J</i> = 8.5 Hz, 1H), 7.44 (d, <i>J</i> = 7.2 Hz, 1H), 6.91 (s, 2H), 5.08 (dd, <i>J</i> = 12.8, 5.4 Hz, 1H), 4.23 (t, <i>J</i> = 6.1 Hz, 2H), 3.84 (s, 6H), 3.62 (s, 3H), 3.53 (s, 2H), 3.17 – 3.11 (m, 3H), 2.93 – 2.88 (m, 2H), 2.64 – 2.59 (m, 2H), 2.42 – 2.31 (m, 3H), 2.19 (s, 6H), 2.07 – 1.98 (m, 1H), 1.95 – 1.84 (m, 2H), 1.81 – 1.74 (m, 2H), 1.71 – 1.54 (m, 5H), 1.30 – 1.08 (m, 3H).
D82	LCMS (ESI) m/z: [M+H] ⁺ = 838.98.	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.56 (s, 2H, FA), 8.27 (s, 1H), 7.87 – 7.77 (m, 2H), 7.47 (dd, <i>J</i> = 7.7, 2.6 Hz, 2H), 7.03 (s, 2H), 5.21 – 5.10 (m, 1H), 4.30 (t, <i>J</i> = 5.7 Hz, 2H), 4.24 (s, 2H), 4.17 – 4.08 (m, 1H), 4.00 (s, 7H), 3.75 (s, 3H), 3.29 – 3.14 (m, 2H), 3.10 – 2.98 (m, 2H), 2.95 – 2.86 (m, 1H), 2.81 – 2.69 (m, 9H), 2.50 (dd, <i>J</i> = 15.0, 8.0 Hz, 1H), 2.21 – 2.11 (m, 1H), 2.04 – 1.80 (m, 7H), 1.74 – 1.63 (m, 2H).
D83	LCMS (ESI) m/z: [M+H] ⁺ = 863.	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.11 (s, 1H), 9.40 (s, 1H, TFA), 8.63 (s, 1H), 8.45 (s, 1H), 8.01 (s, 1H), 7.86 (d, <i>J</i> = 8.3 Hz, 1H), 7.45 (d, <i>J</i> = 2.3 Hz, 1H), 7.38 (dd, <i>J</i> = 8.3, 2.3 Hz, 1H), 7.02 (s, 2H), 5.13 (dd, <i>J</i> = 12.8, 5.4 Hz, 1H), 4.26 (dd, <i>J</i> = 9.4, 5.4 Hz, 4H), 3.93 (s, 7H), 3.63 (s, 4H), 3.40 (d, <i>J</i> = 1.3 Hz, 1H), 3.02 – 2.82 (m, 3H), 2.76 (d, <i>J</i> = 4.7 Hz, 7H), 2.66 – 2.53 (m, 2H), 2.53 – 2.52 (m, 1H), 2.26 – 1.90 (m, 7H), 1.77 (s, 1H), 1.60 (s, 1H).
D84	LCMS (ESI) m/z: [M+H] ⁺ = 845.40.	¹ H NMR (400 MHz, DMSO-d ₆) δ 11.10 (s, 1H), 8.82 (t, <i>J</i> = 8.0 Hz, 1H), 8.48 (d, <i>J</i> = 67.2 Hz, 1H), 8.19 (s, 1H, FA), 7.96 (d, <i>J</i> = 2.3 Hz, 1H), 7.82 (t, <i>J</i> = 7.8 Hz, 1H), 7.53 (d, <i>J</i> = 8.5 Hz, 1H), 7.45 (d, <i>J</i> = 7.2 Hz, 1H), 6.93 (s, 2H), 6.57 (s, 1H), 5.09 (dd, <i>J</i> = 12.9, 5.5 Hz, 1H), 4.81 – 4.45 (m, 1H), 4.23 (t, <i>J</i> = 6.4 Hz, 2H), 3.86 (s, 6H), 3.65 – 3.61 (m, 4H), 3.15 – 3.08 (m, 1H), 2.95 – 2.78 (m, 3H), 2.62 – 2.57 (m, 2H), 2.34 – 2.25 (m, 7H), 2.20 – 1.92 (m, 4H), 1.90 – 1.73 (m, 3H), 1.66 – 1.36 (m, 6H).
D85	LCMS (ESI) m/z: [M+H] ⁺ = 845.35	¹ H NMR (400 MHz, DMSO-d ₆) δ 11.12 (s, 1H), 8.85 (d, <i>J</i> = 8.0 Hz, 1H), 8.50 (d, <i>J</i> = 66.8 Hz, 1H), 8.14 (s, 1H, FA), 8.00 (d, <i>J</i> = 1.1 Hz, 1H), 7.85 (d, <i>J</i> = 8.2 Hz, 1H), 7.44 (d, <i>J</i> = 2.3 Hz, 1H), 7.36 (dd, <i>J</i> = 8.3, 2.2 Hz, 1H), 7.03 (s, 2H), 6.53 (s, 1H), 5.13 (dd, <i>J</i> = 13.0, 5.3 Hz, 1H), 4.27 – 4.17 (m, 4H), 3.93 (s, 7H), 3.64 (d, <i>J</i> = 1.5 Hz, 3H), 2.96 – 2.84 (m, 2H), 2.76 (s, 6H), 2.63 – 2.58 (m, 2H), 2.47 – 2.34 (m, 2H), 2.12 – 1.95 (m, 3H), 1.89 – 1.68 (m, 3H), 1.66 – 1.40 (m, 5H), 1.30 – 1.21 (m, 1H).

Compound No.	LCMS	¹ H NMR
D86	LCMS (ESI) m/z: [M+H] ⁺ = 881.45.	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.31 (br s, 1H, FA), 8.27 (s, 1H), 7.88 (s, 1H), 7.73 (d, <i>J</i> = 8.5 Hz, 1H), 7.42 (s, 1H), 7.30 (d, <i>J</i> = 8.5 Hz, 1H), 7.06 (s, 2H), 5.10 (dd, <i>J</i> = 12.4, 5.3 Hz, 1H), 4.42 (s, 2H), 4.22 – 4.12 (m, 1H), 4.02 (s, 6H), 3.75 (s, 3H), 3.69 – 3.53 (m, 7H), 3.22 – 3.08 (m, 4H), 2.92 (s, 9H), 2.82 – 2.69 (m, 5H), 2.26 (d, <i>J</i> = 14.0 Hz, 2H), 2.16 – 1.95 (m, 3H), 1.93 – 1.81 (m, 2H), 1.81 – 1.67 (m, 2H).
D87	LCMS (ESI) m/z: [M+H] ⁺ = 841.35.	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.11 (s, 1H), 8.61 (d, <i>J</i> = 7.9 Hz, 1H), 8.39 (s, 1H), 8.18 (s, 1H, FA), 7.93 (s, 1H), 7.82 (d, <i>J</i> = 8.3 Hz, 1H), 7.42 (d, <i>J</i> = 2.2 Hz, 1H), 7.34 (d, <i>J</i> = 8.4 Hz, 1H), 6.91 (s, 2H), 5.11 (dd, <i>J</i> = 13.0, 5.3 Hz, 1H), 4.19 (t, <i>J</i> = 6.4 Hz, 2H), 4.03 (s, 1H), 3.85 (s, 6H), 3.64 – 3.56 (m, 5H), 2.75 – 2.72 (m, 1H), 2.69 – 2.60 (m, 3H), 2.60 – 2.53 (m, 4H), 2.30 – 2.22 (m, 7H), 1.97 – 1.66 (m, 8H), 1.60 – 1.43 (m, 5H).
D88	LCMS (ESI) m/z: [M+H] ⁺ = 841.35.	¹ H NMR (400 MHz, DMSO-d ₆) δ 11.10 (s, 1H), 8.60 (d, <i>J</i> = 7.9 Hz, 1H), 8.36 (d, <i>J</i> = 2.4 Hz, 1H), 8.19 (s, 2H, FA), 7.92 (s, 1H), 7.87 – 7.74 (m, 1H), 7.51 (d, <i>J</i> = 9.0 Hz, 1H), 7.42 (dd, <i>J</i> = 7.2, 2.6 Hz, 1H), 6.90 (s, 2H), 5.11 – 5.04 (m, 1H), 4.23 (t, <i>J</i> = 6.3 Hz, 2H), 4.03 (s, 1H), 3.85 (s, 6H), 3.61 (s, 3H), 3.55 (s, 2H), 2.93 – 2.84 (m, 1H), 2.78 – 2.70 (m, 1H), 2.69 – 2.54 (m, 7H), 2.21 (s, 6H), 2.08 – 1.99 (m, 1H), 1.93 – 1.70 (m, 7H), 1.59 – 1.47 (m, 5H).
D89	LCMS (ESI) m/z: [M+H] ⁺ = 827.35.	¹ H NMR (400 MHz, DMSO-d ₆) δ 11.12 (s, 1H), 8.61 (d, <i>J</i> = 7.7 Hz, 1H), 8.42 (s, 1H), 8.21 (s, 1H, FA), 7.94 (s, 1H), 7.84 (d, <i>J</i> = 8.3 Hz, 1H), 7.44 (d, <i>J</i> = 2.3 Hz, 1H), 7.36 (dd, <i>J</i> = 8.3, 2.3 Hz, 1H), 6.91 (s, 2H), 5.12 (dd, <i>J</i> = 13.0, 5.4 Hz, 1H), 4.19 (t, <i>J</i> = 6.5 Hz, 2H), 3.84 (s, 6H), 3.74 – 3.67 (m, 1H), 3.62 (s, 3H), 3.55 (s, 2H), 2.95 – 2.84 (m, 3H), 2.64 – 2.54 (m, 2H), 2.35 – 2.29 (m, 2H), 2.21 (s, 6H), 2.07 – 1.94 (m, 3H), 1.83 – 1.73 (m, 4H), 1.62 – 1.42 (m, 6H).
D90	LCMS (ESI) m/z: [M+H] ⁺ = 863.35..	¹ H NMR (400 MHz, DMSO-d ₆) δ 11.12 (s, 1H), 8.88 (d, <i>J</i> = 8.8 Hz, 1H), 8.60 (s, 1H), 8.15 (s, 0.3H, FA), 7.98 (s, 1H), 7.84 (d, <i>J</i> = 8.3 Hz, 1H), 7.44 (d, <i>J</i> = 2.3 Hz, 1H), 7.36 (dd, <i>J</i> = 8.3, 2.3 Hz, 1H), 6.97 (s, 2H), 6.53 (s, 0.3H, FA salt), 5.13 (dd, <i>J</i> = 12.9, 5.3 Hz, 1H), 4.35 (s, 1H), 4.20 (t, <i>J</i> = 6.5 Hz, 2H), 3.88 (s, 6H), 3.82 (s, 2H), 3.63 (s, 3H), 3.15 (s, 1H), 2.95 – 2.84 (m, 2H), 2.65 – 2.55 (m, 3H), 2.44 (s, 8H), 2.18 (t, <i>J</i> = 11.3 Hz, 1H), 2.10 – 2.01 (m, 1H), 1.91 – 1.74 (m, 4H), 1.57 – 1.41 (m, 4H).

Example 30 – Preparation of Compounds D91-D220, DD1, and DD2

In analogy to the procedures described in the examples above, compounds D91-D220, DD1, and DD2 were prepared using the appropriate starting materials

Compound No.	LCMS	¹ H NMR
D91	662.30	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.27 – 8.21 (m, 1H), 7.92 (s, 1H), 7.74 – 7.70 (m, 1H), 7.65 – 7.60 (m, 1H), 7.56 – 7.50 (m, 1H), 6.99 (s, 2H), 5.13 (dd, J = 13.3, 5.2 Hz, 1H), 4.53 – 4.38 (m, 2H), 4.18 – 4.10 (m, 2H), 4.10 – 4.01 (m, 2H), 3.97 (s, 6H), 3.83 – 3.74 (m, 2H), 3.71 (s, 3H), 3.67 – 3.57 (m, 1H), 2.99 – 2.85 (m, 1H), 2.84 – 2.75 (m, 1H), 2.56 – 2.40 (m, 1H), 2.26 – 2.15 (m, 1H).
D92	637.35	¹ H NMR (300 MHz, Methanol-d ₄) δ 7.82 – 7.78 (m, 1H), 7.73 (s, 1H), 7.70 – 7.64 (m, 2H), 7.60 – 7.52 (m, 2H), 7.05 (s, 2H), 5.16 (dd, J = 13.3, 5.2 Hz, 1H), 4.58 – 4.42 (m, 2H), 4.27 (s, 2H), 4.24 – 4.15 (m, 2H), 4.00 (s, 6H), 3.97 – 3.89 (m, 2H), 3.80 – 3.70 (m, 4H), 3.03 – 2.75 (m, 2H), 2.60 – 2.41 (m, 1H), 2.29 – 2.16 (m, 1H).
D93	674.35	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.98 (s, 1H), 8.68 (d, J = 7.7 Hz, 1H), 8.40 (s, 1H), 7.97 (s, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.38 – 7.22 (m, 3H), 7.19 (t, J = 1.9 Hz, 1H), 7.15 – 7.06 (m, 1H), 5.11 (dd, J = 13.2, 5.1 Hz, 1H), 4.41 – 4.18 (m, 2H), 4.06 – 3.92 (m, 3H), 3.80 – 3.76 (m, 3H), 3.60 (s, 3H), 3.02 – 2.83 (m, 3H), 2.60 (d, J = 16.5 Hz, 1H), 2.48 – 2.31 (m, 1H), 1.96 (dd, J = 27.3, 11.8 Hz, 3H), 1.70 (d, J = 12.2 Hz, 2H).
D94	808.55	¹ H NMR (300 MHz, Methanol-d ₄) δ 7.53 – 7.48 (m, 2H), 7.40 – 7.33 (m, 2H), 7.01 – 6.98 (m, 2H), 6.28 (s, 1H), 5.15 (dd, J = 13.3, 5.1 Hz, 1H), 4.51 – 4.42 (m, 2H), 4.41 – 4.35 (m, 2H), 4.06 – 3.96 (m, 10H), 3.71 (s, 3H), 3.49 – 3.40 (m, 4H), 3.25 – 3.07 (m, 6H), 3.02 – 2.85 (m, 3H), 2.84 – 2.76 (m, 1H), 2.60 – 2.51 (m, 1H), 2.50 – 2.40 (m, 2H), 2.25 – 2.14 (m, 1H), 2.11 – 1.97 (m, 2H), 1.83 – 1.48 (m, 5H).
D95	605.36	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.96 (s, 1H), 10.49 (s, 1H), 8.67 (s, 1H), 8.23–8.16 (m, 1H), 8.00 (s, 1H), 7.52 (t, J = 2.2 Hz, 1H), 7.38 (dd, J = 7.8, 1.9 Hz, 1H), 7.27 (t, J = 8.2 Hz, 1H), 6.94 (s, 2H), 6.80 (dd, J = 8.0, 2.5 Hz, 1H), 5.17 (dd, J = 10.7, 5.2 Hz, 1H), 3.86 (s, 6H), 3.64 (s, 3H), 3.63–3.55 (m, 2H), 2.81–2.70 (m, 1H), 2.68–2.56 (m, 1H), 2.32–2.10 (m, 8H).

Compound No.	LCMS	¹ H NMR
D96	631.35	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.96 (s, 1H), 8.72 (d, J = 7.7 Hz, 1H), 8.46 (s, 1H), 7.96 (s, 1H), 7.18 (t, J = 8.4 Hz, 1H), 6.86 (d, J = 2.2 Hz, 2H), 6.70 – 6.61 (m, 3H), 6.51 (d, J = 8.0 Hz, 1H), 5.26 (dd, J = 10.4, 5.2 Hz, 1H), 4.01 (s, 1H), 3.89 (s, 6H), 3.82 (d, J = 12.1 Hz, 2H), 3.67 (s, 3H), 2.88 (q, J = 10.2, 8.1 Hz, 2H), 2.81 – 2.62 (m, 2H), 2.31 – 2.12 (m, 2H), 1.94 (d, J = 12.2 Hz, 2H), 1.81 – 1.64 (m, 2H).
D97	711.20	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.54 (s, 1H, FA), 7.43 (s, 1H), 7.37 (d, J = 8.2 Hz, 1H), 7.01 – 6.91 (m, 3H), 6.85 (s, 1H), 6.77 (d, J = 8.3 Hz, 1H), 6.29 (s, 1H), 5.16 – 5.08 (m, 1H), 4.44 – 4.30 (m, 2H), 4.18 – 3.99 (m, 2H), 3.98 – 3.92 (m, 6H), 3.75 – 3.67 (m, 7H), 3.62 (s, 1H), 3.08 – 2.95 (m, 2H), 2.88 (s, 3H), 2.82 – 2.70 (m, 1H), 2.50 – 2.39 (m, 1H), 2.22 – 2.11 (m, 1H), 2.05 – 2.00 (m, 4H).
D98	789.2	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.97 (s, 1H), 8.86 (s, 1H), 8.57 (s, 1H, FA), 7.92 (s, 1H), 7.43 (d, J = 8.3 Hz, 1H), 7.28 (d, J = 8.5 Hz, 1H), 7.23 – 7.05 (m, 2H), 6.79 (d, J = 2.3 Hz, 2H), 6.60 – 6.50 (m, 1H), 5.10 (dd, J = 13.2, 5.1 Hz, 1H), 4.42 – 4.12 (m, 3H), 3.90 – 3.73 (m, 8H), 3.60 (s, 3H), 3.24 – 3.09 (m, 1H), 3.00 – 2.84 (m, 2H), 2.82 – 2.69 (m, 2H), 2.64 – 2.54 (m, 2H), 2.46 – 2.32 (m, 2H), 2.27 – 2.07 (m, 1H), 2.03 – 1.95 (m, 1H), 1.93 – 1.72 (m, 4H), 1.66 – 1.49 (m, 2H).
D99	779.3	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.97 (s, 1H), 8.16 (s, FA, 1H), 7.88 (s, 1H), 7.70 (d, J = 5.4 Hz, 1H), 7.61 (d, J = 5.3 Hz, 1H), 7.38 (d, J = 8.2 Hz, 1H), 6.97 (s, 2H), 6.73 – 6.61 (m, 2H), 5.08 (dd, J = 13.3, 5.1 Hz, 1H), 4.36 – 4.14 (m, 2H), 3.88 (s, 6H), 3.81 (s, 2H), 3.62 (s, 3H), 3.58 (s, 4H), 3.13 – 3.02 (m, 2H), 2.99 – 2.78 (m, 2H), 2.64 – 2.55 (m, 1H), 2.47 – 2.38 (m, 2H), 2.38 – 2.20 (m, 4H), 2.19 – 2.06 (m, 2H), 2.03 – 1.92 (m, 1H), 1.87 – 1.53 (m, 7H), 1.32 – 1.06 (m, 2H).
D100	809.55	¹ H NMR (300 MHz, Methanol-d ₄) δ 7.66 (s, 1H), 7.41 (d, J = 8.2 Hz, 1H), 7.01 (s, 2H), 6.88 (s, 1H), 6.83 – 6.78 (m, 1H), 6.76 (s, 1H), 5.14 (dd, J = 13.2, 5.2 Hz, 1H), 4.56 – 4.30 (m, 4H), 4.04 – 3.97 (m, 9H), 3.86 – 3.76 (m, 3H), 3.75 – 3.71 (m, 4H), 3.69 – 3.53 (m, 4H), 3.36 – 3.34 (m, 1H), 3.23 – 3.07 (m, 5H), 2.99 – 2.78 (m, 2H), 2.62 – 2.43 (m, 1H), 2.37 – 1.99 (m, 9H), 1.72 – 1.61 (m, 1H).

Compound No.	LCMS	¹ H NMR
D101	804.55	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.61 (s, 1H) FA, 8.36 (s, 1H), 8.04 (s, 1H), 7.46 (d, J = 8.2 Hz, 1H), 7.10 (s, 2H), 6.94 – 6.88 (m, 1H), 6.87 – 6.81 (m, 1H), 5.20 (dd, J = 13.2, 5.1 Hz, 1H), 4.54 – 4.39 (m, 4H), 4.08 (s, 6H), 3.81 (s, 3H), 3.76 – 3.72 (m, 4H), 3.65 – 3.55 (m, 2H), 3.26 – 3.11 (m, 2H), 3.02 – 2.81 (m, 2H), 2.77 – 2.40 (m, 7H), 2.31 – 2.18 (m, 1H), 2.16 – 2.07 (m, 2H), 2.00 (s, 5H), 1.72 – 1.49 (m, 2H).
D102	874.5	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.95 (s, 1H), 8.88 (d, J = 8.9 Hz, 1H), 8.59 (s, 1H), 8.17 (s, 2H, FA), 7.96 (s, 1H), 7.50 (d, J = 8.7 Hz, 1H), 7.05 (d, J = 7.9 Hz, 2H), 6.93 (s, 2H), 5.05 (dd, J = 13.3, 5.1 Hz, 1H), 4.38 – 4.16 (m, 3H), 3.85 (s, 8H), 3.63 (s, 5H), 3.19 – 3.14 (m, 2H), 2.95 – 2.76 (m, 5H), 2.64 – 2.58 (m, 1H), 2.41 – 2.36 (m, 2H), 2.26 (d, J = 4.0 Hz, 6H), 2.21 – 2.15 (m, 1H), 2.00 – 1.86 (m, 2H), 1.82 – 1.73 (m, 3H), 1.54 – 1.50 (m, 1H), 1.46 – 1.38 (m, 2H), 1.30 – 1.19 (m, 2H).
D103	650.2	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.98 (s, 1H), 9.42 (d, 1H), 8.46 (s, 1H), 8.06 – 7.94 (m, 3H), 7.86 – 7.73 (m, 2H), 7.42 (d, 1H), 6.82 – 6.72 (m, 2H), 5.11 (dd, 1H), 4.91 – 4.78 (m, 1H), 4.42 – 4.15 (m, 4H), 3.89 – 3.79 (m, 2H), 3.61 (s, 3H), 3.01 – 2.83 (m, 1H), 2.66 – 2.53 (m, 1H), 2.45 – 2.28 (m, 1H), 2.05 – 1.95 (m, 1H).
D104	927.45	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.95 (s, 1H), 10.14 – 9.84 (m, 2H, TFA), 9.07 (s, 1H), 8.61 (s, 1H), 8.02 (s, 1H), 7.52 (d, J = 8.3 Hz, 1H), 7.03 (d, J = 2.9 Hz, 2H), 6.54 – 6.45 (m, 2H), 5.05 (dd, J = 13.2, 5.2 Hz, 1H), 4.71 – 4.57 (m, 1H), 4.43 – 4.33 (m, 2H), 4.31 – 4.16 (m, 4H), 4.08 – 4.00 (m, 2H), 3.93 (s, 6H), 3.78 (s, 2H), 3.69 (s, 3H), 3.51 (s, 5H), 3.45 (s, 2H), 3.39 (s, 2H), 3.19 (s, 2H), 3.01 – 2.89 (m, 3H), 2.80 (s, 3H), 2.70 – 2.54 (m, 1H), 2.38 – 2.32 (m, 1H), 2.10 (s, 4H), 1.94 (d, J = 14.0 Hz, 3H).
D105	688.3	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.95 (s, 1H), 9.07 (s, 1H, TFA), 8.84 – 8.76 (m, 1H), 8.48 (s, 1H), 8.01 (s, 1H), 7.40 – 7.18 (m, 2H), 7.09 – 7.02 (m, 4H), 5.21 – 5.13 (m, 1H), 4.26 (d, J = 5.0 Hz, 2H), 4.15 – 4.01 (m, 2H), 3.93 (s, 6H), 3.64 (s, 3H), 3.30 – 3.14 (m, 2H), 2.78 (d, J = 4.5 Hz, 6H), 2.75 – 2.71 (m, 1H), 2.70 – 2.61 (m, 2H), 2.23 – 2.13 (m, 2H), 2.06 – 1.97 (m, 2H), 1.93 – 1.82 (m, 2H).

Compound No.	LCMS	¹ H NMR
D106	696.3	¹ H NMR (300 MHz, Methanol-d ₄) δ 7.78 – 7.67 (m, 2H), 7.60 (d, J = 5.4 Hz, 1H), 7.44 (d, J = 8.3 Hz, 1H), 7.37 – 7.28 (m, 2H), 7.04 (s, 2H), 5.15 (dd, J = 13.3, 5.1 Hz, 1H), 4.49 – 4.32 (m, 2H), 4.20 (s, 2H), 3.98 (s, 6H), 3.76 (s, 3H), 3.60 (s, 1H), 3.47 (d, J = 10.6 Hz, 2H), 3.25 – 3.12 (m, 3H), 3.00 – 2.80 (m, 4H), 2.51 (dd, J = 12.9, 4.8 Hz, 1H), 2.24 – 2.03 (m, 5H), 1.84 (s, 2H).
D107	825.4	¹ H NMR (400 MHz, DMSO-d ₆) δ 8.15 (s, 1H, FA), 7.86 (s, 1H), 7.68 (d, J = 5.4 Hz, 1H), 7.64 (d, J = 8.3 Hz, 1H), 7.60 (d, J = 5.4 Hz, 1H), 6.93 (s, 2H), 6.78 (s, 1H), 6.65 (dd, J = 8.4, 2.2 Hz, 1H), 5.78 – 5.68 (m, 1H), 5.63 (dd, J = 9.5, 4.0 Hz, 1H), 5.28 – 5.19 (m, 1H), 3.85 (s, 6H), 3.74 (s, 4H), 3.61 (s, 3H), 3.56 (s, 2H), 3.51 (s, 1H), 3.22 – 3.16 (m, 2H), 3.12 – 2.98 (m, 2H), 2.87 – 2.78 (m, 1H), 2.65 – 2.54 (m, 2H), 2.47 – 2.38 (m, 2H), 2.11 – 2.03 (m, 1H), 1.87 – 1.80 (m, 1H), 1.76 – 1.72 (m, 4H), 0.89 – 0.83 (m, 3H), 0.83 – 0.77 (m, 3H).
D108	688.35	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.56 (s, 1H, FA salt), 8.24 (s, 1H), 7.84 (s, 1H), 7.17 (t, J = 8.1 Hz, 1H), 7.05 (s, 2H), 6.74 – 6.64 (m, 2H), 6.57 (d, J = 8.2 Hz, 1H), 5.09 (dd, J = 9.6, 4.8 Hz, 1H), 4.34 (s, 2H), 4.01 (s, 7H), 3.74 (s, 5H), 2.94 – 2.88 (m, 1H), 2.85 (s, 6H), 2.81 – 2.71 (m, 3H), 2.43 – 2.13 (m, 2H), 2.10 – 2.00 (m, 2H), 1.85 – 1.75 (m, 2H).
D109	670.2	¹ H NMR (300 MHz, DMSO-d ₆) δ 8.36 (s, 1H), 7.86 (s, 1H), 7.48 (d, J = 8.4 Hz, 1H), 7.38 – 7.32 (m, 1H), 7.29 (s, 1H), 6.77 (d, J = 2.2 Hz, 2H), 6.56 (t, J = 2.2 Hz, 1H), 5.07 (dd, J = 13.2, 5.1 Hz, 1H), 4.42 – 4.17 (m, 2H), 3.98 (s, 1H), 3.82- 3.71 (m, 8H), 3.58 (s, 3H), 3.04 – 2.80 (m, 3H), 2.61 (d, J = 17.7 Hz, 1H), 2.41 – 2.30 (m, 1H), 2.05 – 1.87 (m, 3H), 1.71 (dd, J = 22.0, 10.0 Hz, 2H).
D110	724.3	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.57 (s, 1H, FA salt), 7.68 (s, 1H), 7.44 – 7.35 (m, 2H), 7.00 (s, 2H), 6.87 (d, J = 2.1 Hz, 1H), 6.79 (dd, J = 8.2, 2.3 Hz, 1H), 5.14 (dd, J = 13.1, 5.1 Hz, 1H), 4.48 – 4.30 (m, 2H), 4.14 (s, 2H), 3.98 (s, 6H), 3.73 (s, 7H), 3.33 – 3.20 (m, 1H), 3.08 (s, 4H), 2.99 – 2.73 (m, 2H), 2.58 – 2.41 (m, 1H), 2.17 (d, J = 12.6 Hz, 1H), 2.07 (s, 4H), 1.41 (d, J = 6.8 Hz, 6H).
D111	718.35	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.97 (s, 1H), 7.89 (s, 1H), 7.74 – 7.55 (m, 2H), 7.39 (d, J = 8.8 Hz, 1H), 6.95 (s, 2H), 6.77 – 6.67 (m, 2H), 5.17 – 5.00 (m, 1H), 4.42 – 4.11 (m, 2H), 3.87 (s, 8H), 3.72 – 3.55 (m, 7H), 3.02 – 2.81 (m, 1H), 2.75 – 2.54 (m, 4H), 2.46 – 2.28 (m, 2H), 2.00 (s, 3H).

Compound No.	LCMS	¹ H NMR
D112	875.45	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.42 (d, J = 15.6 Hz, 1H), 7.87 (s, 1H), 7.55 (d, J = 8.5 Hz, 1H), 7.41 (d, J = 7.6 Hz, 2H), 7.08 (s, 2H), 5.27 – 5.10 (m, 1H), 4.44 (d, J = 14.5 Hz, 5H), 4.02 (s, 6H), 3.75 (s, 3H), 3.63 (s, 8H), 3.46 (s, 3H), 3.14 (d, J = 12.3 Hz, 1H), 3.01 – 2.89 (m, 9H), 2.90 – 2.77 (m, 1H), 2.78 – 2.38 (m, 3H), 2.26 – 2.16 (m, 1H), 2.10 – 1.91 (m, 2H).
D113	696.3	¹ H NMR (300 MHz, DMSO-d ₆) δ 8.32 (s, 1H, FA), 7.80 (s, 1H), 7.69 – 7.56 (m, 2H), 7.43 (d, J = 8.2 Hz, 1H), 7.28 – 7.13 (m, 2H), 7.01 – 6.88 (m, 2H), 5.04 – 4.89 (m, 1H), 4.31 (d, 2H), 4.19 (d, J = 16.2 Hz, 2H), 3.91 – 3.72 (m, 6H), 3.60 (s, 5H), 3.48 (s, 1H), 3.33 – 2.91 (m, 4H), 2.90 – 2.71 (m, 2H), 2.71 – 2.56 (m, 1H), 2.43 – 2.31 (m, 1H), 2.29 – 2.12 (m, 1H), 2.11 – 1.80 (m, 4H), 1.70 (d, J = 13.8 Hz, 1H), 1.48 (s, 1H).
D114	713.35	¹ H NMR (300 MHz, DMSO-d ₆ +a drop of D ₂ O) δ 8.45 (s, 1H), 7.97 (s, 1H), 7.41 (d, J = 8.3 Hz, 1H), 7.01 (s, 2H), 6.91 – 6.83 (m, 1H), 6.80 (d, J = 2.3 Hz, 1H), 5.06 (dd, J = 13.3, 5.1 Hz, 1H), 4.58 (t, J = 5.7 Hz, 1H), 4.38 – 4.10 (m, 4H), 3.92 (s, 6H), 3.53 – 3.45 (m, 1H), 3.42 – 3.36 (m, 3H), 3.39 – 3.25 (m, 3H), 2.92 – 2.75 (m, 1H), 2.77 (s, 6H), 2.66 – 2.54 (m, 1H), 2.43 – 2.24 (m, 2H), 2.17 – 2.07 (m, 1H), 2.05 – 1.95 (m, 1H).
D115	642.3	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.99 (s, 1H), 9.39 (d, J = 7.1 Hz, 1H), 8.43 (s, 1H), 7.92 (s, 1H), 7.42 (d, J = 8.8 Hz, 1H), 6.78 (dd, J = 6.6, 2.3 Hz, 4H), 6.58 (t, J = 2.2 Hz, 1H), 5.11 (dd, J = 13.2, 5.0 Hz, 1H), 4.84 (d, J = 6.8 Hz, 1H), 4.40 - 4.15 (m, 4H), 3.82 (s, 8H), 3.60 (s, 3H), 2.95 - 2.83 (m, 1H), 2.62 (s, 1H), 2.45 - 2.34 (m, 1H), 2.05 - 1.94 (m, 1H).
D116	669.35	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.99 (s, 1H), 9.41 (d, J = 7.1 Hz, 1H), 8.45 (s, 1H), 8.16 (s, 0.2H, FA), 7.98 (s, 1H), 7.43 (d, J = 8.8 Hz, 1H), 6.95 (s, 2H), 6.82 - 6.72 (m, 2H), 5.11 (dd, J = 13.2, 5.0 Hz, 1H), 4.89 - 4.79 (m, 1H), 4.40 - 4.15 (m, 4H), 3.87 (s, 6H), 3.84 - 3.74 (m, 4H), 3.62 (s, 3H), 2.95 - 2.83 (m, 1H), 2.63 (s, 1H), 2.39 (s, 7H), 2.05 - 1.95 (m, 1H).
D117	718.3	¹ H NMR (300 MHz, DMSO) δ 10.98 (s, 1H), 8.99 (d, J = 7.6 Hz, 1H), 8.43 (s, 1H), 8.05 – 7.94 (m, 3H), 7.86 – 7.73 (m, 2H), 7.44 (d, J = 8.3 Hz, 1H), 7.38 – 7.17 (m, 2H), 5.10 (dd, J = 13.3, 5.1 Hz, 1H), 4.48 – 4.40 (m, 1H), 4.39 – 4.18 (m, 2H), 3.62 (s, 3H), 3.31 - 3.12 (m, 5H), 3.01 – 2.83 (m, 1H), 2.65 - 2.55 (m, 2H), 2.45 – 2.34 (m, 1H), 2.33 – 2.19 (m, 2H), 2.05 – 1.85 (m, 3H), 1.76 - 1.70 (m, 4H).

Compound No.	LCMS	¹ H NMR
D118	751.35	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.99 (s, 1H), 8.98 – 8.89 (m, 1H), 8.59 (d, J = 2.3 Hz, 1H), 8.15 (s, 0.2H, FA salt), 8.02 (s, 1H), 7.46 (d, J = 8.5 Hz, 1H), 7.36 (dt, J = 8.6, 2.2 Hz, 1H), 7.27 (d, J = 2.3 Hz, 1H), 7.20 – 7.10 (m, 2H), 5.12 (dd, J = 13.2, 5.2, 1H), 4.70 – 4.49 (m, 1H), 4.36 (d, J = 16.9 Hz, 1H), 4.29 – 4.08 (m, 2H), 3.91 (s, 3H), 3.87 (s, 1H), 3.62 (s, 5H), 3.51 – 3.42 (m, 1H), 3.21 – 3.08 (m, 1H), 3.01 – 2.83 (m, 1H), 2.66 – 2.55 (m, 1H), 2.45 – 2.37 (m, 1H), 2.27 (s, 6H), 2.08 – 1.92 (m, 3H).
D119	726.35	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.56 (s, 1H, FA salt), 7.75 (s, 1H), 7.59 (s, 1H), 7.41 (d, J = 8.2 Hz, 1H), 7.04 (s, 2H), 6.88 (s, 1H), 6.80 (d, J = 8.3 Hz, 1H), 5.19 – 5.08 (m, 1H), 4.72 (s, 2H), 4.40 (d, J = 5.2 Hz, 2H), 4.27 (s, 2H), 4.00 (s, 6H), 3.82 – 3.62 (m, 8H), 3.42 (s, 3H), 3.24 – 3.18 (m, 3H), 3.00 – 2.71 (m, 2H), 2.56 – 2.45 (m, 1H), 2.15 – 2.09 (m, 5H).
D120	712.3	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.57 (s, 1H), 7.63 (s, 1H), 7.39 (d, J = 8.2 Hz, 1H), 6.93 (s, 2H), 6.85 (d, J = 2.2 Hz, 1H), 6.80 – 6.73 (m, 2H), 5.13 (dd, J = 13.3, 5.1 Hz, 1H), 4.47 – 4.27 (m, 2H), 4.02 (s, 5H), 3.95 (s, 6H), 3.72 (s, 3H), 3.70 (s, 4H), 3.06 – 2.72 (m, 6H), 2.60 – 2.37 (m, 1H), 2.23 – 2.11 (m, 1H), 2.01 (t, J = 5.6 Hz, 4H).
D121	696.35	¹ H NMR (300 MHz, DMSO-d ₆) δ 8.26 (s, 1H, FA), 7.83 (s, 1H), 7.67 (d, J = 5.4 Hz, 1H), 7.60 (d, J = 5.4 Hz, 1H), 7.50 (d, J = 8.4 Hz, 1H), 7.00 (d, J = 9.3 Hz, 2H), 6.91 (d, J = 1.9 Hz, 2H), 5.01 (dd, J = 13.3, 5.1 Hz, 1H), 4.31 (d, J = 16.9 Hz, 1H), 4.21 (d, 1H), 3.80 (d, J = 1.6 Hz, 7H), 3.71 – 3.60 (m, 6H), 3.50 (s, 1H), 3.28 – 3.01 (m, 2H), 2.98 – 2.77 (m, 1H), 2.59 (d, J = 17.1 Hz, 4H), 2.39 – 2.24 (m, 1H), 2.05 – 1.90 (m, 2H), 1.89 – 1.78 (m, 1H), 1.77 – 1.58 (m, 3H), 1.57 – 1.42 (m, 1H).
D122	613.25	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.97 (s, 1H), 7.86 (s, 1H), 7.69 (d, J = 5.4 Hz, 1H), 7.60 (d, J = 5.3 Hz, 1H), 7.39 (d, J = 8.3 Hz, 1H), 6.96 (s, 2H), 6.86 (dd, J = 8.4, 2.4 Hz, 1H), 6.79 (d, J = 2.3 Hz, 1H), 5.10 (dd, J = 13.3, 5.1 Hz, 1H), 4.33 (d, J = 16.4 Hz, 1H), 4.25 – 4.07 (m, 2H), 3.85 (s, 6H), 3.62 (s, 4H), 3.55 – 3.40 (m, 3H), 2.99 – 2.83 (m, 1H), 2.71 – 2.55 (m, 2H), 2.46 – 2.34 (m, 1H), 2.18 – 2.08 (m, 1H), 2.08 – 1.97 (m, 1H).

Compound No.	LCMS	¹ H NMR
D123	627.2	¹ H NMR (400 MHz, DMSO-d ₆ with a drop of D ₂ O) δ 8.30 (s, 0.1H, FA), 7.82 (s, 1H), 7.67 (d, J = 5.4 Hz, 1H), 7.60 (d, J = 5.4 Hz, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.35 – 7.28 (m, 1H), 7.23 – 7.18 (m, 1H), 6.90 (s, 2H), 5.08 (dd, J = 13.3, 5.1 Hz, 1H), 4.40 – 4.18 (m, 2H), 3.88 – 3.78 (m, 8H), 3.60 (s, 3H), 3.42 – 3.32 (m, 1H), 2.97 – 2.83 (m, 1H), 2.82 – 2.70 (m, 2H), 2.68 – 2.55 (m, 1H), 2.49 – 2.31 (m, 3H), 2.05 – 1.97 (m, 1H), 1.55 (d, J = 12.4 Hz, 2H).
D124	687.35	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.18 (s, 1H), 8.67 (d, J = 7.7 Hz, 1H), 8.41 (s, 1H), 8.22 (s, 1H, FA), 7.94 (s, 1H), 7.23 – 7.14 (m, 1H), 6.89 (d, J = 14.8 Hz, 4H), 6.67 (d, J = 7.4 Hz, 1H), 4.46 (s, 2H), 4.00 – 3.87 (m, 1H), 3.84 (s, 6H), 3.75 (s, 1H), 3.72 (s, 1H), 3.61 (s, 3H), 3.56 (s, 2H), 3.28 (t, J = 6.8 Hz, 2H), 2.81 (t, J = 11.9 Hz, 2H), 2.54 (d, J = 6.8 Hz, 2H), 2.22 (s, 6H), 1.93 – 1.85 (m, 2H), 1.72 – 1.59 (m, 2H).
D125	552.1	¹ H NMR (400 MHz, DMSO-d ₆) δ 11.02 (s, 1H), 8.14 – 7.99 (m, 3H), 7.76 – 7.70 (m, 2H), 7.70 – 7.59 (m, 4H), 5.16 (dd, J = 13.3, 5.1 Hz, 1H), 4.57 (d, J = 17.5 Hz, 1H), 4.43 (d, J = 17.5 Hz, 1H), 3.63 (s, 3H), 3.00 – 2.87 (m, 1H), 2.70 – 2.58 (m, 1H), 2.45 – 2.32 (m, 1H), 2.11 – 2.01 (m, 1H).
D126	846.4	¹ H NMR (400 MHz, DMSO-d ₆) δ 8.62 (d, J = 7.7 Hz, 1H), 8.41 (s, 1H), 8.26 (s, 1H, FA), 7.94 (s, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.32 (d, J = 8.4 Hz, 1H), 7.21 (s, 1H), 6.90 (s, 2H), 5.10 (dd, J = 13.3, 5.1 Hz, 1H), 4.39 – 4.16 (m, 2H), 4.01 – 3.97 (m, 1H), 3.90 (d, J = 12.3 Hz, 1H), 3.84 (s, 6H), 3.72 (d, J = 10.4 Hz, 1H), 3.78 – 3.56 (m, 3H), 3.52 (s, 2H), 3.07 – 3.02 (m, 1H), 2.98 – 2.82 (m, 5H), 2.64 – 2.55 (m, 3H), 2.52 – 2.28 (m, 1H), 2.19 (s, 6H), 2.03 – 1.87 (m, 3H), 1.82 – 1.77 (m, 2H), 1.58 – 1.51 (m, 2H).
D127	846.35	¹ H NMR (400 MHz, DMSO-d ₆) δ 8.61 (d, J = 7.6 Hz, 1H), 8.41 (s, 1H), 8.20 (s, 1H, FA), 7.94 (s, 1H), 7.52 (d, J = 8.5 Hz, 1H), 7.17 – 7.08 (m, 2H), 6.93 (s, 2H), 5.05 (dd, J = 13.2, 5.1 Hz, 1H), 4.45 – 4.16 (m, 2H), 4.12 (s, 1H), 4.01 (d, J = 12.4 Hz, 1H), 3.86 (s, 6H), 3.78 – 3.65 (m, 3H), 3.62 (s, 3H), 3.15 (d, J = 12.9 Hz, 1H), 3.05 – 2.82 (m, 5H), 2.64 – 2.55 (m, 3H), 2.42 – 2.34 (m, 1H), 2.32 (s, 6H), 2.01 – 1.87 (m, 3H), 1.81 – 1.77 (m, 2H), 1.58 – 1.50 (m, 2H).

Compound No.	LCMS	¹ H NMR
D128	678.1	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.99 (s, 1H), 8.70 (d, J = 7.7 Hz, 1H), 8.43 (s, 1H), 8.08 – 7.91 (m, 3H), 7.80 (d, J = 6.7 Hz, 2H), 7.47 (d, J = 8.5 Hz, 1H), 7.31 (d, J = 25.7 Hz, 2H), 5.12 (dd, J = 13.2, 5.1 Hz, 1H), 4.44 – 4.15 (m, 2H), 4.11 - 3.90 (m, 1H), 3.82 (d, J = 12.5 Hz, 2H), 3.61 (s, 3H), 3.01 – 2.91 (m, 2H), 2.90 (s, 1H), 2.74 (s, 1H), 2.73 - 2.70 (m, 1H), 2.68 - 2.55 (m, 1H), 2.43 - 2.31 (m, 1H), 2.07 – 1.85 (m, 3H), 1.80 - 1.61 (m, 2H).
D129	704.3	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.99 (s, 1H), 8.92 (dd, J = 9.0, 2.9 Hz, 1H), 8.57 (d, J = 2.9 Hz, 1H), 7.89 (s, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.36 (d, J = 8.5, 2.6 Hz, 1H), 7.26 (s, 1H), 7.09 (s, 1H), 7.01 (s, 1H), 6.87 (s, 1H), 5.17 – 5.07 (m, 1H), 4.62 – 4.57 (m, 1H), 4.36 (d, J = 16.8 Hz, 1H), 4.28 – 4.10 (m, 2H), 3.92 – 3.80 (m, 4H), 3.61 (s, 3H), 3.48 – 3.40 (m, 1H), 3.20 – 3.09 (m, 1H), 2.99 – 2.86 (m, 1H), 2.72 – 2.56 (m, 3H), 2.44 – 2.36 (m, 1H), 2.13 – 1.92 (m, 3H), 1.24 (t, J = 7.6 Hz, 3H).
D130	839.4	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.00 (s, 1H), 9.26 – 8.96 TFA (m, 1H), 8.83 (s, 1H), 8.47 (s, 1H), 8.02 (s, 1H), 7.49 (d, J = 8.3 Hz, 1H), 7.38 – 7.22 (m, 2H), 7.02 (s, 2H), 5.11 (dd, J = 13.3, 5.1 Hz, 1H), 4.45 – 4.11 (m, 5H), 4.09 – 3.76 (m, 9H), 3.67 – 3.61 (m, 5H), 3.28 – 3.06 (m, 6H), 3.04 – 2.85 (m, 3H), 2.84 – 2.71 (m, 6H), 2.69 – 2.56 (m, 2H), 2.46 – 2.26 (m, 2H), 2.23 – 1.92 (m, 4H), 1.92 – 1.72 (m, 2H).
D131	706.25	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.98 (s, 1H), 8.94 - 8.87 (m, 1H), 8.56 (d, J = 2.8 Hz, 1H), 7.92 (s, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.40 - 7.32 (m, 1H), 7.26 (d, J = 1.5 Hz, 1H), 6.79 (d, J = 2.2 Hz, 2H), 6.57 (t, J = 2.2 Hz, 1H), 5.15 - 5.07 (m, 1H), 4.70 - 4.51 (m, 1H), 4.35 (d, J = 16.8 Hz, 1H), 4.27 - 4.18 (m, 1H), 4.14 (s, 1H), 3.88 (d, J = 13.0 Hz, 1H), 3.82 (s, 6H), 3.60 (s, 3H), 3.47 - 3.40 (m, 1H), 3.15 - 3.11 (m, 1H), 2.94 - 2.86 (m, 1H), 2.64 - 2.56 m, 1H), 2.42 - 2.38 (m, 1H), 2.04 - 1.89 (m, 3H).
D132	696.35	¹ H NMR (400 MHz, DMSO-d ₆) δ 7.76 (s, 1H), 7.38 (d, J = 8.1 Hz, 1H), 7.29 (d, J = 1.3 Hz, 1H), 6.89 (s, 2H), 6.73 – 6.66 (m, 2H), 5.02 (dd, J = 13.3, 5.1 Hz, 1H), 4.36 – 4.12 (m, 2H), 3.84 (s, 6H), 3.72 – 3.62 (m, 4H), 3.60 – 3.55 (m, 7H), 2.93 – 2.80 (m, 1H), 2.70 – 2.52 (m, 6H), 2.52 – 2.25 (m, 1H), 2.43 – 2.27 (m, 1H), 2.03 – 1.95 (m, 1H), 1.80 – 1.76 (m, 4H).

Compound No.	LCMS	¹ H NMR
D133	753.3	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.95 (s, 1H), 8.20 (s, 1H, FA), 7.96 (s, 1H), 7.87 (s, 1H), 7.47 (d, J = 8.2 Hz, 1H), 6.91 (s, 2H), 6.54 – 6.43 (m, 2H), 5.04 (dd, J = 13.3, 5.1 Hz, 1H), 4.36 – 4.11 (m, 2H), 3.85 (s, 6H), 3.62 (s, 8H), 3.57 – 3.51 (m, 3H), 3.30 – 3.25 (m, 2H), 3.08 – 3.02 (m, 2H), 2.99 – 2.78 (m, 1H), 2.64 – 2.58 (m, 2H), 2.45 – 2.24 (m, 4H), 2.00 – 1.92 (m, 1H), 1.76 – 1.70 (m, 4H).
D134	846.35	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.38 (s, 1H), 7.89 (s, 1H), 7.49 (d, J = 8.4 Hz, 1H), 7.41 – 7.34 (m, 2H), 7.07 (s, 2H), 5.16 (dd, J = 13.3, 5.1 Hz, 1H), 4.43 (d, J = 10.6 Hz, 4H), 4.02 (s, 6H), 4.00 – 3.93 (m, 3H), 3.76 (s, 3H), 3.69 – 3.57 (m, 2H), 3.39 (s, 2H), 3.24 (d, J = 13.0 Hz, 1H), 2.92 (s, 9H), 2.85 – 2.81 (m, 1H), 2.55 – 2.46 (m, 1H), 2.30 – 2.15 (m, 5H), 1.99 – 1.87 (m, 2H).
D135	846.5	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.55 (s, 1H, FA), 8.37 (s, 1H), 7.86 (s, 1H), 7.47 (d, J = 8.3 Hz, 1H), 7.40 – 7.33 (m, 2H), 7.05 (s, 2H), 5.15 (d, J = 8.1 Hz, 1H), 4.49 – 4.41 (m, 3H), 4.35 (d, J = 13.8 Hz, 2H), 4.01 (s, 6H), 3.86 (d, J = 12.1 Hz, 2H), 3.76 (s, 3H), 3.37 (s, 1H), 3.16 – 3.10 (m, 1H), 2.98 – 2.91 (m, 1H), 2.89 – 2.79 (m, 9H), 2.71 – 2.61 (m, 2H), 2.57 – 2.49 (m, 2H), 2.25 – 2.17 (m, 1H), 2.07 – 1.97 (m, 4H), 1.81 – 1.68 (m, 2H).
D136	670.3	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.97 (s, 1H), 8.68 (s, TFA, 1H), 7.93 (s, 1H), 7.72 (d, J = 5.3 Hz, 1H), 7.66 – 7.57 (m, 2H), 7.20 – 7.12 (m, 2H), 7.08 (s, 2H), 5.07 (dd, J = 13.2, 5.1 Hz, 1H), 4.50 (d, J = 13.9, 4.3 Hz, 1H), 4.43 – 4.19 (m, 3H), 3.97 (s, 6H), 3.95 – 3.74 (m, 4H), 3.73 – 3.62 (m, 4H), 3.61 – 3.53 (m, 1H), 2.99 – 2.85 (m, 1H), 2.64 – 2.57 (m, 1H), 2.45 – 2.36 (m, 1H), 2.04 – 1.93 (m, 1H), 1.50 (dd, J = 6.5, 3.3 Hz, 6H).
D137	858.6	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.36 (s, 1H), 7.90 (d, J = 1.6 Hz, 1H), 7.57 (d, J = 9.0 Hz, 1H), 7.08 (d, J = 1.3 Hz, 2H), 6.79 (d, J = 7.2 Hz, 2H), 5.11 (dd, J = 13.4, 5.1 Hz, 1H), 4.45 – 4.31 (m, 6H), 4.12 – 3.90 (m, 9H), 3.88 – 3.81 (m, 1H), 3.79 – 3.66 (m, 4H), 3.62 – 3.54 (m, 2H), 3.03 – 2.85 (m, 8H), 2.84 – 2.74 (m, 1H), 2.55 – 2.10 (m, 9H).

Compound No.	LCMS	¹ H NMR
D138	739.45	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.99 (s, 1H), 8.97 (s, 1H, TFA), 8.81 (d, J = 4.9 Hz, 1H), 8.29 (s, 1H), 8.00 (s, 1H), 7.41 (d, J = 8.8 Hz, 1H), 7.04 (s, 2H), 6.71 (dd, J = 5.7, 2.4 Hz, 2H), 5.08 (dd, J = 13.3, 5.1 Hz, 1H), 4.39 – 4.13 (m, 4H), 3.95 (s, 6H), 3.76 (s, 2H), 3.64 (s, 4H), 3.38 (d, J = 12.2 Hz, 2H), 3.19 – 3.09 (m, 2H), 2.94 – 2.82 (m, 1H), 2.79 (d, J = 4.2 Hz, 3H), 2.60 (d, J = 16.2 Hz, 1H), 2.43 – 2.25 (m, 1H), 2.14 (d, J = 13.7 Hz, 2H), 2.06 – 1.96 (m, 3H).
D139	707.35	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.97 (s, 1H), 8.49 (d, J = 1.6 Hz, 1H), 8.14 (d, J = 1.8 Hz, 2H), 7.39 (d, J = 8.0 Hz, 1H), 6.97 (s, 2H), 6.70 (d, J = 7.5 Hz, 2H), 5.08 (dd, J = 13.2, 5.1 Hz, 1H), 4.36–4.15 (m, 2H), 3.90 (s, 8H), 3.63 (d, J = 4.3 Hz, 8H), 2.96–2.85 (m, 2H), 2.77 (s, 2H), 2.63–2.60 (m, 1H), 2.38 (dd, J = 13.2, 4.6 Hz, 1H), 2.06–1.95 (m, 2H), 1.87 (s, 3H)
D140	846.25	¹ H NMR (300 MHz, Acetonitrile-d ₃) δ 8.29 (s, 1H), 7.74 (s, 1H), 7.46 (d, J = 8.3 Hz, 1H), 7.39 – 7.27 (m, 2H), 6.98 (s, 2H), 5.07 (dd, J = 13.3, 5.2 Hz, 1H), 4.87 – 4.65 (m, 1H), 4.42 – 4.23 (m, 3H), 3.94 (s, 7H), 3.83 (s, 1H), 3.64 (d, J = 20.7 Hz, 4H), 3.55 – 3.37 (m, 2H), 3.30 – 2.99 (m, 3H), 2.81 – 2.80 (m, 6H), 2.52 – 2.30 (m, 3H), 2.27 – 2.10 (m, 4H), 1.87 (s, 2H), 1.73 (s, 1H), 1.32 (d, J = 21.7 Hz, 2H).
D141	846.2	¹ H NMR (300 MHz, Acetonitrile-d ₃) δ 8.29 (s, 1H), 7.75 (s, 1H), 7.48 (d, J = 8.2 Hz, 1H), 7.41 – 7.30 (m, 2H), 6.97 (s, 2H), 5.07 (dd, J = 13.3, 5.1 Hz, 1H), 4.79 (d, J = 22.1 Hz, 1H), 4.32 (q, J = 10.1, 9.0 Hz, 3H), 3.93 (s, 7H), 3.67 (s, 4H), 3.62 – 3.48 (m, 3H), 2.95 – 2.90 (m, 4H), 2.80 (s, 6H), 2.43 (dd, J = 13.1, 5.0 Hz, 1H), 2.22 (q, J = 22.0, 16.5 Hz, 5H), 1.94 – 1.82 (m, 2H), 1.74 (s, 1H), 1.31 (d, J = 21.7 Hz, 2H).
D142	860.5	¹ H NMR (400 MHz, DMSO-d ₆) δ 8.58 (d, J = 1.2 Hz, 1H), 8.28 (s, 1H, FA), 7.95 (s, 1H), 7.43 (d, J = 8.4 Hz, 1H), 7.28 (dd, J = 8.5, 2.4 Hz, 1H), 7.18 (d, J = 2.3 Hz, 1H), 6.92 (s, 2H), 5.16 (dd, J = 13.4, 5.1 Hz, 1H), 4.42 – 4.13 (m, 3H), 3.84 (s, 6H), 3.80 (s, 2H), 3.62 (s, 3H), 3.57 (s, 2H), 3.17 (s, 1H), 3.00 (s, 3H), 2.96 (dd, J = 12.8, 5.2 Hz, 2H), 2.80 – 2.69 (m, 3H), 2.62 – 2.58 (m, 2H), 2.43 – 2.35 (m, 2H), 2.22 (s, 6H), 2.04 – 1.97 (m, 1H), 1.84 – 1.80 (m, 4H), 1.71 – 1.46 (m, 2H).

Compound No.	LCMS	¹ H NMR
D143	777.55	¹ H NMR (400 MHz, DMSO-d ₆ with a drop of D ₂ O) δ 8.5 - 8.50 (m, 1H), 8.28 (s, 1H), 7.95 (s, 1H), 7.47 (d, J = 8.4 Hz, 1H), 7.38 - 7.31 (m, 1H), 7.26 (s, 1H), 6.97 (s, 2H), 5.12 (dd, J = 13.3, 4.9 Hz, 1H), 4.58 - 4.53 (m, 1H), 4.36 (d, J = 16.9 Hz, 1H), 4.22 (dd, J = 17.0, 3.6 Hz, 1H), 4.13 (s, 1H), 4.04 (s, 2H), 3.88 (s, 7H), 3.61 (s, 3H), 3.41 - 3.28 (m, 1H), 3.11 (t, J = 12.3 Hz, 1H), 2.99 (s, 3H), 2.97 - 2.88 (m, 1H), 2.81 - 2.72 (m, 1H), 2.59 (s, 6H), 2.42 - 2.34 (m, 1H), 2.06 - 2.01 (m, 2H), 1.96 - 1.91 (m, 1H).
D144	670.2	¹ H NMR (400 MHz, Methanol-d ₄) δ 7.77 (s, 1H), 7.71 (d, J = 5.4 Hz, 1H), 7.62 (d, J = 5.4 Hz, 1H), 7.53 (d, J = 8.2 Hz, 1H), 7.38 (d, J = 10.2 Hz, 2H), 7.09 (s, 2H), 5.24 - 5.12 (m, 1H), 4.69 - 4.53 (m, 2H), 4.52 - 4.37 (m, 3H), 4.04 (s, 6H), 3.88 (s, 2H), 3.76 (s, 3H), 3.74 - 3.51 (m, 3H), 3.00 - 2.86 (m, 1H), 2.85 - 2.76 (m, 1H), 2.61 - 2.42 (m, 1H), 2.25 - 2.15 (m, 1H), 1.62 (d, J = 6.4 Hz, 6H).
D145	858.6	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.57 (br s, 2H, FA), 8.36 (d, J = 1.5 Hz, 1H), 7.88 (s, 1H), 7.35 (d, J = 8.4 Hz, 1H), 7.01 (d, J = 11.0 Hz, 4H), 5.15 (dd, J = 13.7, 6.0 Hz, 1H), 4.67 - 4.62 (m, 3H), 4.45 - 4.36 (m, 3H), 4.18 (s, 2H), 3.99 (s, 6H), 3.91 - 3.81 (m, 2H), 3.76 (s, 3H), 3.67 (s, 1H), 3.53 (s, 2H), 2.94 - 2.81 (m, 2H), 2.72 (s, 6H), 2.58 - 2.13 (m, 9H).
D146	727.3	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.99 (s, 1H), 8.68 (m, J = 7.7 Hz, 1H), 8.41 (s, 1H), 8.18 (d, J = 2.2 Hz, 1H), 7.44 (m, J = 8.5 Hz, 1H), 7.21 (m, J = 2.3 Hz, 1H), 6.95 (s, 2H), 5.11 (dd, J = 13.3, 5.1 Hz, 1H), 4.45 - 4.26 (m, 1H), 4.25 - 4.12 (m, 1H), 4.05 - 3.95 (m, 2H), 3.92 (s, 6H), 3.83 - 3.81 (m, 1H), 3.80 - 3.76 (m, 2H), 3.62 (s, 3H), 3.00 - 2.81 (m, 3H), 2.55 (s, 2H), 2.39 (s, 6H), 2.06 - 1.96 (m, 1H), 1.95 - 1.81 (m, 2H), 1.78 - 1.55 (m, 2H).
D147	645.3	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.52 (s, 0.2H, FA), 7.75 (s, 1H), 7.71 (d, J = 5.5 Hz, 1H), 7.61 (d, J = 5.5 Hz, 1H), 7.49 (d, J = 8.2 Hz, 1H), 7.38 - 7.32 (m, 2H), 7.04 (s, 2H), 5.16 (dd, J = 13.3, 5.2 Hz, 1H), 4.49 - 4.35 (m, 2H), 4.16 (s, 2H), 3.99 (s, 6H), 3.42 (s, 4H), 3.17 (m, 4H), 2.94 - 2.85 (m, 1H), 2.85 - 2.75 (m, 1H), 2.56 - 2.45 (m, 1H), 2.24 - 2.13 (m, 1H).

Compound No.	LCMS	¹ H NMR
D148	860.5	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.98 (s, 1H), 8.41 (d, J = 8.9 Hz, 1H), 7.95 (d, J = 1.3 Hz, 1H), 7.42 (d, J = 8.5 Hz, 1H), 7.27 (dd, J = 8.5, 2.4 Hz, 1H), 7.17 (d, J = 2.4 Hz, 1H), 6.99 (d, J = 4.5 Hz, 2H), 5.10 (dd, J = 13.2, 5.1 Hz, 1H), 4.43 – 4.03 (m, 5H), 3.91 (d, J = 3.2 Hz, 6H), 3.82 (d, J = 11.9 Hz, 2H), 3.59 (s, 3H), 3.16 (s, 1H), 2.92 (s, 2H), 2.77 (s, 3H), 2.75 – 2.56 (m, 11H), 2.46 – 2.30 (m, 2H), 1.99 (d, J = 12.0 Hz, 1H), 1.80 (s, 4H), 1.56 (d, J = 12.7 Hz, 2H).
D149	767.4	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.56 (s, 1H, FA), 8.27 (s, 1H), 7.85 (s, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.39 – 7.30 (m, 2H), 7.05 (s, 2H), 5.15 (dd, J = 13.3, 5.2 Hz, 1H), 4.53 (t, J = 8.3 Hz, 1H), 4.52 – 4.34 (m, 2H), 4.31 (s, 2H), 4.01 (s, 6H), 3.75 (s, 3H), 3.31 – 3.17 (m, 4H), 2.99 – 2.72 (m, 8H), 2.59 – 2.43 (m, 1H), 2.46 – 2.36 (m, 2H), 2.23 – 2.13 (m, 1H), 2.01 – 1.97 (m, 2H), 1.88 (t, J = 5.6 Hz, 2H), 1.82 (t, J = 5.6 Hz, 2H).
D150	810.55	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.54 (s, FA 2H), 8.27 (s, 1H), 7.87 (s, 1H), 7.47 (d, J = 8.2 Hz, 1H), 7.35 (d, J = 10.4 Hz, 2H), 7.07 (s, 2H), 5.16 (dd, J = 13.3, 5.2 Hz, 1H), 4.53 – 4.33 (m, 4H), 4.11 – 3.97 (m, 7H), 3.96 – 3.86 (m, 2H), 3.75 (s, 3H), 3.02 – 2.87 (m, 8H), 2.87 – 2.65 (m, 6H), 2.58 – 2.43 (m, 1H), 2.30 – 2.01 (m, 6H), 1.94 – 1.69 (m, 4H).
D151	763.35	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.98 (s, 1H), 9.17 (s, 1H), 9.01 – 8.91 (m, 1H), 8.59 (d, J = 1.8 Hz, 1H), 8.02 (s, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.23 – 7.12 (m, 2H), 7.04 (s, 2H), 5.13 – 5.01 (m, 1H), 4.62 (s, 1H), 4.41 – 4.16 (m, 6H), 4.01 (s, 1H), 3.93 (s, 6H), 3.63 (s, 3H), 3.49 (dd, J = 30.5, 13.7 Hz, 1H), 3.22 (t, J = 12.3 Hz, 1H), 2.92 (s, 1H), 2.78 (d, J = 4.6 Hz, 6H), 2.60 (d, J = 17.0 Hz, 1H), 2.40 (d, J = 13.6 Hz, 1H), 2.00 (dd, J = 20.3, 10.8 Hz, 3H).
D152	763.35	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.00 (s, 1H), 9.08 (s, 1H), 9.00 – 8.90 (m, 1H), 8.60 (d, J = 2.3 Hz, 1H), 8.02 (s, 1H), 7.47 (d, J = 8.5 Hz, 1H), 7.42 – 7.32 (m, 1H), 7.28 (d, J = 9.0 Hz, 1H), 7.04 (s, 2H), 5.18 – 5.05 (m, 1H), 4.60 (s, 1H), 4.36 (d, J = 16.9 Hz, 1H), 4.25 (d, J = 4.4 Hz, 3H), 4.23 – 4.08 (m, 1H), 3.93 (s, 6H), 3.63 (s, 3H), 3.54 – 3.07 (m, 3H), 3.02 – 2.84 (m, 1H), 2.82 – 2.80 (m, 1H), 2.78 (d, J = 4.6 Hz, 6H), 2.61 (d, J = 16.5 Hz, 1H), 2.46 – 2.35 (m, 1H), 1.98 (d, J = 25.6 Hz, 3H).

Compound No.	LCMS	¹ H NMR
D153	794.2	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.35 (s, 3H, FA), 7.62 (d, J = 5.4 Hz, 1H), 7.47 – 7.37 (m, 2H), 6.90 – 6.82 (m, 3H), 6.79 (d, 1H), 5.14 (dd, J = 13.3, 5.1 Hz, 1H), 4.47 – 4.32 (m, 4H), 3.95 (s, 6H), 3.75 (s, 3H), 3.72 (s, 4H), 3.59 (d, J = 12.0 Hz, 2H), 3.23 – 3.19 (m, 1H), 3.01 – 3.75 (m, 6H), 2.68 (s, 3H), 2.57 – 2.44 (m, 1H), 2.41 (s, 3H), 2.23 – 2.15 (m, 1H), 2.13 – 2.01 (m, 7H), 1.63 (s, 2H).
D154	683.3	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.99 (s, 1H), 9.50 – 9.43 (m, 1H, TFA), 7.94 (s, 1H), 7.72 (d, J = 5.4 Hz, 1H), 7.67 – 7.60 (m, 2H), 7.34 – 7.24 (m, 2H), 7.09 (s, 2H), 5.09 (dd, J = 13.3, 5.1 Hz, 1H), 4.97 – 4.62 (m, 1H), 4.59 – 4.49 (m, 1H), 4.40 (d, J = 17.0 Hz, 1H), 4.28 (d, J = 16.9 Hz, 1H), 4.09 (d, J = 13.1 Hz, 1H), 3.98 (s, 6H), 3.83 (d, J = 13.9 Hz, 1H), 3.64 (s, 3H), 3.58 (d, J = 13.5 Hz, 2H), 3.29 (t, J = 11.8 Hz, 1H), 3.07 (d, J = 12.9 Hz, 1H), 2.93 (ddd, J = 17.9, 13.5, 5.4 Hz, 1H), 2.77 – 2.54 (m, 3H), 2.40 (td, J = 13.1, 4.5 Hz, 1H), 2.14 (s, 3H), 2.03 – 1.88 (m, 2H).
D155	763.35	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.55 (s, 1H, FA), 8.36 (d, J = 0.7 Hz, 1H), 7.87 (s, 1H), 7.68 (d, J = 9.3 Hz, 1H), 7.20 – 7.14 (m, 2H), 7.07 (s, 2H), 5.17 – 5.08 (m, 1H), 4.73 – 4.63 (m, 1H), 4.50 – 4.42 (m, 2H), 4.38 (s, 2H), 4.34 – 4.22 (m, 1H), 4.09 (d, J = 13.7 Hz, 1H), 4.02 (s, 6H), 3.75 (s, 3H), 3.44 – 3.38 (m, 1H), 3.23 – 3.14 (m, 1H), 2.98 – 2.92 (m, 1H), 2.89 (s, 6H), 2.83 – 2.76 (m, 1H), 2.55 – 2.44 (m, 1H), 2.23 – 2.13 (m, 2H), 2.13 – 2.02 (m, 1H).
D156	763.35	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.56 (s, 1H, FA), 8.38 (s, 1H), 7.87 (s, 1H), 7.50 (d, J = 8.3 Hz, 1H), 7.43 – 7.35 (m, 2H), 7.07 (s, 2H), 5.20 – 5.13 (m, 1H), 4.71 – 4.59 (m, 2H), 4.51 – 4.41 (m, 2H), 4.37 (s, 2H), 4.10 (s, 1H), 4.02 (s, 6H), 3.93 (d, J = 12.9 Hz, 1H), 3.75 (s, 3H), 3.16 – 3.08 (m, 1H), 2.98 – 2.91 (m, 1H), 2.87 (s, 6H), 2.84 – 2.78 (m, 1H), 2.58 – 2.47 (m, 1H), 2.26 – 2.15 (m, 2H), 2.13 – 2.04 (m, 1H).
D157	844.35	¹ H NMR (400 MHz, DMSO-d ₆) δ 8.55 (s, 1H), 7.90 (s, 1H), 7.43 (d, J = 8.4 Hz, 1H), 7.27 (d, J = 8.0 Hz, 1H), 7.17 (s, 2H), 7.11 (s, 1H), 5.05 (dd, J = 13.4, 4.8 Hz, 1H), 4.40 – 4.15 (m, 3H), 3.86 (s, 4H), 3.82 – 3.80 (m, 3H), 3.61 (s, 3H), 3.16 (s, 1H), 2.95 – 2.80 (m, 2H), 2.80 – 2.65 (m, 4H), 2.64 – 2.54 (m, 3H), 2.51 (s, 6H), 2.45 – 2.35 (m, 2H), 2.04 – 1.96 (m, 1H), 1.87 – 1.75 (m, 4H), 1.64 – 1.47 (m, 2H), 1.17 (t, J = 7.6 Hz, 3H).

Compound No.	LCMS	¹ H NMR
D158	696.35	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.98 (s, 1H), 8.92 (s, 1H, TFA salt), 7.53 (s, 2H), 7.42 (d, J = 8.9 Hz, 1H), 6.84 (s, 2H), 6.72 (s, 2H), 5.08 (dd, J = 13.3, 5.1 Hz, 1H), 4.39 – 4.17 (m, 4H), 3.88 (s, 6H), 3.77 (s, 2H), 3.65 (s, 2H), 3.62 (s, 3H), 3.21 – 3.12 (m, 2H), 2.98 – 2.85 (m, 1H), 2.64–2.60 (m, 2H), 2.57 (s, 1H), 2.42 – 2.37 (m, 1H), 2.35 (s, 3H), 2.14 (d, J = 14.0 Hz, 2H), 2.00 (t, J = 11.7 Hz, 3H).
D159	849.4	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.57 (s, 1H, FA), 8.39 (d, J = 5.2 Hz, 1H), 7.86 (s, 1H), 7.50 (d, J = 8.4 Hz, 1H), 7.34 (s, 1H), 7.23 (d, J = 8.3, 2.4 Hz, 1H), 7.05 (s, 2H), 5.17 (dd, J = 13.3, 6.9, 5.1 Hz, 1H), 4.49 – 4.39 (m, 3H), 4.35 (s, 2H), 4.11 (t, 2H), 4.01 (s, 6H), 3.75 (s, 3H), 3.29 – 3.14 (m, 1H), 3.07 – 2.98 (m, 1H), 2.97 – 2.88 (m, 1H), 2.86 (s, 6H), 2.83 – 2.76 (m, 1H), 2.59 – 2.47 (m, 3H), 2.45 – 2.33 (m, 1H), 2.32 – 2.25 (m, 1H), 2.24 – 2.15 (m, 1H), 2.08 – 1.98 (m, 1H), 1.98 – 1.92 (m, 1H), 1.92 – 1.83 (m, 2H), 1.69 – 1.52 (m, 4H).
D160	822.4	¹ H NMR (400 MHz, Methanol-d ₄) δ 7.82 (d, J = 8.2 Hz, 1H), 7.67 (s, 1H), 7.30 (d, J = 2.3 Hz, 1H), 7.25 (dd, J = 8.3, 2.3 Hz, 1H), 7.14 (d, J = 1.3 Hz, 1H), 7.04 (d, J = 3.1 Hz, 2H), 5.12 (dd, J = 12.5, 5.4 Hz, 1H), 4.98 (d, J = 6.5 Hz, 1H), 4.40 (s, 2H), 4.00–3.99 (s, 6H), 3.69–3.63 (s, 3H), 3.60 – 3.49 (m, 4H), 3.37 (s, 1H), 3.23 – 3.12 (m, 2H), 3.12 – 3.07 (m, 2H), 3.07 – 2.93 (m, 1H), 2.92 – 2.74 (m, 4H), 2.66 (d, J = 1.2 Hz, 3H), 2.65 (s, 1H), 2.05 (m, 1H), 2.16–2.05 (m, 6H), 2.03 – 1.97 (m, 3H), 1.64 (q, J = 12.1 Hz, 2H).
D161	807.43	
D162	846.35	¹ H NMR (400 MHz, Methanol-d ₄ with a drop of D ₂ O) δ 8.37 (s, 1H), 8.36 (br s, 1H, FA), 7.87 (s, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.39 – 7.31 (m, 2H), 7.08 (s, 2H), 5.15 (dd, J = 13.3, 5.2 Hz, 1H), 4.49 – 4.34 (m, 5H), 4.02 (s, 6H), 3.86 (d, J = 12.3 Hz, 2H), 3.75 (s, 3H), 3.30 – 3.26 (m, 1H), 3.16 – 3.09 (m, 1H), 2.92 (s, 7H), 2.86 – 2.74 (m, 3H), 2.71 – 2.60 (m, 2H), 2.56 – 2.48 (m, 2H), 2.24 – 2.15 (m, 1H), 2.05 – 1.92 (m, 4H), 1.71 (q, J = 12.6 Hz, 2H).

Compound No.	LCMS	¹ H NMR
D163	849.4	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.99 (s, 1H), 8.88 (d, J = 8.8 Hz, 1H), 8.59 (s, 1H), 8.24 (s, 1H, FA), 7.97 (s, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.17 (d, J = 2.2 Hz, 1H), 7.05 (d, J = 8.4, 2.2 Hz, 1H), 6.93 (s, 2H), 5.08 (dd, J = 13.2, 5.1 Hz, 1H), 4.33 (q, J = 22.5 Hz, 3H), 4.07 (t, J = 6.3 Hz, 2H), 3.85 (s, 6H), 3.62 (s, 5H), 3.20 – 3.08 (m, 1H), 2.97 – 2.83 (m, 2H), 2.66 – 2.56 (m, 1H), 2.46 – 2.31 (m, 4H), 2.26 (s, 6H), 2.20 – 2.08 (m, 1H), 2.05 – 1.92 (m, 1H), 1.91 – 1.82 (m, 1H), 1.83 – 1.71 (m, 3H), 1.57 – 1.38 (m, 4H).
D164	763.2	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.97 (s, 1H), 8.97 – 8.90 (m, 1H), 8.57 (d, J = 2.5 Hz, 1H), 8.27 (s, 1H, FA), 7.96 (s, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.23 – 7.14 (m, 2H), 6.91 (s, 2H), 5.10 – 5.02 (m, 1H), 4.75 – 4.56 (m, 1H), 4.41 – 4.16 (m, 3H), 4.04 – 3.92 (m, 1H), 3.84 (s, 6H), 3.51 (s, 3H), 3.57–3.46 (m, 2H), 3.22 (t, J = 12.3 Hz, 1H), 2.97 – 2.85 (m, 1H), 2.69 – 2.56 (m, 1H), 2.45 – 2.32 (m, 1H), 2.17 (s, 6H), 2.06 – 1.89 (m, 3H).
D165	763.35	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.55 (s, FA, 1H), 8.37 (s, 1H), 7.86 (s, 1H), 7.54 – 7.45 (m, 1H), 7.43 – 7.32 (m, 2H), 7.07 (s, 2H), 5.23 – 5.11 (m, 1H), 4.74 – 4.56 (m, 1H), 4.48 – 4.35 (m, 4H), 4.12 – 4.02 (m, 7H), 3.97 – 3.87 (m, 1H), 3.78 – 3.72 (s, 3H), 3.27 – 3.05 (m, 2H), 2.88 – 2.78 (m, 8H), 2.56 – 2.47 (m, 1H), 2.28 – 2.14 (m, 2H), 2.13 – 2.05 (m, 1H).
D166	875.5	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.98 (s, 1H), 9.06 (s, 1H, TFA salt), 8.91 (dd, J = 9.0, 2.8 Hz, 1H), 8.61 (s, 1H), 8.01 (s, 1H), 7.51 (d, J = 8.4 Hz, 1H), 7.38 – 7.27 (m, 2H), 7.03 (s, 2H), 5.10 (dd, J = 13.2, 5.1 Hz, 1H), 4.38 (d, J = 17.0 Hz, 2H), 4.28 – 4.19 (m, 3H), 3.92 (s, 6H), 3.63 (s, 3H), 3.57 – 3.45 (m, 7H), 3.37 – 3.35 (m, 4H), 3.05 – 2.99 (m, 1H), 2.93 – 2.89 (m, 1H), 2.88 – 2.83 (m, 2H), 2.80 – 2.74 (m, 6H), 2.65 – 2.58 (m, 2H), 2.43 – 2.36 (m, 2H), 2.05 – 1.96 (m, 1H), 1.94 – 1.76 (m, 2H).
D167	846.4	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.98 (s, 1H), 8.88 (d, J = 8.7 Hz, 1H), 8.60 (s, 1H), 8.23 (s, 2H, FA salt), 7.97 (s, 1H), 7.43 (d, J = 8.5 Hz, 1H), 7.28 (dd, J = 8.5, 2.3 Hz, 1H), 7.17 (d, J = 2.3 Hz, 1H), 6.93 (s, 2H), 5.10 (dd, J = 13.3, 5.1 Hz, 1H), 4.53 – 4.09 (m, 4H), 3.86 (s, 6H), 3.80 (s, 2H), 3.64 (d, J = 8.8 Hz, 5H), 3.20 – 3.14 (m, 1H), 2.99 – 2.83 (m, 2H), 2.74 (t, J = 11.9 Hz, 2H), 2.65 – 2.54 (m, 3H), 2.44 – 2.34 (m, 1H), 2.29 (s, 6H), 2.04 – 1.94 (m, 1H), 1.85 – 1.79 (m, 4H), 1.62 – 1.52 (m, 2H).

Compound No.	LCMS	¹ H NMR
D168	629.15	¹ H NMR (400 MHz, Methanol-d ₄) δ 7.77 (s, 1H), 7.71 (d, J = 5.4 Hz, 1H), 7.64 – 7.56 (m, 2H), 7.26 (d, J = 8.5 Hz, 1H), 7.21 (s, 1H), 7.08 (s, 2H), 5.38 – 5.06 (m, 2H), 4.76 (s, 2H), 4.65 (d, J = 16.6 Hz, 2H), 4.55 – 4.40 (m, 2H), 4.37 – 4.32 (m, 2H), 4.08 – 3.95 (m, 6H), 3.75 (s, 3H), 2.98 – 2.86 (m, 1H), 2.85 – 2.76 (m, 1H), 2.58 – 2.45 (m, 1H), 2.22 – 2.18 (m, 1H).
D169	643.1	¹ H NMR (400 MHz, Methanol-d ₄) δ 7.90 (d, J = 8.3 Hz, 1H), 7.77 (s, 1H), 7.71 (d, J = 5.4 Hz, 1H), 7.61 (d, J = 5.4 Hz, 1H), 7.37 (d, J = 2.2 Hz, 1H), 7.32 (dd, J = 8.3, 2.3 Hz, 1H), 7.08 (s, 2H), 5.34 (s, 1H), 5.15 (dd, J = 12.5, 5.4 Hz, 1H), 4.78 (dd, J = 12.0, 6.3 Hz, 2H), 4.64 (s, 2H), 4.38 (d, J = 10.8 Hz, 2H), 4.00 (s, 6H), 3.75 (s, 3H), 2.96 – 2.83 (m, 1H), 2.83 – 2.66 (m, 2H), 2.20 – 2.10 (m, 1H).
D170	629.1	¹ H NMR (400 MHz, Methanol-d ₄) δ 7.83 – 7.74 (m, 2H), 7.71 (d, J = 5.4 Hz, 1H), 7.61 (d, J = 5.4 Hz, 1H), 7.13 – 7.05 (m, 4H), 5.38 – 5.08 (m, 2H), 4.77 (s, 2H), 4.66 (s, 2H), 4.55 – 4.40 (m, 2H), 4.35 (s, 2H), 4.07 – 3.92 (m, 6H), 3.75 (s, 3H), 3.00 – 2.86 (m, 1H), 2.85 – 2.75 (m, 1H), 2.57 – 2.42 (m, 1H), 2.27 – 2.10 (m, 1H).
D171	889.45	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.00 (s, 1H), 9.08 (s, 1H, TFA salt), 8.83 (d, J = 8.7 Hz, 1H), 8.53 (s, 1H), 7.52 (d, J = 8.3 Hz, 1H), 7.40 – 7.28 (m, 2H), 6.82 (d, J = 2.2 Hz, 2H), 5.11 (dd, J = 13.2, 5.0 Hz, 1H), 4.42 – 4.22 (m, 5H), 3.86 (s, 6H), 3.62 (s, 3H), 3.50 – 3.45 (m, 8H), 3.07 – 2.95 (m, 2H), 2.95 – 2.90 (m, 1H), 2.89 – 2.74 (m, 9H), 2.68 – 2.54 (m, 2H), 2.45 – 2.30 (m, 6H), 2.01 – 1.79 (m, 3H).
D172	941.40	¹ H NMR (300 MHz, MeOD) δ 8.27 (s, 1H), 7.42 (d, J = 8.2 Hz, 1H), 6.92 – 6.76 (m, 4H), 5.14 (dd, J = 13.2, 5.1 Hz, 1H), 4.85 – 4.68 (m, 1H), 4.67 – 4.51 (m, 2H), 4.48 – 4.31 (m, 4H), 4.23 – 4.18 (m, 2H), 3.96 (s, 7H), 3.81 – 3.70 (m, 7H), 3.69 – 3.39 (m, 8H), 3.26 – 3.05 (m, 2H), 3.02 – 2.72 (m, 5H), 2.60 – 2.40 (m, 4H), 2.36 – 2.08 (m, 7H).
D173	822.35	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.39 (s, 1H, FA), 7.82 (d, J = 8.3 Hz, 1H), 7.71 (s, 1H), 7.36 (d, J = 1.4 Hz, 1H), 7.33 – 7.22 (m, 2H), 7.04 (s, 2H), 5.13 (dd, J = 12.4, 5.4 Hz, 1H), 5.03 – 4.96 (m, 1H), 4.69 – 4.59 (m, 1H), 4.40 (s, 2H), 4.01 (s, 6H), 3.74 (s, 3H), 3.63 – 3.52 (m, 2H), 3.22 – 3.13 (m, 2H), 3.11 – 2.96 (m, 3H), 2.93 – 2.70 (m, 5H), 2.64 – 2.56 (m, 5H), 2.23 – 2.04 (m, 6H), 2.02 – 1.87 (m, 4H), 1.91 – 1.53 (m, 2H).

Compound No.	LCMS	¹ H NMR
D174	794.25	¹ H NMR (400 MHz, DMSO-d ₆) δ 7.82 (s, 1H), 7.69 – 7.59 (m, 2H), 7.51 (d, J = 8.3 Hz, 1H), 7.16 – 7.07 (m, 2H), 6.99 (s, 2H), 4.99 (dd, J = 13.3, 5.1 Hz, 1H), 4.86 – 4.78 (m, 1H), 4.42 – 4.24 (m, 2H), 4.21 (d, J = 6.4 Hz, 2H), 3.88 (s, 6H), 3.60 (s, 3H), 3.37 (dd, J = 28.0, 12.1 Hz, 4H), 3.16 (s, 1H), 3.01 (t, J = 12.7 Hz, 2H), 2.92 (d, J = 6.9 Hz, 2H), 2.90 – 2.78 (m, 2H), 2.70 – 2.64 (m, 1H), 2.39 (s, 2H), 2.08 – 1.73 (m, 11H), 1.44 (q, J = 12.1 Hz, 2H).
D175	915.35	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.99 (s, 1H), 9.07 (s, 1H, TFA salt), 8.93 (d, J = 8.8 Hz, 1H), 8.62 (s, 1H), 8.02 (s, 1H), 7.42 (d, J = 8.9 Hz, 1H), 7.03 (s, 2H), 6.77 – 6.65 (m, 2H), 5.08 (dd, J = 13.2, 5.1 Hz, 1H), 4.49 – 4.38 (m, 1H), 4.39 – 4.14 (m, 5H), 3.93 (s, 6H), 3.70 (s, 2H), 3.64 (s, 3H), 3.29 (s, 6H), 3.07 – 2.95 (m, 2H), 2.95 – 2.89 (m, 1H), 2.91 – 2.69 (m, 9H), 2.68 – 2.56 (m, 2H), 2.45 – 2.28 (m, 2H), 2.17 – 1.78 (m, 7H).
D176	682.45	¹ H NMR (400 MHz, DMSO-d ₆) δ 11.00 (s, 1H), 9.32 (d, J = 7.7 Hz, 1H, TFA), 7.94 (s, 1H), 7.72 (d, J = 5.4 Hz, 1H), 7.63 (d, J = 5.4 Hz, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.49 – 7.39 (m, 2H), 7.09 (s, 2H), 5.14 (dd, J = 13.3, 5.1 Hz, 1H), 4.53 (dd, J = 13.2, 7.9 Hz, 1H), 4.40 (d, J = 16.9 Hz, 1H), 4.27 (dd, J = 17.3, 1.8 Hz, 1H), 4.09 (d, J = 13.1 Hz, 1H), 3.98 (s, 6H), 3.88 (d, J = 13.7 Hz, 1H), 3.73 (s, 2H), 3.64 (s, 2H), 3.51 (s, 1H), 3.47 (d, J = 7.4 Hz, 1H), 3.31 (s, 1H), 3.08 (d, J = 12.8 Hz, 1H), 3.00 – 2.87 (m, 1H), 2.61 (d, J = 19.7 Hz, 3H), 2.40 (dt, J = 13.3, 6.7 Hz, 1H), 2.22 (d, J = 10.8 Hz, 2H), 2.12 (q, J = 8.9, 8.5 Hz, 1H), 2.06 – 1.98 (m, 1H), 1.92 (d, J = 11.0 Hz, 1H).
D177	749.25	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.57 (s, 1H, FA), 8.39 (s, 1H), 7.86 (s, 1H), 7.49 (d, J = 8.2 Hz, 1H), 7.05 (s, 3H), 7.03 – 6.97 (m, 1H), 5.24 – 5.12 (m, 2H), 4.48 – 4.35 (m, 2H), 4.21 (s, 2H), 4.06 – 3.97 (m, 7H), 3.96 – 3.83 (m, 2H), 3.75 (s, 3H), 3.57 (t, J = 8.4 Hz, 1H), 2.99 – 2.87 (m, 1H), 2.85 – 2.80 (m, 1H), 2.74 (s, 6H), 2.56 – 2.46 (m, 1H), 2.24 – 2.15 (m, 1H).
D178	682.2	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.94 (s, 1H), 8.28 (s, 1H), 7.87 (s, 1H), 7.69 (d, J = 5.4 Hz, 1H), 7.60 (d, J = 5.3 Hz, 1H), 7.47 (d, J = 8.3 Hz, 1H), 6.92 (s, 2H), 6.54 – 6.44 (m, 2H), 5.03 (dd, J = 13.3, 5.1 Hz, 1H), 4.30 (d, J = 16.9 Hz, 1H), 4.17 (d, J = 16.8 Hz, 1H), 3.85 (s, 6H), 3.61 (s, 6H), 3.52 (s, 2H), 2.98 – 2.83 (m, 1H), 2.58 (d, J = 17.1 Hz, 1H), 2.46 – 2.28 (m, 6H), 2.02 – 1.88 (m, 1H), 1.72 (t, J = 5.3 Hz, 4H).

Compound No.	LCMS	¹ H NMR
D179	848.25	¹ H NMR (400 MHz, DMSO-d ₆) δ 11.06 (s, 1H), 9.01 (s, 1H), 8.95 (s, 1H, TFA), 8.61 (s, 1H), 8.02 (s, 1H), 7.73 (d, J = 7.8 Hz, 1H), 7.03 (s, 2H), 6.71 (d, J = 7.9 Hz, 1H), 6.17 (s, 1H), 5.24 (dd, J = 12.4, 5.2 Hz, 1H), 4.25 (d, J = 5.0 Hz, 2H), 3.93 (s, 9H), 3.64 (s, 3H), 2.92 – 2.83 (m, 4H), 2.81 – 2.75 (m, 7H), 2.68 – 2.59 (m, 2H), 2.51 – 2.41 (m, 2H), 2.17 – 2.04 (m, 2H), 1.98 – 1.82 (m, 4H), 1.64 – 1.47 (m, 2H).
D180	749.3	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.38 (s, 1H), 7.88 (s, 1H), 7.69 (d, J = 8.8 Hz, 1H), 7.08 (s, 2H), 6.88– 6.68 (m, 2H), 5.32 – 5.07 (m, 2H), 4.54– 4.3 (m, 4H), 4.03 (s, 6H), 3.99–3.88 (m, 2H), 3.75 (s, 3H), 3.67–3.54 (m, 1H), 2.92 (s, 7H), 2.83–2.72 (m, 2H), 2.58 – 2.38 (m, 1H), 2.23–2.09 (m, 1H).
D181	832.35	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.56 (s, 1H, FA), 8.32 (s, 1H), 7.86 (s, 1H), 7.65 (d, 1H), 7.11 (d, J = 7.6 Hz, 2H), 7.05 (s, 2H), 5.12 (dd, J = 13.3, 5.1 Hz, 1H), 4.83 – 4.77 (m, 1H), 4.48 – 4.35 (d, J = 16.8 Hz, 2H), 4.32 (s, 2H), 4.01 (s, 6H), 3.93 (d, J = 13.0 Hz, 2H), 3.75 (s, 3H), 3.45 – 3.38 (m, 2H), 3.08 – 2.95 (m, 3H), 2.95 – 2.89 (m, 1H), 2.84 (s, 6H), 2.81 – 2.70 (m, 2H), 2.57 – 2.42 (m, 2H), 2.21 – 2.13 (m, 1H), 2.04 (t, J = 12.7 Hz, 2H), 1.74 – 1.56 (m, 2H).
D182	832.35	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.65 (br s, FA, 1H), 8.33 (s, 1H), 7.86 (s, 1H), 7.46 (d, J = 8.3 Hz, 1H), 7.39 – 7.30 (m, 2H), 7.06 (s, 2H), 5.15 (dd, J = 13.4, 5.1 Hz, 1H), 4.83 – 4.78 (m, 1H), 4.51 – 4.39 (m, 2H), 4.33 (s, 2H), 4.01 (s, 6H), 3.87 – 3.68 (m, 5H), 3.48 – 3.39 (m, 2H), 3.08 – 2.96 (m, 1H), 2.97 – 2.88 (m, 3H), 2.85 (s, 6H), 2.83 – 2.71 (m, 2H), 2.58 – 2.39 (m, 2H), 2.23 – 2.15 (m, 1H), 2.13 – 1.98 (m, 2H), 1.79 – 1.59 (m, 2H).
D183	696.15	¹ H NMR (400 MHz, DMSO-d ₆) δ 11.08 (s, 1H), 8.21 (s, 1H, FA), 7.87 (s, 1H), 7.69 (d, J = 5.4 Hz, 1H), 7.66 – 7.55 (m, 2H), 6.93 (s, 2H), 6.78 (d, J = 2.1 Hz, 1H), 6.69 – 6.60 (m, 1H), 5.12 – 4.97 (m, 1H), 3.85 (s, 6H), 3.73 (s, 4H), 3.62 (s, 3H), 3.53 (s, 2H), 2.97 – 2.81 (m, 1H), 2.70 – 2.53 (m, 2H), 2.46 – 2.31 (m, 4H), 2.07 – 1.95 (m, 1H), 1.80 – 1.67 (m, 4H).

Compound No.	LCMS	¹ H NMR
D184	807.35	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.09 (s, 1H), 9.45 (s, 1H, TFA salt), 9.23 (s, 1H, TFA salt), 7.85 (s, 1H), 7.69 (dd, J = 8.3, 2.6 Hz, 1H), 7.33 (d, J = 1.4 Hz, 1H), 7.03 (s, 2H), 6.78 (d, J = 2.2 Hz, 1H), 6.66 (dd, J = 8.3, 2.1 Hz, 1H), 5.06 (dd, J = 12.9, 5.4 Hz, 1H), 4.35 – 4.19 (m, 2H), 3.99 – 3.79 (m, 10H), 3.61 (s, 3H), 3.54 – 3.50 (m, 2H), 3.48 – 3.46 (m, 2H), 3.25 – 3.16 (m, 2H), 3.10 – 2.83 (m, 7H), 2.66 – 2.60 (m, 1H), 2.56 – 2.53 (m, 3H), 2.20 – 2.10 (m, 2H), 2.06 – 1.88 (m, 5H), 1.58 – 1.39 (m, 2H).
D185	793.25	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.49 (s, 1H, FA), 7.80 – 7.57 (m, 4H), 7.07 (s, 2H), 6.83 (d, J = 2.0 Hz, 1H), 6.67 (dd, J = 8.4, 2.1 Hz, 1H), 5.07 (dd, J = 12.4, 5.4 Hz, 1H), 4.39 (s, 2H), 4.01 (s, 6H), 3.79 (d, J = 16.3 Hz, 7H), 3.55 (d, J = 11.6 Hz, 2H), 3.23 – 3.07 (m, 2H), 2.96 – 2.81 (m, 1H), 2.81 – 2.67 (m, 2H), 2.58 (s, 4H), 2.39 (s, 2H), 2.16 – 2.00 (m, 3H), 1.99 – 1.89 (m, 5H), 1.55 (s, 2H).
D186	682.2	¹ H NMR (400 MHz, DMSO-d ₆) δ 7.82 (s, 1H), 7.73 – 7.55 (m, 2H), 7.40 (d, J = 8.9 Hz, 1H), 6.98 (s, 2H), 6.83 – 6.67 (m, 2H), 5.09 – 4.91 (m, 1H), 4.44 – 4.12 (m, 4H), 3.89 (s, 6H), 3.73 (s, 2H), 3.61 (s, 5H), 3.34 (d, J = 12.2 Hz, 2H), 3.09 (t, J = 11.9 Hz, 2H), 2.90 – 2.75 (m, 1H), 2.70 – 2.57 (m, 1H), 2.44 – 2.28 (m, 1H), 2.17 – 1.88 (m, 5H).
D187	846.1	¹ H NMR (400 MHz, DMSO-d ₆) δ 11.09 (s, 1H), 8.97 (d, J = 8.4 Hz, 1H), 8.53 (s, 1H), 8.18 (s, 1H, FA), 7.98 (s, 1H), 7.68 (d, J = 8.5 Hz, 1H), 7.36 (s, 1H), 7.28 (dd, J = 8.7, 2.3 Hz, 1H), 6.92 (s, 2H), 5.08 (dd, J = 12.9, 5.4 Hz, 1H), 4.71 – 4.58 (m, 1H), 4.01 (d, J = 12.9 Hz, 2H), 3.85 (s, 6H), 3.62 (s, 3H), 3.56 (s, 2H), 3.08 (t, J = 11.7 Hz, 3H), 2.96 – 2.76 (m, 3H), 2.73 – 2.53 (m, 4H), 2.22 (s, 6H), 2.08 – 1.86 (m, 3H), 1.53 – 1.46 (m, 2H).
D188	927.58	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.55 (s, 2H, FA), 8.36 (s, 1H), 7.85 (s, 1H), 7.39 (d, J = 8.2 Hz, 1H), 7.06 (s, 2H), 6.85 (d, J = 2.1 Hz, 1H), 6.77 (dd, J = 8.2, 2.2 Hz, 1H), 5.14 (dd, J = 13.2, 5.1 Hz, 1H), 4.62 (s, 1H), 4.47 (s, 2H), 4.46 – 4.32 (m, 2H), 4.22 (t, J = 9.6 Hz, 2H), 4.02 (s, 6H), 3.95 (t, J = 9.3 Hz, 2H), 3.75 (s, 3H), 3.67 (s, 4H), 3.23 – 3.04 (m, 2H), 2.99 – 2.89 (m, 2H), 2.85 – 2.74 (m, 1H), 2.69 (d, J = 6.9 Hz, 2H), 2.55 – 2.45 (m, 5H), 2.39 (s, 3H), 2.29 (t, J = 11.7 Hz, 1H), 2.21 – 2.13 (m, 1H), 2.08 – 1.99 (m, 1H), 1.98 – 1.86 (m, 4H), 1.31 (s, 2H).

Compound No.	LCMS	¹ H NMR
D189	808.35	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.14 (s, 1H), 9.22 (s, 2H, TFA), 7.94 – 7.83 (m, 2H), 7.75 – 7.60 (m, 2H), 7.37 – 7.26 (m, 2H), 7.06 (d, J = 1.7 Hz, 2H), 5.17 – 4.97 (m, 2H), 4.27 (d, J = 27.8 Hz, 2H), 3.94 (s, 6H), 3.63 (s, 3H), 3.55 – 3.49 (m, 1H), 3.46 (s, 3H), 3.26 – 3.17 (m, 2H), 3.06 – 2.83 (m, 6H), 2.68 – 2.53 (m, 3H), 2.10 – 1.79 (m, 10H), 1.58 – 1.39 (m, 2H).
D190	763.15	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.11 (s, 1H), 9.25 (d, J = 8.5 Hz, 1H), 8.55 (s, 1H), 8.17 (s, 1H, FA), 7.99 (s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.09 (d, J = 2.2 Hz, 1H), 6.97 (dd, J = 8.5, 2.2 Hz, 1H), 6.93 (s, 2H), 5.16 – 5.04 (m, 2H), 4.14 – 4.01 (m, 3H), 3.86 (s, 6H), 3.66 – 3.57 (m, 6H), 3.00 – 2.81 (m, 1H), 2.65 – 2.54 (m, 2H), 2.25 (s, 6H), 2.07 – 2.01 (m, 1H).
D191	832.4	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.56 (s, FA, 1H), 8.34 (s, 1H), 7.84 (s, 1H), 7.62 (d, J = 8.3 Hz, 1H), 7.02 (s, 2H), 6.82 (d, J = 2.1 Hz, 1H), 6.65 (dd, J = 8.3, 2.1 Hz, 1H), 5.07 (dd, J = 12.4, 5.4 Hz, 1H), 4.60 - 4.39 (m, 1H), 4.27 (s, 2H), 4.15 (t, J = 7.8 Hz, 2H), 4.00 (s, 6H), 3.96 - 3.83 (m, 2H), 3.72 (s, 3H), 3.63 - 3.51 (m, 1H), 3.28 - 3.21 (m, 1H), 3.09 - 3.00 (m, 1H), 2.95 – 2.60 (m, 9H), 2.58 - 2.39 (m, 1H), 2.36 - 2.23 (m, 1H), 2.18 – 1.93 (m, 3H).
D192	777.25	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.12 (s, 1H), 9.05 (s, 1H, TFA), 8.94 (d, J = 8.8 Hz, 1H), 8.57 (s, 1H), 8.02 (s, 1H), 7.72 (d, J = 8.5 Hz, 1H), 7.51 (s, 1H), 7.41 (d, J = 8.6 Hz, 1H), 7.04 (s, 2H), 5.10 (dd, J = 12.8, 5.3 Hz, 1H), 4.76 – 4.63 (m, 1H), 4.58 – 4.52 (m, 1H), 4.25 (d, J = 4.8 Hz, 2H), 4.18 (d, J = 13.6 Hz, 1H), 3.93 (s, 6H), 3.76 – 3.51 (m, 5H), 2.93 – 2.83 (m, 1H), 2.82 – 2.75 (m, 6H), 2.66 – 2.54 (m, 2H), 2.09 – 1.92 (m, 3H).
D193	794.2	¹ H NMR (300 MHz, DMSO-d ₆) δ 8.28 (s, 3H), 8.08 (d, J = 5.4 Hz, 1H), 7.76 (s, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.50 (d, J = 5.1 Hz, 1H), 7.03 (s, 1H), 6.96 (d, J = 8.4 Hz, 1H), 6.82 (s, 2H), 5.02 (dd, J = 13.2, 5.1 Hz, 1H), 4.85 - 4.74 (m, 1H), 4.38 (d, J = 17.1 Hz, 1H), 4.24 (d, J = 17.1 Hz, 1H), 3.96 (s, 2H), 3.86 (s, 6H), 3.62 (s, 3H), 3.16 (d, J = 9 Hz, 2H), 2.96 - 2.80 (m, 1H), 2.74 - 2.52 (m, 3H), 2.48 - 2.12 (m, 9H), 2.05 - 1.90 (m, 1H), 1.85 - 1.50 (m, 9H), 1.40 - 1.20 (m, 2H).

Compound No.	LCMS	¹ H NMR
D194	642.15	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.97 (s, 1H), 8.15 (s, 1H), 7.88 (s, 1H), 7.69 (d, J = 5.4 Hz, 1H), 7.60 (d, J = 5.3 Hz, 1H), 7.42 (d, J = 8.5 Hz, 1H), 7.25 (dd, J = 8.5, 2.4 Hz, 1H), 7.14 (d, J = 2.3 Hz, 1H), 6.94 (s, 2H), 5.09 (dd, J = 13.3, 5.1 Hz, 1H), 4.37 – 4.14 (m, 2H), 3.87 (s, 6H), 3.62 (d, J = 3.5 Hz, 5H), 3.17 (t, J = 4.9 Hz, 4H), 2.91 (ddd, J = 17.2, 13.6, 5.4 Hz, 1H), 2.61 (d, J = 5.0 Hz, 5H), 2.45 – 2.33 (m, 1H), 2.03 – 1.95 (m, 1H).
D195	874.2	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.00 (s, 1H), 8.89 (d, J = 9.0 Hz, 1H), 8.59 (s, 1H), 8.26 (s, 3H, FA), 7.96 (s, 1H), 7.65 (d, J = 7.8 Hz, 1H), 7.50 (s, 1H), 7.41 (d, J = 8.0 Hz, 1H), 6.92 (s, 2H), 5.11 (dd, J = 13.2, 5.1 Hz, 1H), 4.43 – 4.29 (m, 2H), 3.84 (s, 6H), 3.65 – 3.59 (m, 5H), 3.24 – 3.00 (m, 3H), 2.98 – 2.79 (m, 3H), 2.66 – 2.55 (m, 7H), 2.21 (s, 6H), 2.22 – 2.04 (m, 3H), 2.04 – 1.88 (m, 2H), 1.79 – 1.76 (m, 6H).
D196	875.35	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.91 (dd, J = 8.8 Hz, 0.16H, TFA salt), 8.34 (s, 1H), 7.88 (s, 1H), 7.73 (d, J = 9.0 Hz, 1H), 7.20 (d, J = 7.7 Hz, 2H), 7.07 (s, 2H), 5.14 (dd, J = 13.3, 5.1 Hz, 1H), 4.51 (s, 3H), 4.43 (d, J = 15.7 Hz, 2H), 4.02 (s, 6H), 3.75 (s, 3H), 3.68 (d, J = 11.2 Hz, 4H), 3.62 (s, 4H), 3.49 – 3.43 (m, 2H), 3.38 (s, 2H), 3.17 (d, J = 11.5 Hz, 1H), 2.99 (t, J = 5.3 Hz, 2H), 2.92 (s, 6H), 2.80 (d, J = 17.3 Hz, 1H), 2.65 (dd, J = 28.9, 12.3 Hz, 1H), 2.57 – 2.41 (m, 2H), 2.22 – 2.14 (m, 1H), 2.12 – 2.04 (m, 1H), 2.02 – 1.97 (m, 1H).
D197	735.34	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.00 (s, 1H), 7.86 (d, J = 2.1 Hz, 1H), 7.41 (d, J = 8.2 Hz, 1H), 7.16 (s, 2H), 7.09 (d, J = 2.1 Hz, 1H), 6.87 (d, J = 2.1 Hz, 1H), 6.79 (dd, J = 8.2, 2.1 Hz, 1H), 5.13 (dd, J = 13.3, 5.1 Hz, 1H), 4.54 (d, J = 31.5 Hz, 2H), 4.37 (dd, J = 16.3, 9.0 Hz, 4H), 4.17 (d, J = 23.2 Hz, 2H), 4.02 (s, 6H), 3.76 (s, 7H), 3.54 (d, J = 12.4 Hz, 4H), 3.18 – 2.98 (m, 2H), 2.91 (s, 4H), 2.79 (ddd, J = 17.6, 4.7, 2.4 Hz, 1H), 2.50 (qd, J = 13.2, 4.7 Hz, 1H), 2.34 – 2.02 (m, 4H).
D198	736.2	¹ H NMR (300 MHz, DMSO-d ₆) δ 8.74 (s, 1H), 8.35 (s, 1H), 7.40 (s, 1H), 7.14 (s, 2H), 6.70 (s, 2H), 5.06 (dd, J = 13.1, 5.1 Hz, 1H), 4.45 – 4.27 (m, 3H), 4.19 (d, J = 16.7 Hz, 3H), 4.02 (d, J = 10.1 Hz, 2H), 3.95 (s, 6H), 3.88 (s, 1H), 3.72 (s, 2H), 3.67 (s, 3H), 3.65 (s, 2H), 3.43 (s, 2H), 3.16 (s, 1H), 3.05 – 2.81 (m, 3H), 2.76 – 2.54 (m, 1H), 2.28 (s, 2H), 2.12 (d, J = 13.6 Hz, 2H), 2.02 – 1.80 (m, 3H).

Compound No.	LCMS	¹ H NMR
D199	794.2	¹ H NMR (300 MHz, DMSO-d ₆) δ 8.28 (s, 3H), 8.08 (d, J = 5.4 Hz, 1H), 7.76 (s, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.50 (d, J = 5.1 Hz, 1H), 7.03 (s, 1H), 6.96 (d, J = 8.4 Hz, 1H), 6.82 (s, 2H), 5.02 (dd, J = 13.2, 5.1 Hz, 1H), 4.85 - 4.74 (m, 1H), 4.38 (d, J = 17.1 Hz, 1H), 4.24 (d, J = 17.1 Hz, 1H), 3.96 (s, 2H), 3.86 (s, 6H), 3.62 (s, 3H), 3.16 (d, J = 9 Hz, 2H), 2.96 - 2.80 (m, 1H), 2.74 - 2.52 (m, 3H), 2.48 - 2.12 (m, 9H), 2.05 - 1.90 (m, 1H), 1.85 - 1.50 (m, 9H), 1.40 - 1.20 (m, 2H).
D200	875.45	¹ H NMR (400 MHz, Methanol-d ₄) δ 8.48 – 8.35 (m, 1H), 7.87 (s, 1H), 7.54 (d, J = 8.8 Hz, 1H), 7.46 – 7.34 (m, 2H), 7.07 (s, 2H), 5.18 (ddd, J = 20.4, 13.3, 5.1 Hz, 1H), 4.55 – 4.44 (m, 5H), 4.47 – 4.36 (m, 6H), 4.02 (s, 3H), 3.70 - 3.54 (m, 6H), 3.65 – 3.60 (m, 2H), 3.49 – 3.42 (m, 1H), 3.15 – 3.08 (m, 2H), 3.01 – 2.94 (m, 2H), 2.92 (s, 6H), 2.88 - 2.86 (m, 3H), 2.85 – 2.82 (m, 1H), 2.83 – 2.73 (m, 1H), 2.59 – 2.52 (m, 1H), 2.51 – 2.37 (m, 1H), 2.24 – 2.15 (m, 1H), 2.00 – 1.95 (m, 1H).
D201	752.35	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.97 (s, 1H), 9.18 (s, 1H), 7.93 (s, 1H), 7.42 – 7.36 (m, 1H), 6.95 (s, 2H), 6.68 (d, J = 7.2 Hz, 2H), 5.08 (dd, J = 13.3, 5.1 Hz, 1H), 4.29 (s, 1H), 4.17 (d, J = 24.7 Hz, 3H), 3.93 (s, 8H), 3.68 (s, 3H), 3.58 (s, 6H), 2.98 – 2.76 (m, 2H), 2.61 (s, 1H), 2.56 (d, J = 7.4 Hz, 2H), 2.45 – 2.29 (m, 5H), 2.05 – 1.93 (m, 1H), 1.79 – 1.71 (m, 4H).
D202	697.3	¹ H NMR (400 MHz, DMSO-d ₆) δ 11.08 (s, 1H), 9.24 (s, 1H), 8.21 (s, 1H, FA), 8.06 (s, 1H), 7.63 (d, J = 8.3 Hz, 1H), 6.91 (s, 2H), 6.78 (s, 1H), 6.65 (d, J = 8.4, 2.1 Hz, 1H), 5.05 (dd, J = 12.9, 5.4 Hz, 1H), 3.85 (s, 7H), 3.73 (s, 4H), 3.66 (s, 4H), 3.52 (s, 2H), 2.95 – 2.81 (m, 1H), 2.60 (s, 1H), 2.40 (s, 3H), 2.05 – 1.95 (m, 1H), 1.73 (s, 4H).
D203	683.5	¹ H NMR (300 MHz, Methanol-d ₄) δ 9.04 (s, 1H), 7.79 (s, 1H), 7.42 (d, J = 8.2 Hz, 1H), 7.10 – 6.94 (m, 2H), 6.89 (d, J = 2.2 Hz, 1H), 6.85 – 6.75 (m, 1H), 5.15 (dd, J = 13.3, 5.1 Hz, 1H), 4.57 – 4.26 (m, 4H), 4.11 – 3.92 (m, 7H), 3.78 (s, 7H), 3.56 (s, 2H), 3.09 (s, 1H), 3.05 – 2.72 (m, 2H), 2.68 – 2.38 (m, 1H), 2.37 – 1.94 (m, 5H).

Compound No.	LCMS	¹ H NMR
D204	683.2	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.98 (s, 1H), 9.28 (s, 1H), 8.47 (s, 1H, FA), 8.10 (s, 1H), 7.29 (d, J = 8.2 Hz, 1H), 7.02 (s, 2H), 6.96 – 6.87 (m, 2H), 6.20 (s, 1H, FA salt), 5.08 (dd, J = 13.3, 5.1 Hz, 1H), 4.51 (s, 2H), 4.38 – 4.09 (m, 2H), 3.86 (s, 6H), 3.68 (s, 3H), 3.63 (s, 3H), 3.51 (s, 2H), 3.21 – 3.13 (m, 2H), 2.98 – 2.87 (m, 1H), 2.65 – 2.56 (m, 2H), 2.47 – 2.35 (m, 1H), 2.14 (s, 2H), 2.01 – 1.91 (m, 1H), 1.79 (s, 2H).
D205	666.45	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.97 (s, 1H), 7.42 (d, J = 8.4 Hz, 1H), 7.31 (d, J = 1.2 Hz, 1H), 7.25 (dd, J = 8.5, 2.4 Hz, 1H), 7.14 (d, J = 2.3 Hz, 1H), 6.59 – 6.52 (m, 2H), 5.09 (dd, J = 13.3, 5.1 Hz, 1H), 4.39 – 4.16 (m, 2H), 3.81 (s, 6H), 3.62 (s, 2H), 3.54 (s, 3H), 3.22 – 3.11 (m, 4H), 2.98 – 2.84 (m, 1H), 2.72 – 2.56 (m, 5H), 2.46 – 2.36 (m, 1H), 2.33 (s, 3H), 2.04 (s, 3H), 2.02 – 1.94 (m, 1H).
D206	630.2	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.99 (s, 1H), 9.25 (s, 1H), 8.14 (s, 0.1H, FA), 8.09 (s, 1H), 7.67 (d, J = 8.3 Hz, 1H), 7.09 (s, 1H), 7.05 – 6.97 (m, 3H), 6.54 (s, 0.2H, FA salt), 5.09 (dd, J = 13.2, 5.1 Hz, 2H), 4.47 – 4.15 (m, 6H), 3.90 (s, 8H), 3.67 (s, 3H), 3.03 – 2.77 (m, 1H), 2.71 – 2.60 (m, 1H), 2.43 – 2.30 (m, 1H), 2.10 – 1.93 (m, 1H).
D207	682.3	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.97 (s, 1H), 8.22 (s, 1H, FA), 8.09 (d, J = 5.3 Hz, 1H), 7.78 (s, 1H), 7.52 (d, J = 5.3 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 6.78 (s, 2H), 6.69 (d, J = 7.9 Hz, 2H), 5.08 (dd, J = 13.3, 5.1 Hz, 1H), 4.37–4.11 (m, 2H), 3.84 (s, 6H), 3.63 (s, 3H), 3.55 (d, J = 10.1 Hz, 6H), 2.98–2.82 (m, 1H), 2.62 (s, 1H), 2.45–2.21 (s, 5H), 2.06–1.90 (m, 1H), 1.72 (t, J = 5.5 Hz, 4H).
D208	696.25	¹ H NMR (300 MHz, DMSO-d ₆) δ 11.07 (s, 1H), 8.55 (d, J = 3.1 Hz, 1H), 8.16 (FA, s, 1H), 7.89 (d, J = 3.2 Hz, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.32 (s, 1H), 6.81 (d, J = 16.7 Hz, 3H), 6.72 – 6.57 (m, 1H), 5.17 – 4.96 (m, 1H), 3.85 (s, 6H), 3.81 – 3.68 (m, 5H), 3.57 (s, 3H), 3.49 (s, 4H), 2.98 – 2.79 (m, 2H), 2.76 – 2.63 (m, 1H), 2.63 – 2.55 (m, 1H), 2.07 – 1.90 (m, 1H), 1.82 – 1.65 (m, 4H).
D209	697.3	¹ H NMR (300 MHz, Methanol-d ₄) δ 9.10 (s, 1H), 8.01 (s, 1H), 7.66 (d, J = 8.3 Hz, 1H), 7.03 (s, 2H), 6.86 (d, J = 2.1 Hz, 1H), 6.70 (dd, J = 8.3, 2.1 Hz, 1H), 5.08 (dd, J = 12.4, 5.4 Hz, 1H), 4.21 (s, 2H), 4.01 (s, 6H), 3.88 (s, 4H), 3.77 (s, 3H), 3.28 – 3.00 (m, 4H), 2.97 – 2.58 (m, 3H), 2.22 – 1.99 (m, 5H).

Compound No.	LCMS	¹ H NMR
D210	667.35	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.96 (s, 1H), 8.74 (s, 1H), 8.30 (s, 1H), 8.14 (s, 1H, FA), 7.37 (d, J = 8.0 Hz, 1H), 7.06 (s, 2H), 6.70–6.69 (m, 2H), 5.08 (dd, J = 13.2, 5.1 Hz, 1H), 4.33–4.16 (m, 2H), 3.88 (s, 6H), 3.72–3.65 (m, 5H), 3.58 (s, 4H), 2.98–2.82 (m, 1H), 2.66–2.56 (m, 4H), 2.45–2.24 (m, 2H), 2.05–1.96 (m, 1H), 1.78 (s, 4H).
D211	662.3	¹ H NMR (300 MHz, MeOD) δ 8.17 – 8.06 (m, 3H), 7.77 – 7.68 (m, 3H), 7.57 (d, J = 7.1 Hz, 2H), 7.51 (d, J = 8.6 Hz, 1H), 5.17 (dd, J = 13.3, 5.2 Hz, 1H), 4.56 – 4.37 (m, 2H), 4.25 – 4.12 (m, 1H), 3.85 (d, J = 12.7 Hz, 2H), 3.75 (s, 3H), 3.26 – 3.19 (m, 2H), 3.03 – 2.74 (m, 2H), 2.62 – 2.41 (m, 1H), 2.25 – 2.13 (m, 3H), 2.03 – 1.85 (m, 2H).
D212	630.3	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.99 (s, 1H), 9.23 (s, 1H), 8.24 (s, 1H, FA), 8.06 (s, 1H), 7.50 (d, J = 8.4 Hz, 1H), 7.12 (dd, J = 8.2, 2.5 Hz, 1H), 7.02 (d, J = 2.4 Hz, 1H), 6.91 (s, 2H), 5.09 (dd, J = 13.1, 5.0 Hz, 1H), 4.85 – 4.75 (m, 1H), 4.45 – 4.16 (m, 2H), 3.85 (s, 6H), 3.72 – 3.63 (m, 7H), 3.13 – 3.07 (m, 2H), 2.94 – 2.83 (m, 1H), 2.65 – 2.59 (m, 1H), 2.42 – 2.35 (m, 1H), 2.04 – 1.98 (m, 1H).
D213	630.15	¹ H NMR (300 MHz, Methanol-d ₄) δ 9.10 (s, 1H), 8.01 (s, 1H), 7.56 (d, J = 8.3 Hz, 1H), 7.27 – 7.16 (m, 2H), 7.02 (s, 2H), 5.23 – 5.04 (m, 2H), 4.54 – 4.43 (m, 4H), 4.43 – 4.39 (m, 2H), 4.12 – 3.93 (m, 8H), 3.77 (s, 3H), 3.00 – 2.86 (m, 1H), 2.85 – 2.75 (m, 1H), 2.60 – 2.42 (m, 1H), 2.25 – 2.13 (m, 1H).
D214	697.15	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.96 (s, 1H), 7.99 (s, 1H), 7.36 (d, J = 8.0 Hz, 1H), 6.88 (s, 2H), 6.68 (d, J = 8.1 Hz, 2H), 5.08 (dd, J = 13.3, 5.1 Hz, 1H), 4.38 – 4.13 (m, 2H), 3.85 (s, 6H), 3.63 (s, 3H), 3.57 (d, J = 4.5 Hz, 6H), 2.97 – 2.83 (m, 1H), 2.77 (s, 3H), 2.63 – 2.54 (m, 2H), 2.37 (dd, J = 13.2, 4.6 Hz, 2H), 2.02 – 1.94 (m, 1H), 1.73 (t, J = 5.5 Hz, 4H).
D215	683.2	¹ H NMR (400 MHz, Methanol-d ₄) δ 9.47 (s, 1H), 7.99 (s, 1H), 7.38 (d, J = 8.2 Hz, 1H), 7.19 (s, 2H), 6.86 (d, J = 2.2 Hz, 1H), 6.77 (m, J = 8.2, 2.3 Hz, 1H), 5.16 – 5.07 (m, 1H), 4.37 (d, J = 7.8 Hz, 2H), 4.30 (s, 2H), 3.98 (s, 6H), 3.78 (s, 3H), 3.74 (s, 4H), 3.24 (s, 4H), 2.96 – 2.83 (m, 1H), 2.83 – 2.73 (m, 1H), 2.56 – 2.40 (m, 1H), 2.21 – 2.09 (m, 5H).

Compound No.	LCMS	¹ H NMR
D216	682.3	¹ H NMR (300 MHz, DMSO-d ₆) δ 10.97 (s, 1H), 8.55 (d, J = 3.2 Hz, 1H), 7.89 (d, J = 3.2 Hz, 1H), 7.44 – 7.27 (m, 2H), 6.84 (s, 2H), 6.76 – 6.62 (m, 2H), 5.08 (dd, J = 13.1, 5.1 Hz, 1H), 4.38 – 4.12 (m, 2H), 3.86 (s, 6H), 3.67 – 3.53 (m, 6H), 3.50 (s, 3H), 3.02 – 2.80 (m, 1H), 2.66 – 2.52 (m, 4H), 2.43 – 2.26 (m, 2H), 2.06 – 1.91 (m, 1H), 1.75 (s, 4H).
D217	667.45	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.74 (s, 1H), 8.16 (s, 1H), 7.42 (d, J = 8.2 Hz, 1H), 7.38 (s, 2H), 6.89 (d, J = 2.1 Hz, 1H), 6.81 (dd, J = 8.2, 2.3 Hz, 1H), 5.14 (dd, J = 13.3, 5.1 Hz, 1H), 4.45 – 4.36 (m, 4H), 4.05 (s, 6H), 3.91 – 3.68 (m, 7H), 3.62 – 3.40 (m, 2H), 3.29 – 3.12 (m, 2H), 3.01 – 2.74 (m, 2H), 2.50 (qd, J = 13.0, 4.7 Hz, 1H), 2.39 – 1.98 (m, 5H).
D218	747.45	¹ H NMR (300 MHz, Methanol-d ₄) δ 8.59 (s, 1H), 8.24 (s, 1H, FA), 7.86 (s, 1H), 7.56 (d, J = 8.3 Hz, 1H), 7.48 – 7.37 (m, 2H), 7.30 (s, 2H), 5.23 (ddd, J = 13.2, 5.2, 2.2 Hz, 1H), 4.71 (dd, J = 15.5, 7.7 Hz, 1H), 4.53 – 4.41 (m, 4H), 4.10 (d, J = 1.1 Hz, 7H), 3.98 (d, J = 13.1 Hz, 1H), 3.84 (s, 3H), 3.32 (d, J = 13.3 Hz, 1H), 3.20 (d, J = 6.3 Hz, 1H), 3.05 – 2.96 (m, 7H), 2.92 – 2.82 (m, 1H), 2.58 (qd, J = 13.1, 4.7 Hz, 1H), 2.33 – 2.09 (m, 3H).
D219	654.4	¹ H NMR (300 MHz, DMSO-d ₆) δ 8.08 (s, 1H), 7.68 (s, 1H), 7.50 (d, J = 8.3 Hz, 1H), 7.36 (d, J = 14.9 Hz, 2H), 6.93 (d, J = 2.2 Hz, 2H), 6.51 (s, 1H), 5.03 (dd, J = 13.4, 5.1 Hz, 1H), 4.43 – 4.20 (m, 2H), 4.06 – 3.93 (m, 3H), 3.78 (s, 6H), 3.59 (s, 3H), 3.01 (t, J = 12.1 Hz, 2H), 2.88 – 2.72 (m, 1H), 2.70 – 2.62 (m, 1H), 2.43 – 2.24 (m, 1H), 1.97 (dd, J = 22.7, 10.4 Hz, 3H), 1.73 (t, J = 10.8 Hz, 2H).
D220	794.7	¹ H NMR (400 MHz, Methanol-d ₄) δ 7.78 – 7.69 (m, 3H), 7.61 (d, J = 5.4 Hz, 1H), 7.08 (s, 2H), 7.06 – 6.97 (m, 2H), 5.14 (dd, J = 13.4, 5.2 Hz, 1H), 4.55 – 4.37 (m, 4H), 4.02 (s, 6H), 3.76 (s, 3H), 3.65 (d, J = 12.5 Hz, 2H), 3.59 – 3.53 (m, 1H), 3.40 – 3.33 (m, 1H), 3.28 – 3.16 (m, 2H), 3.10 (d, J = 6.7 Hz, 2H), 3.04 – 2.87 (m, 3H), 2.84 – 2.75 (m, 1H), 2.74 – 2.64 (m, 1H), 2.57 – 2.41 (m, 2H), 2.36 – 2.21 (m, 2H), 2.21 – 1.93 (m, 9H), 1.71 – 1.57 (m, 2H).
DD1	775.10	¹ H NMR (300 MHz, DMSO-d ₆) δ 12.39 (s, 1H), 9.05 – 8.89 (m, 2H), 8.61 (d, J = 8.4 Hz, 2H), 8.32 (dd, J = 6.4, 2.9 Hz, 1H), 7.96 (s, 1H), 7.57 (s, 1H), 7.36 – 7.24 (m, 2H), 6.90 (s, 2H), 4.87 (d, J = 47.4 Hz, 2H), 4.55 (s, 1H), 3.83 (s, 7H), 3.62 (s, 4H), 3.46 (s, 2H), 2.13 (s, 8H).

Compound No.	LCMS	¹ H NMR
DD2	654.20	¹ H NMR (300 MHz, Methanol-d ₄) δ 9.05 (s, 1H), 8.44 – 8.36 (m, 2H), 7.74 – 7.67 (m, 2H), 7.61 – 7.50 (m, 2H), 7.36 – 7.27 (m, 2H), 7.00 (s, 2H), 4.12 – 3.86 (m, 12H), 3.75 (s, 3H), 3.11 – 2.98 (m, 4H).

Example 31 – BRD9 bromodomain TR-FRET Competition Binding Assay

This example demonstrates the ability of the compounds of the disclosure to biochemically inhibit BRD9 bromodomain in a competition binding assay.

Procedure: His-Flag-BRD9 (P133-K239; Swiss Prot Q9H8M2; SEQ ID NO:1 mgssshhhhhhenlyfq/gdykdddkgslevlfqg/PAENESTPIQQLLEHFLRQLQRKDPHGFFAFPVTDIAIPGYSMII KHPMDFGTMKDKIVANEYKSVTEFKADFKLMCDNAMTYNRPDTVYYKLAKKILHAGFKMMSK) was cloned, expressed, purified, and then treated with TEV protease. Cleaved His tag was removed by purification. The binding of a biotinylated small molecule ligand of BRD9 was assessed via the LANCE® TR-FRET platform (PerkinElmer), and the compounds were assayed for inhibitory activity against this interaction.

Results: A mixture of biotinylated-ligand and SureLight™ Allophycocyanin-Streptavidin (APC-SA, PerkinElmer AD0201) in 50 mM HEPES (pH 7.4), 50 mM NaCl, 1 mM TCEP (pH 7), 0.01% (v/v) Tween-20, 0.01% (w/v) bovine serum albumin was added to a white 384-well PerkinElmer Proxiplate Plus plate. DMSO or 3-fold serially diluted compounds were then added to the Proxiplate followed by addition of Flag-BRD9. After a 10-minute incubation at room temperature, Eu-W1024 anti-FLAG (PerkinElmer, AD0273) was added. The final reaction mixture that contained 3.75 nM biotinylated ligand, 3 nM Flag-BRD9, 7.5 nM SureLight™ Allophycocyanin-Streptavidin, and 0.2 nM Eu-W1024 anti-FLAG was incubated at room temperature for 90 minutes.

The plates were then read on a PerkinElmer Envision plate reader to determine the ratio of emission at 665 nm over 615 nm. Data was normalized to a DMSO control (100%) and a no protein control (0%) and then fit to a four parameter, non-linear curve fit to calculate an IC₅₀ (μM) as shown in Table 5. As shown by the results in Table 5, a number of compounds of the present disclosure exhibit an IC₅₀ value of < 1 μM for BRD9 binding, indicating their affinity for targeting BRD9.

Table 5. Bromodomain TR-FRET Binding

Compound No.	Bromodomain TR-FRET BRD9 IC ₅₀ (nM)
B1	+++
B2	++++
B3	+++
B4	+++
B5	++++
B6	++++
B7	++

Compound No.	Bromodomain TR-FRET BRD9 IC ₅₀ (nM)
B8	+++
B9	+++
B10	+++
B11	++
D1	++
D2	++++
D3	+++
D4	+++
D5	++
D6	++++
D7	++
D8	++
D9	+++
D10	++++
D11	++++
D12	++++
D13	++++
D14	+++
D15	++++

“+” indicates inhibitory effect of ≥ 1000 nM;

“++” indicates inhibitory effect of ≥ 100 nM;

“+++” indicates inhibitory effect of ≥ 10 nM;

“++++” indicates inhibitory effect of < 10 nM;

“NT” indicates not tested

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Example 32 – SYO1 BRD9 NanoLuc Degradation Assay

This example demonstrates the ability of the compounds of the disclosure to degrade a Nanoluciferase-BRD9 fusion protein in a cell-based degradation assay.

Procedure: A stable SYO-1 cell line expressing 3xFLAG-NLuc-BRD9 was generated. On day 0 cells were seeded in 30 μ L media into each well of 384-well cell culture plates. The seeding density was 8000 cells/well. On day 1, cells were treated with 30 nL DMSO or 30 nL of 3-fold serially DMSO-diluted compounds (10 points in duplicates with 1 μ M as final top dose). Subsequently plates were incubated for 6 hours in a standard tissue culture incubator and equilibrated at room temperature for 15 minutes. Nanoluciferase activity was measured by adding 15 μ L of freshly prepared Nano-Glo Luciferase Assay Reagent (Promega N1130), shaking the plates for 10 minutes and reading the bioluminescence using an EnVision reader.

Results: The Inhibition% was calculated using the following formula: $\% \text{Inhibition} = 100 \times (\text{Lum}_{\text{HC}} - \text{Lum}_{\text{Sample}}) / (\text{Lum}_{\text{HC}} - \text{Lum}_{\text{LC}})$. DMSO treated cells are employed as High Control (HC) and 1 μ M of a known BRD9 degrader standard treated cells are employed as Low Control (LC). The data was fit to a four parameter, non-linear curve fit to calculate IC₅₀ (μ M) values as shown in Table 6A and Table 6B. As

shown by the results in Table 6A and Table 6B, a number of compounds of the present disclosure exhibit an IC₅₀ value of < 1 μ M for the degradation of BRD9, indicating their use as compounds for reducing the levels and/or activity of BRD9 and their potential for treating BRD9-related disorders.

5

Table 6A. SYO1 BRD9-NanoLuc Degradation

Compound No.	SYO1 BRD9-NanoLuc degradation IC ₅₀ (nM)
D1	+
D2	+++
D3	++++
D4	+++
D5	+
D6	+
D7	++
D8	++
D9	+
D10	++++
D11	+
D12	++++
D13	++++
D14	++
D15	++++

“+” indicates inhibitory effect of $\geq$ 1000 nM;

“++” indicates inhibitory effect of $\geq$ 100 nM;

“+++” indicates inhibitory effect of $\geq$ 10 nM;

“++++” indicates inhibitory effect of < 10 nM;

“NT” indicates not tested

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Table 6B. SYO1 BRD9-NanoLuc Degradation

Compound No.	SYO1 BRD9-NanoLuc degradation IC ₅₀ (nM)
D16	++++
D17	++++
D18	++++
D19	++++
D20	++++
D21	++++
D22	++++
D23	++++
D24	++++
D25	++++
D26	++++

Compound No.	SYO1 BRD9-NanoLuc degradation IC ₅₀ (nM)
D27	++++
D28	++++
D29	++++
D30	+++
D31	+++
D32	++
D33	++++
D34	++
D35	++++
D36	++++
D37	++++
D38	++++
D39	++++
D40	++++
D41	++++
D42	++++
D43	++++
D44	+++
D45	+
D46	++++
D47	+++
D48	+++
D49	++++
D50	++++
D51	+++
D52	+++
D53	+++
D54	++
D55	++
D56	+++
D57	++++
D58	+++
D59	+++
D60	++++
D61	++
D62	+++
D63	++
D64	++
D65	++++

Compound No.	SYO1 BRD9-NanoLuc degradation IC ₅₀ (nM)
D66	++++
D67	+++
D68	+++
D69	+++
D70	++++
D71	+++
D72	++++
D73	++++
D74	++++
D75	++++
D76	+++
D77	++++
D78	++++
D79	++++
D80	++
D81	++
D82	++
D83	++++
D84	++++
D85	++++
D86	++++
D87	++++
D88	+++
D89	++++
D90	++++

“+” indicates inhibitory effect of ≥ 1000 nM;

“++” indicates inhibitory effect of ≥ 100 nM;

“+++” indicates inhibitory effect of ≥ 10 nM;

“++++” indicates inhibitory effect of < 10 nM;

“NT” indicates not tested

5

Table 6C. SYO1 BRD9-NanoLuc Degradation

Compound No.	SYO1 BRD9-NanoLuc degradation IC ₅₀ (nM)
D91	++++
D92	++++
D93	++++
D94	++++
D95	++
D96	++++

Compound No.	SYO1 BRD9-NanoLuc degradation IC ₅₀ (nM)
D97	++++
D98	++++
D99	++++
D100	++++
D101	++++
D102	++++
D103	++++
D104	++++
D105	++++
D106	++++
D107	++++
D108	++++
D109	++++
D110	++++
D111	++++
D112	++++
D113	++++
D114	++++
D115	++++
D116	++++
D117	++++
D118	++++
D119	++++
D120	++++
D121	++++
D122	++++
D123	++++
D124	++++
D125	++++
D126	++++
D127	++++
D128	++++
D129	++++
D130	++++
D131	++++
D132	++++
D133	++++
D134	++++
D135	++++

Compound No.	SYO1 BRD9-NanoLuc degradation IC ₅₀ (nM)
D136	++++
D137	++
D138	++++
D139	++++
D140	++++
D141	++++
D142	+
D143	+
D144	++++
D145	++
D146	++++
D147	++++
D148	+
D149	++++
D150	++++
D151	++++
D152	++++
D153	++++
D154	++++
D155	++++
D156	++++
D157	++++
D158	++++
D159	++++
D160	++++
D161	++++
D162	++++
D163	++++
D164	++++
D165	++++
D166	++++
D167	++++
D168	++++
D169	++++
D170	++++
D171	+++
D172	+
D173	++++
D174	++++

Compound No.	SYO1 BRD9-NanoLuc degradation IC ₅₀ (nM)
D175	++++
D176	++++
D177	++++
D178	++++
D179	++++
D180	++++
D181	++++
D182	++++
D183	++++
D184	++++
D185	++++
D186	++++
D187	++++
D188	++++
D189	++++
D190	++++
D191	++++
D192	++++
D193	++++
D194	++++
D195	++++
D196	++++
D197	++++
D198	+++
D199	++++
D200	++++
D201	++++
D202	++++
D203	++++
D204	++
D205	++++
D206	++++
D207	++++
D208	++++
D209	++++
D210	++++
D211	+++
D212	++++
D213	++++

Compound No.	SYO1 BRD9-NanoLuc degradation IC ₅₀ (nM)
D214	++++
D215	++++
D216	++++
D217	++++
D218	+++
D219	++++
D220	++++
DD1	+
DD2	+

“+” indicates inhibitory effect of ≥ 1000 nM;

“++” indicates inhibitory effect of ≥ 100 nM;

“+++” indicates inhibitory effect of ≥ 10 nM;

“++++” indicates inhibitory effect of < 10 nM;

“NT” indicates not tested

5

Other Embodiments

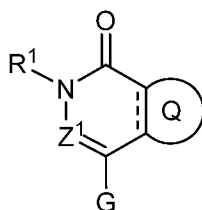
All publications, patents, and patent applications mentioned in this specification are incorporated herein by reference in their entirety to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference in its entirety. Where a term in the present application is found to be defined differently in a document incorporated herein by reference, the definition provided herein is to serve as the definition for the term.

While the invention has been described in connection with specific embodiments thereof, it will be understood that invention is capable of further modifications and this application is intended to cover any variations, uses, or adaptations of the invention following, in general, the principles of the invention and including such departures from the present disclosure that come within known or customary practice within the art to which the invention pertains and may be applied to the essential features hereinbefore set forth, and follows in the scope of the claims.

Other embodiments are in the claims.

Claims

1. A compound having the structure **Formula I**:



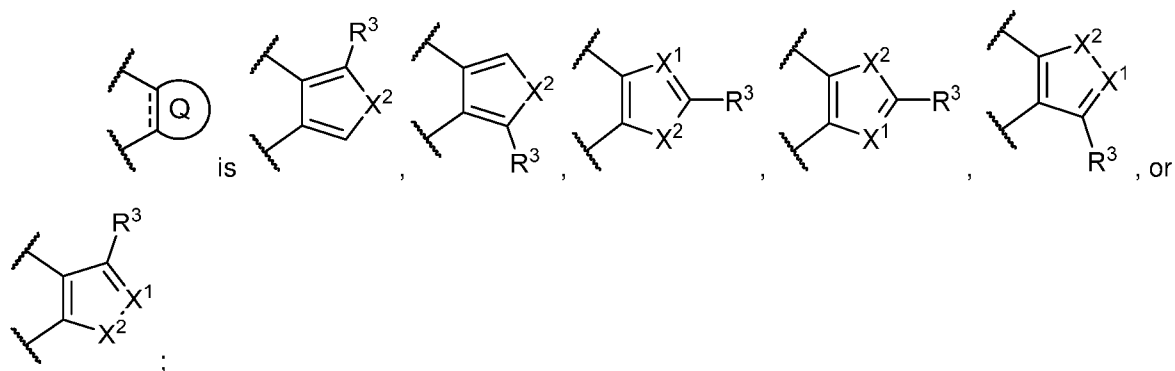
Formula I,

wherein

R¹ is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₁₀ carbocyclyl;

Z¹ is CR² or N;

R² is H, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, or optionally substituted C₂-C₉ heteroaryl;



X¹ is CR^{X1} or N;

X² is O or S;

R^{X1} is H or optionally substituted C₁-C₆ alkyl;

R³ is H, cyano, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₁-C₆ alkoxy, optionally substituted amino, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₃-C₁₀ heterocyclyl, or optionally substituted C₂-C₉ heteroaryl; and

G is optionally substituted C₃-C₁₀ carbocyclyl, C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, or optionally substituted C₂-C₉ heteroaryl,
or a pharmaceutically acceptable salt thereof.

2. A compound having the structure of **Formula II**:

A-L-B

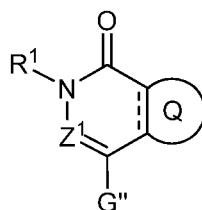
Formula II,

wherein

L is a linker;

B is a degradation moiety; and

A has the structure of **Formula III**:

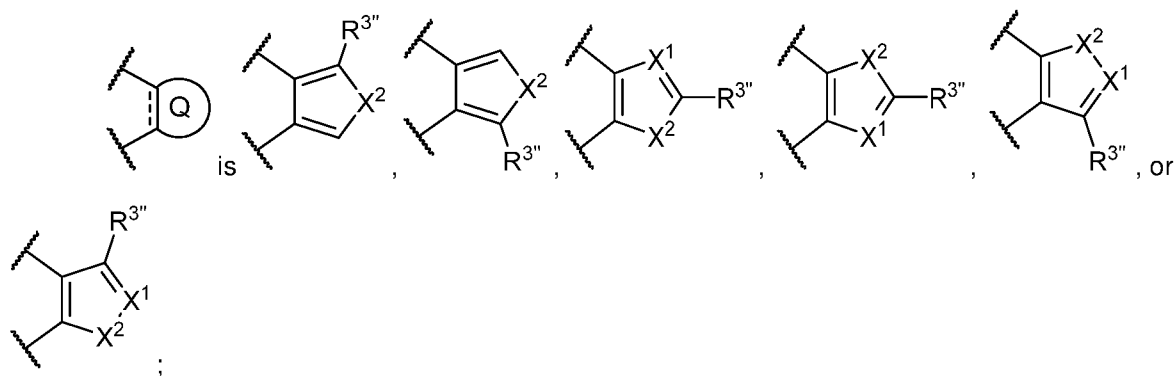
**Formula III,**

wherein

R¹ is, independently, H, optionally substituted C₁-C₆ alkyl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₁₀ carbocyclyl;

Z¹ is CR² or N;

R² is H, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, or optionally substituted C₂-C₉ heteroaryl;



X¹ is CR^{X1} or N;

X² is O or S;

R^{X1} is H or optionally substituted C₁-C₆ alkyl;

R^{3''} is H, , cyano, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₁-C₆ alkoxy, optionally substituted amino, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₃-C₁₀ heterocyclyl, or optionally substituted C₂-C₉ heteroaryl;

R^{3'} is absent, optionally substituted C₁-C₆ alkylene, optionally substituted C₂-C₉ heteroarylene, or optionally substituted C₁-C₆ heteroalkylene;

G'' is , optionally substituted C₃-C₁₀ carbocyclyl, C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, or optionally substituted C₂-C₉ heteroaryl;

G' is optionally substituted C₃-C₁₀ carbocyclylene, C₂-C₉ heterocyclylene, optionally substituted C₆-C₁₀ arylene, or optionally substituted C₂-C₉ heteroarylene; and

A¹ is a bond between A and the linker,

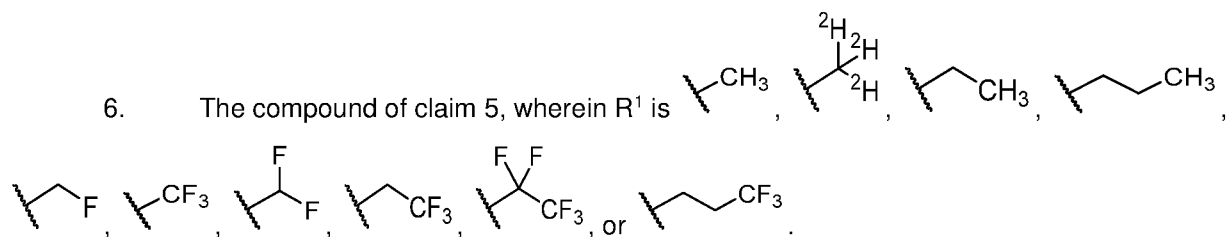
wherein G'' is  or R^{3''} is ,

or a pharmaceutically acceptable salt thereof.

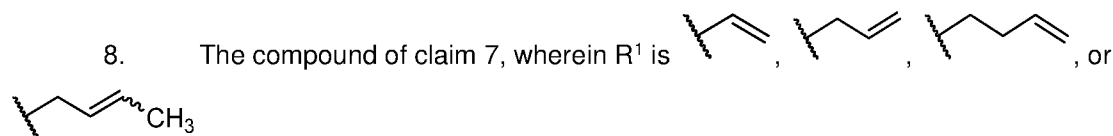
3. The compound of claim 1 or 2, wherein R^1 is H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_2 - C_6 alkenyl, or optionally substituted C_3 - C_{10} carbocyclyl.

4. The compound of claim 3, wherein R^1 is H.

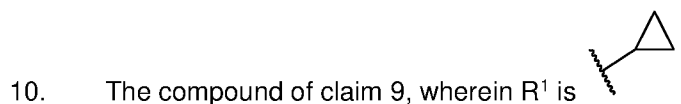
5. The compound of claim 3, wherein R^1 is optionally substituted C_1 - C_6 alkyl.

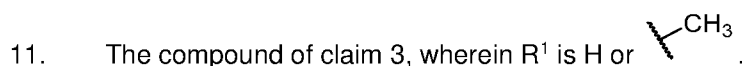


7. The compound of claim 6, wherein R^1 is optionally substituted C_2 - C_6 alkenyl.

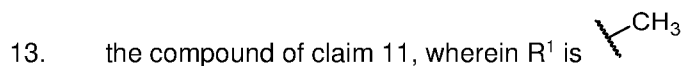


9. The compound of claim 8, wherein R^1 is optionally substituted C_3 - C_{10} carbocyclyl.



11. The compound of claim 3, wherein R^1 is H or .

12. the compound of claim 11, wherein R^1 is H.

13. the compound of claim 11, wherein R^1 is .

14. The compound of any one of claims 1 to 13, wherein Z^1 is N.

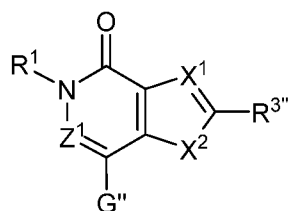
15. The compound of any one of claims 1 to 13, wherein Z^1 is CR^2 .

16. The compound of claim 15, wherein R^2 is H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_3 - C_{10} carbocyclyl, or optionally substituted C_6 - C_{10} aryl.

17. The compound of claim 16, wherein R^2 is H, halogen, or optionally substituted C_1 - C_6 alkyl.

18. The compound of claim 17, wherein R^2 is H, F, or .

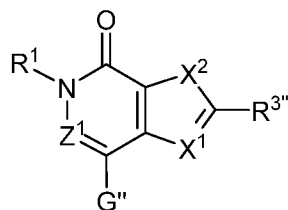
19. The compound of claim 2 to 18, wherein the compound of **Formula III** has the structure of **Formula IIIA**:



Formula IIIA,

or a pharmaceutically acceptable salt thereof.

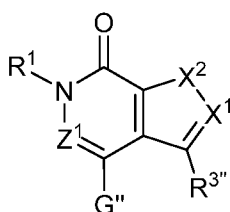
20. The compound of claim 2 to 18, wherein the compound of **Formula III** has the structure of **Formula IIIB**:



Formula IIIB,

or a pharmaceutically acceptable salt thereof.

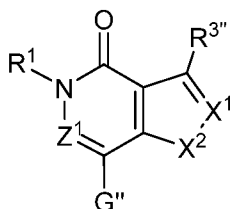
21. The compound of claim 2 to 18, wherein the compound of **Formula III**:



Formula IIIC,

or a pharmaceutically acceptable salt thereof.

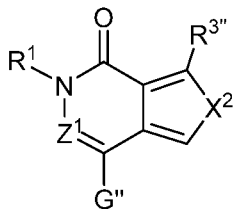
22. The compound of claim 2 to 18, wherein the compound of **Formula III**:



Formula IIID,

or a pharmaceutically acceptable salt thereof.

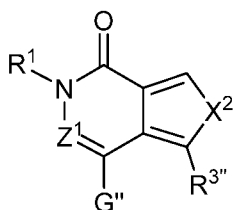
23. The compound of claim 2 to 18, wherein the compound of **Formula IIIE**:



Formula IIIE,

or a pharmaceutically acceptable salt thereof.

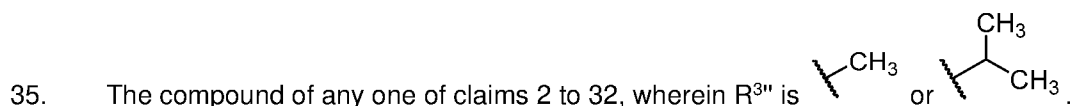
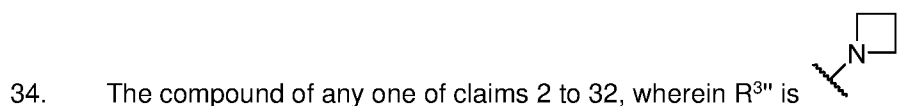
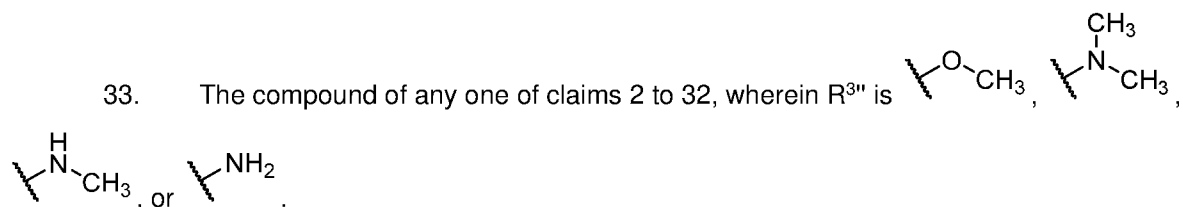
24. The compound of claim 2 to 18, wherein the compound of **Formula IIIF**:



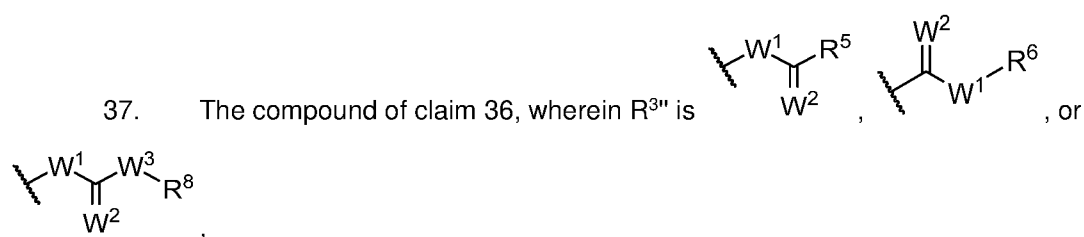
Formula IIIF,

or a pharmaceutically acceptable salt thereof.

25. The compound of any one of claims 2 to 24, wherein X¹ is CH or N.
26. The compound of any one of claims 2 to 24, wherein X¹ is CH.
27. The compound of any one of claims 2 to 26, wherein X² is O.
28. The compound of any one of claims 2 to 26, wherein X² is S.
29. The compound of any one of claims 2 to 28, wherein R^{3''} is H, cyano, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₁-C₆ alkoxy, optionally substituted amino, optionally substituted C₃-C₁₀ heterocyclyl, or optionally substituted C₂-C₉ heteroaryl.
30. The compound of any one of claims 2 to 29, wherein R^{3''} is H.
31. The compound of any one of claims 2 to 29, wherein R^{3''} is cyano.
32. The compound of any one of claims 2 to 29, wherein R^{3''} is optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₁₀ heterocyclyl.



36. The compound of claim 32, wherein R^{3''} is optionally substituted C₁-C₆ heteroalkyl.



wherein

W¹ is NR⁴ or O;

W² is NH, O, or S;

W³ is NR⁷ or O;

R⁴ is H or optionally substituted C₁-C₆ alkyl;

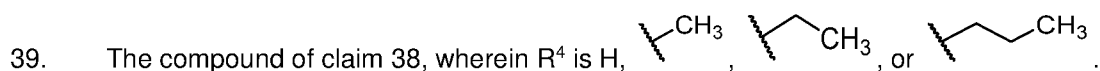
R⁵ is optionally substituted C₁-C₆ alkyl, optionally substituted C₃-C₁₀ carbocyclyl, or optionally substituted C₂-C₉ heterocyclyl;

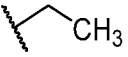
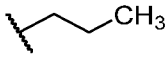
R⁶ is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₃-C₁₀ carbocyclyl, or optionally substituted C₂-C₉ heterocyclyl;

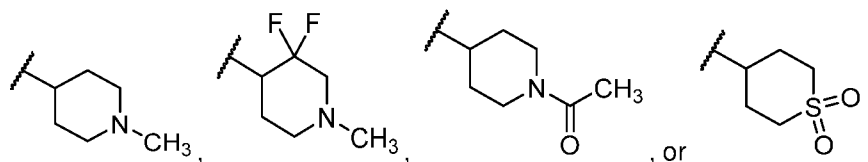
R⁷ is H or optionally substituted C₁-C₆ alkyl; and

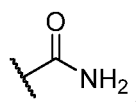
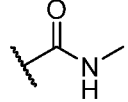
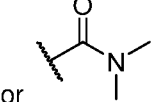
R⁸ is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₃-C₁₀ carbocyclyl, or optionally substituted C₂-C₉ heterocyclyl.

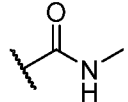
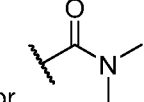
38. The compound of claim 37, wherein W¹ is NR⁴.



40. The compound of claim 39, wherein R^6 is H, , , ,



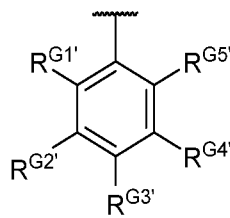
41. The compound of claim 40, wherein $R^{3''}$ is , , or .

42. The compound of claim 41, wherein $R^{3''}$ is  or .

43. The compound of any one of claims 2 to 42, wherein G'' is .

44. The compound of claim 43, wherein G' is optionally substituted C_6 - C_{10} arylene or optionally substituted C_2 - C_9 heteroarylene.

45. The compound of claim 44, wherein G' is optionally substituted C_6 - C_{10} arylene.



46. The compound of claim 45, wherein G' is
wherein

each of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$, and $R^{G5'}$ is, independently, H, A^1 , halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted $-O$ - C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_2 - C_5 heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or $R^{G1'}$ and $R^{G2'}$, $R^{G2'}$ and $R^{G3'}$, $R^{G3'}$ and $R^{G4'}$, and/or $R^{G4'}$ and $R^{G5'}$, together with the carbon atoms to which each is

attached, combine to form ; and

 is optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or optionally substituted C_2 - C_9 heterocyclyl, any of which is optionally substituted with A^1 ,

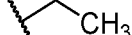
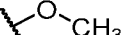
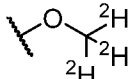
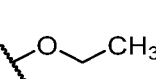
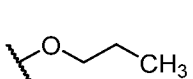
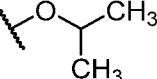
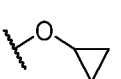
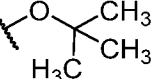
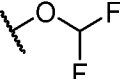
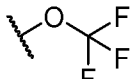
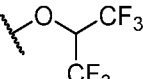
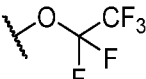
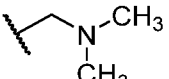
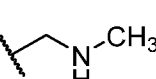
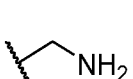
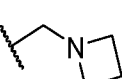
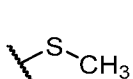
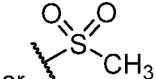
wherein one of R^{G1'}, R^{G2'}, R^{G3'}, R^{G4'}, and R^{G5'} is A¹, or  is substituted with A¹.

47. The compound of claim 46, wherein each of R^{G1'}, R^{G2'}, R^{G3'}, R^{G4'}, and R^{G5'} is, independently, H, A¹, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted -O-C₃-C₆ carbocyclyl, or optionally substituted -C₁-C₃ alkyl-C₂-C₅ heterocyclyl; or R^{G1'} and R^{G2'}, R^{G2'} and R^{G3'}, R^{G3'} and R^{G4'}, and/or R^{G4'} and R^{G5'}, together with the carbon atoms to which each is attached, combine to form ; and

(M) is optionally substituted C₂-C₉ heteroaryl or optionally substituted C₂-C₉ heterocyclyl, any of which is optionally substituted with A¹,

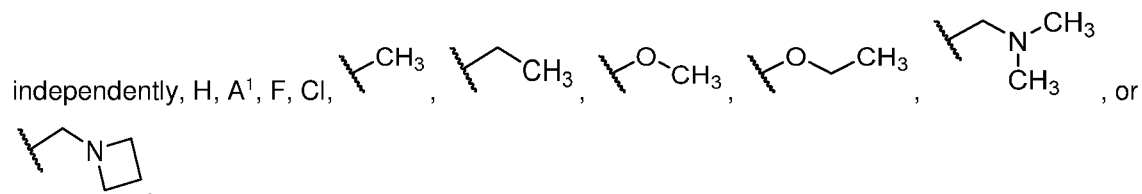
wherein one of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$, and $R^{G5'}$ is A^1 , or $\textcircled{M}$ is substituted with A^1 .

48. The compound of claim 47, wherein each of R^{G1'}, R^{G2'}, R^{G3'}, R^{G4'}, and R^{G5'} is, independently, H, A¹, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted -O-C₃-C₆ carbocyclyl, or optionally substituted -C₁-C₃ alkyl-C₂-C₅ heterocyclyl.

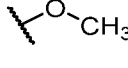
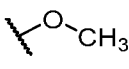
49. The compound of claim 48, wherein each of R^{G1'}, R^{G2'}, R^{G3'}, R^{G4'}, and R^{G5'} is, independently, H, A¹, F, Cl, , , , , , , , , , , , , , , , , , , , , or .

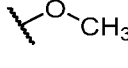
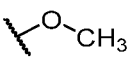
50. The compound of claim 49, wherein each of R^{G1'}, R^{G2'}, R^{G3'}, R^{G4'}, and R^{G5'} is, independently, H, A¹, F, , , , , , , , , , , ,

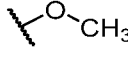
51. The compound of claim 50, wherein each of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$, and $R^{G5'}$ is,

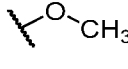


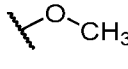
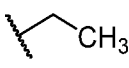
52. The compound of claim 51, wherein $R^{G3'}$ is A^1 .

53. The compound of claim 51, wherein $R^{G1'}$ is H; $R^{G2'}$ is ; $R^{G3'}$ is A^1 ; $R^{G4'}$ is ; and $R^{G5'}$ is H.

54. The compound of claim 51, wherein $R^{G1'}$ is H; $R^{G2'}$ is ; $R^{G3'}$ is A^1 ; $R^{G4'}$ is H; and $R^{G5'}$ is .

55. The compound of claim 51, wherein $R^{G1'}$ is H; $R^{G2'}$ is ; $R^{G3'}$ is A^1 ; $R^{G4'}$ is Cl or F; and $R^{G5'}$ is H.

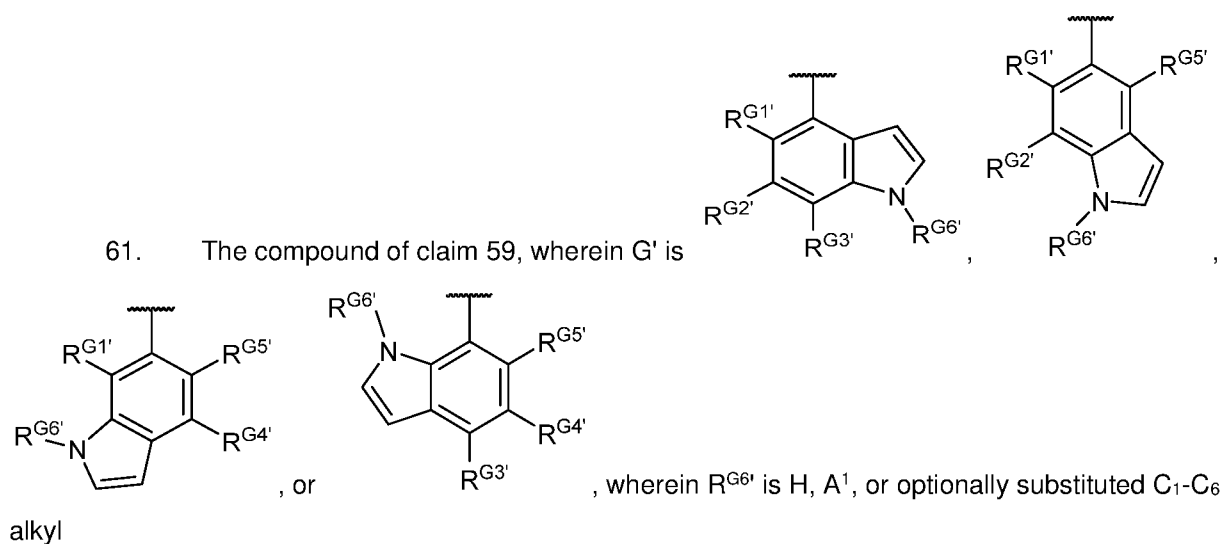
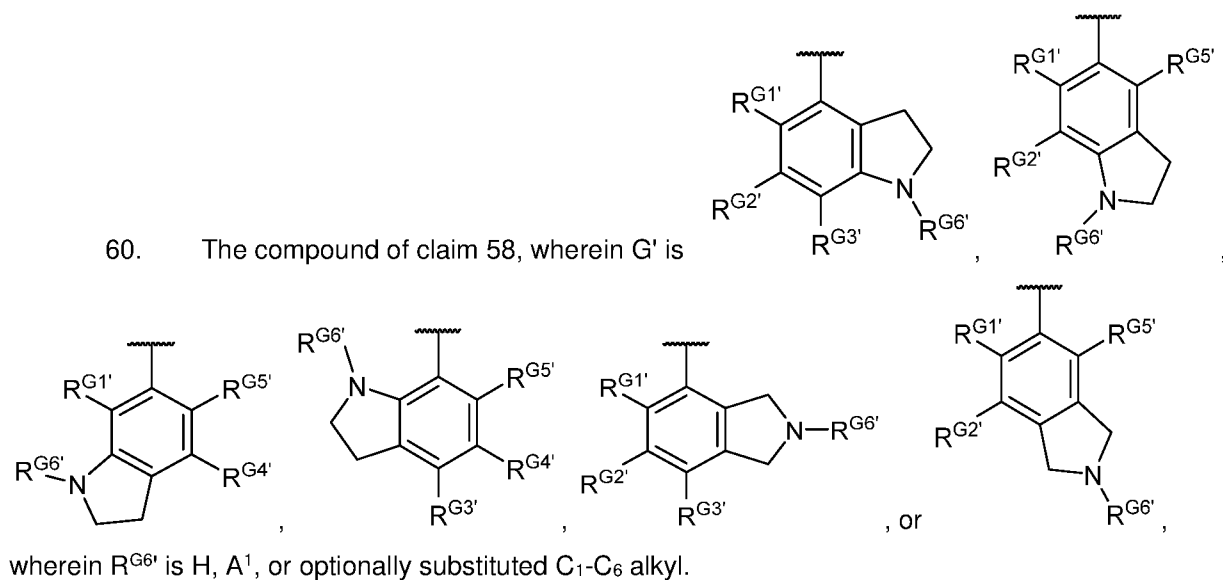
56. The compound of claim 51, wherein $R^{G1'}$ is H; $R^{G2'}$ is ; $R^{G3'}$ is A^1 ; $R^{G4'}$ is H; and $R^{G5'}$ is H.

57. The compound of claim 51, wherein $R^{G1'}$ is H; $R^{G2'}$ is ; $R^{G3'}$ is A^1 ; $R^{G4'}$ is ; and $R^{G5'}$ is H.

58. The compound of claim 47, wherein $R^{G1'}$ and $R^{G2'}$, $R^{G2'}$ and $R^{G3'}$, $R^{G3'}$ and $R^{G4'}$, and/or $R^{G4'}$ and $R^{G5'}$, together with the carbon atoms to which each is attached, combine to form ; and  is optionally substituted C_2 - C_9 heterocyclyl, which is optionally substituted with A^1 , wherein one of $R^{G1'}$, $R^{G2'}$, $R^{G3'}$, $R^{G4'}$, and $R^{G5'}$ is A^1 , or  is substituted with A^1 .

59. The compound of claim 47, wherein $R^{G1'}$ and $R^{G2'}$, $R^{G2'}$ and $R^{G3'}$, $R^{G3'}$ and $R^{G4'}$, and/or $R^{G4'}$ and $R^{G5'}$, together with the carbon atoms to which each is attached, combine to form ; and

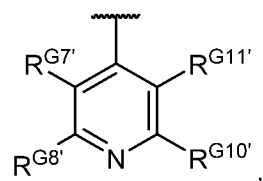
(M) is optionally substituted C₂-C₉ heteroaryl, which is optionally substituted with A¹,
 wherein one of R^{G1'}, R^{G2'}, R^{G3'}, R^{G4'}, and R^{G5'} is A¹, or (M) is substituted with A¹.



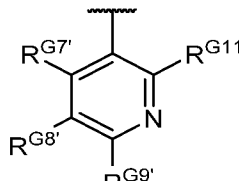
62. The compound of claim 60 or 61, wherein R^{G6'} is H, A¹, or .

63. The compound of claim 62, wherein R^{G6'} is H.

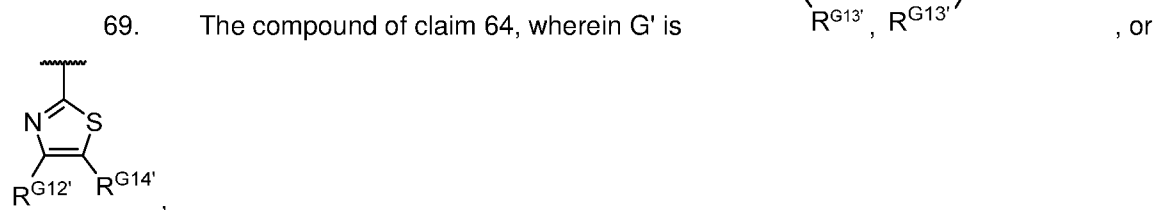
64. The compound of claim 44, wherein G' is optionally substituted C₂-C₉ heteroarylene.

65. The compound of claim 64, wherein G' is
- 
- wherein
- each of $R^{G7'}$, $R^{G8'}$, $R^{G9'}$, $R^{G10'}$, and $R^{G11'}$ is, independently, H, A^1 , halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted $-O$ - C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_2 - C_5 heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or $R^{G7'}$ and $R^{G8'}$, $R^{G8'}$ and $R^{G9'}$, $R^{G9'}$ and $R^{G10'}$, and/or $R^{G10'}$ and $R^{G11'}$, together with the carbon atoms to which each is attached, combine to form $\textcircled{M}$; and
- $\textcircled{M}$ is optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or C_2 - C_9 heterocyclyl, any of which is optionally substituted with A^1 ,
- wherein one of $R^{G7'}$, $R^{G8'}$, $R^{G9'}$, $R^{G10'}$, and $R^{G11'}$ is A^1 ; or $\textcircled{M}$ is substituted with A^1 .

66. The compound of claim 65, wherein each of $R^{G7'}$, $R^{G8'}$, $R^{G9'}$, $R^{G10'}$, and $R^{G11'}$ is, independently, H, A^1 , halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted $-O$ - C_3 - C_6 carbocyclyl, or optionally substituted $-C_1$ - C_3 alkyl- C_2 - C_5 heterocyclyl.

67. The compound of claim 65 or 66, wherein G' is
- 

68. The compound of any one of claims 65 to 67, wherein $R^{G7'}$ is H; $R^{G8'}$ is $\text{---}O-CH_3$; $R^{G9'}$ is A^1 ; and $R^{G11'}$ is H.



wherein

each of $R^{G12'}$, $R^{G13'}$, and $R^{G14'}$ is, independently, H, A^1 , halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted $-O$ - C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_2 - C_5 heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or $R^{G12'}$ and $R^{G14'}$, together with the carbon

atoms to which each is attached, combine to form ; and

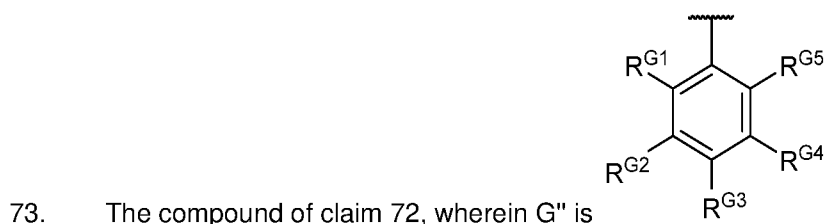
 is optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or optionally substituted C_2 - C_9 heterocyclyl, any of which is optionally substituted with A^1 ,

wherein one of $R^{G12'}$, $R^{G13'}$, and $R^{G14'}$ is A^1 ; or  is substituted with A^1 .

70. The compound of any one of claims 2 to 28, wherein $R^{3''}$ is , and $R^{3'}$ is absent.

71. The compound of claim 70, wherein G'' is optionally substituted C_6 - C_{10} aryl or optionally substituted C_2 - C_9 heteroaryl.

72. The compound of claim 71, wherein G'' is optionally substituted C_6 - C_{10} aryl.



wherein

each of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl,

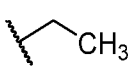
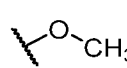
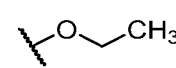
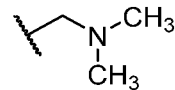
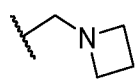
optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, optionally substituted -O-C₃-C₆ carbocyclyl, optionally substituted -C₁-C₃ alkyl-C₃-C₆ carbocyclyl, optionally substituted -C₁-C₃ alkyl-C₂-C₅ heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or R^{G1} and R^{G2}, R^{G2} and R^{G3}, R^{G3} and R^{G4}, and/or R^{G4} and R^{G5}, together with the carbon atoms to which each is attached, combine to form optionally substituted C₆-C₁₀ aryl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heteroaryl, or optionally substituted C₂-C₉ heterocyclyl.

74. The compound of claim 73, wherein each of R^{G1}, R^{G2}, R^{G3}, R^{G4}, and R^{G5} is, independently, H, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted -O-C₃-C₆ carbocyclyl, or optionally substituted -C₁-C₃ alkyl-C₂-C₅ heterocyclyl; or R^{G1} and R^{G2}, R^{G2} and R^{G3}, R^{G3} and R^{G4}, and/or R^{G4} and R^{G5}, together with the carbon atoms to which each is attached, combine to form optionally substituted C₂-C₉ heteroaryl or optionally substituted C₂-C₉ heterocyclyl.

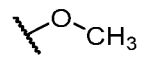
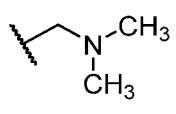
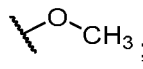
75. The compound of claim 74, wherein each of R^{G1}, R^{G2}, R^{G3}, R^{G4}, and R^{G5} is, independently, H, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted -O-C₃-C₆ carbocyclyl, or optionally substituted -C₁-C₃ alkyl-C₂-C₅ heterocyclyl.

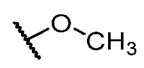
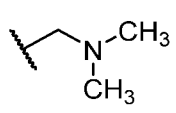
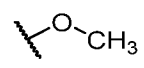
76. The compound of claim 75, wherein each of R^{G1}, R^{G2}, R^{G3}, R^{G4}, and R^{G5} is, independently, H, F, Cl, , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , ,

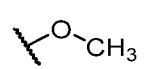
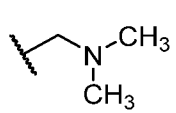
78. The compound of claim 77, wherein each of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is,

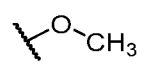
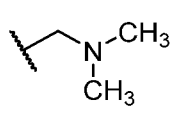
independently, H, F, Cl, , , , , , or .

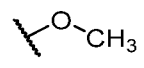
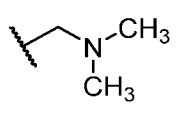
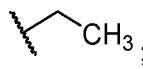
79. The compound of claim 78, wherein two or more of R^{G1} , R^{G2} , R^{G3} , R^{G4} , and R^{G5} is H.

80. The compound of claim 79, wherein R^{G1} is H; R^{G2} is ; R^{G3} is ; R^{G4} is ; and R^{G5} is H.

81. The compound of claim 79, wherein R^{G1} is H; R^{G2} is ; R^{G3} is ; R^{G4} is H; and R^{G5} is .

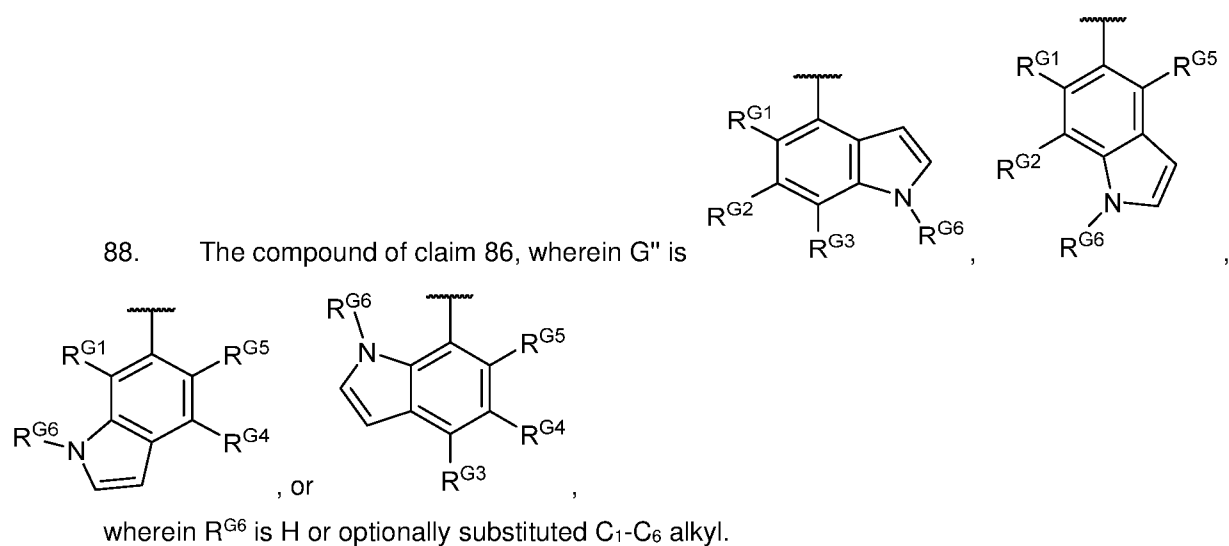
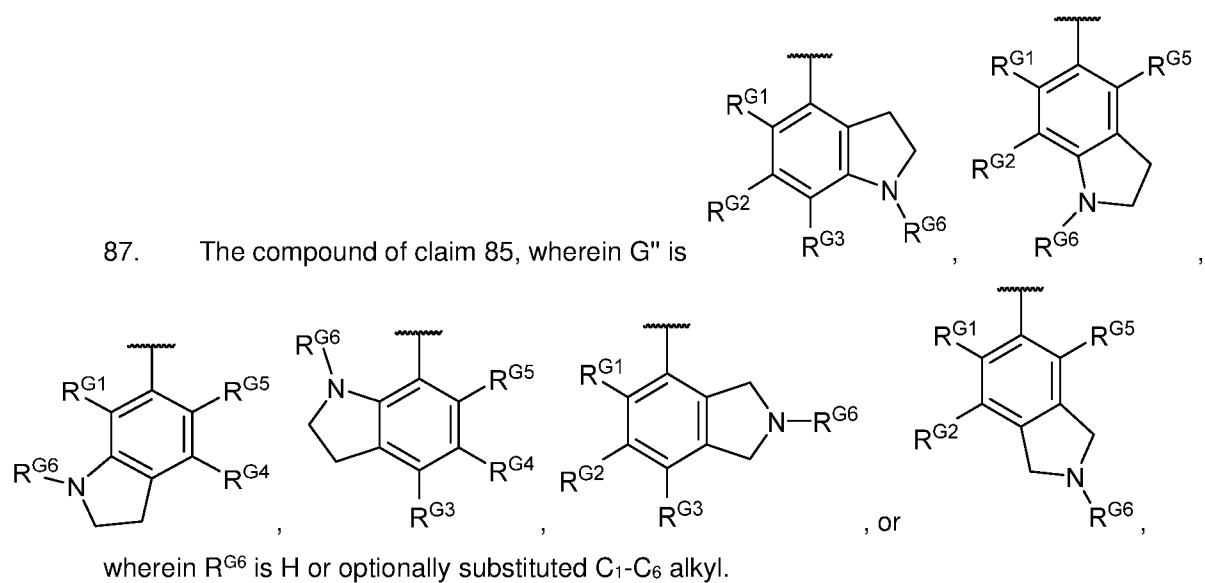
82. The compound of claim 79, wherein R^{G1} is H; R^{G2} is ; R^{G3} is ; R^{G4} is Cl or F; and R^{G5} is H.

83. The compound of claim 79, wherein R^{G1} is H; R^{G2} is ; R^{G3} is ; R^{G4} is H; and R^{G5} is H.

84. The compound of claim 79, wherein R^{G1} is H; R^{G2} is ; R^{G3} is ; R^{G4} is ; and R^{G5} is H.

85. The compound of claim 74, wherein R^{G1} and R^{G2} , R^{G2} and R^{G3} , R^{G3} and R^{G4} , and/or R^{G4} and R^{G5} , together with the carbon atoms to which each is attached, combine to form optionally substituted C₂-C₉ heterocyclyl.

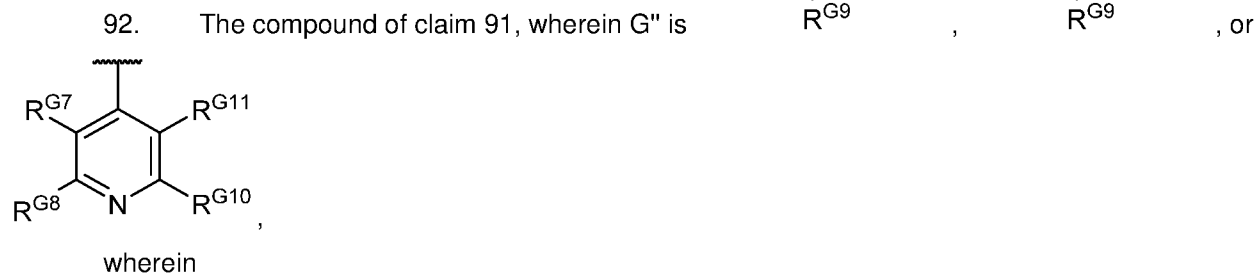
86. The compound of claim 74, wherein R^{G1} and R^{G2} , R^{G2} and R^{G3} , R^{G3} and R^{G4} , and/or R^{G4} and R^{G5} , together with the carbon atoms to which each is attached, combine to form optionally substituted C₂-C₉ heteroaryl.



89. The compound of claim 87 or 88, wherein R^{G6} is H or

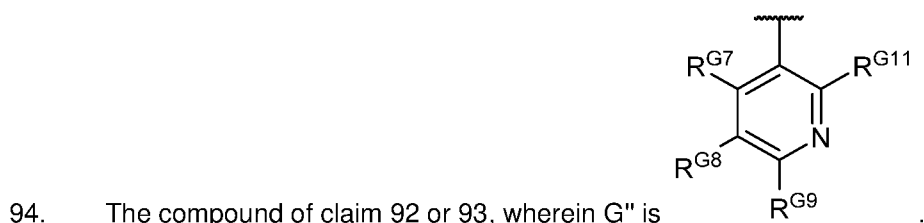
90. The compound of claim 89, wherein R^{G6} is H.

91. The compound of claim 71, wherein G" is optionally substituted C₂-C₉ heteroaryl.

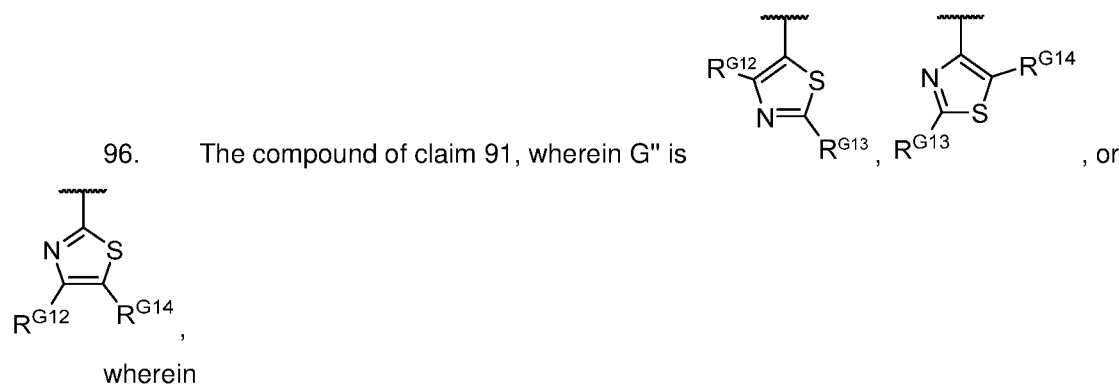


each of R^{G7} , R^{G8} , R^{G9} , R^{G10} , and R^{G11} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted $-O$ - C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_3 - C_6 carbocyclyl, optionally substituted $-C_1$ - C_3 alkyl- C_2 - C_5 heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or R^{G7} and R^{G8} , R^{G8} and R^{G9} , R^{G9} and R^{G10} , and/or R^{G10} and R^{G11} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or C_2 - C_9 heterocyclyl.

93. The compound of claim 92, wherein each of R^{G7} , R^{G8} , R^{G9} , R^{G10} , and R^{G11} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted $-O$ - C_3 - C_6 carbocyclyl, or optionally substituted $-C_1$ - C_3 alkyl- C_2 - C_5 heterocyclyl.



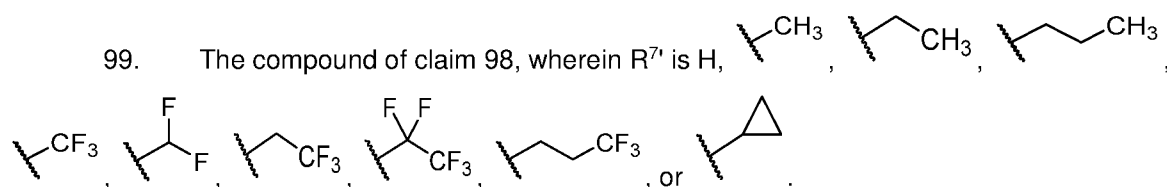
95. The compound of claim 94, wherein R^{G7} is H; R^{G8} is ---OCH_3 ; R^{G9} is H; and R^{G11} is H.

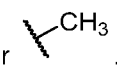


each of R^{G12} , R^{G13} , and R^{G14} is, independently, H, halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted -O- C_3 - C_6 carbocyclyl, optionally substituted - C_1 - C_3 alkyl- C_3 - C_6 carbocyclyl, optionally substituted - C_1 - C_3 alkyl- C_2 - C_5 heterocyclyl, hydroxyl, thiol, or optionally substituted amino; or R^{G12} and R^{G14} , together with the carbon atoms to which each is attached, combine to form optionally substituted C_6 - C_{10} aryl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heteroaryl, or optionally substituted C_2 - C_9 heterocyclyl.

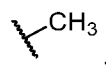
97. The compound of any one of claims 70 to 96, wherein R^{7i} is H, optionally substituted C_1 - C_6 alkyl, or optionally substituted C_3 - C_{10} carbocyclyl.

98. The compound of claim 97, wherein R^{7i} is H or optionally substituted C_1 - C_6 alkyl.

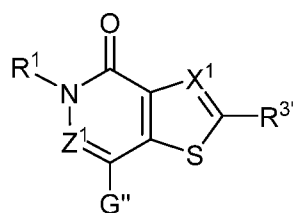


100. The compound of claim 99, wherein R^{7i} is H or .

101. The compound of claim 100, wherein R^{7i} is H.

102. The compound of claim 100, wherein R^{7i} is .

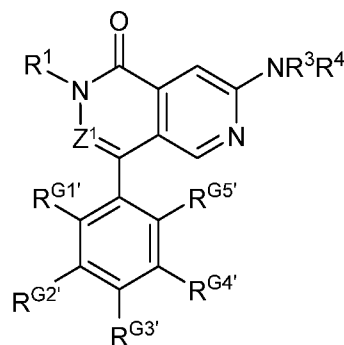
103. The compound of any one of claims 2 to 102, wherein A has the structure of **Formula IIIAa**:



Formula IIIAa,

or a pharmaceutically acceptable salt thereof.

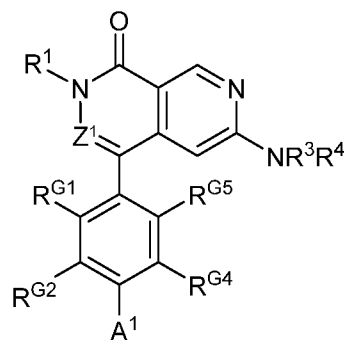
104. The compound of any one of claims 2 to 102, wherein A has the structure of **Formula IIIc**:



Formula IIIc,

or a pharmaceutically acceptable salt thereof.

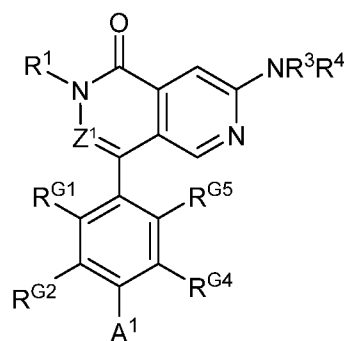
105. The compound of any one of claims 2 to 102, wherein A has the structure of **Formula IIIe**:



Formula IIIe,

or a pharmaceutically acceptable salt thereof.

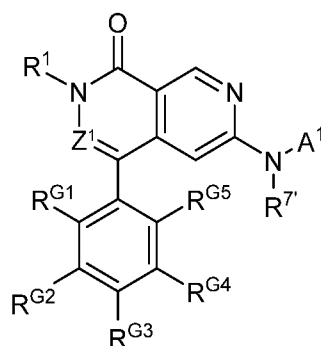
106. The compound of any one of claims 2 to 102, wherein A has the structure of **Formula IIIf**:



Formula IIIf,

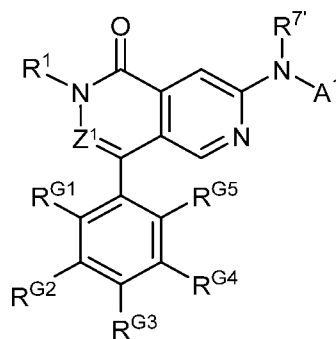
or a pharmaceutically acceptable salt thereof.

107. The compound of any one of claims 2 to 102, wherein A has the structure of **Formula IIIg**:

**Formula IIIg,**

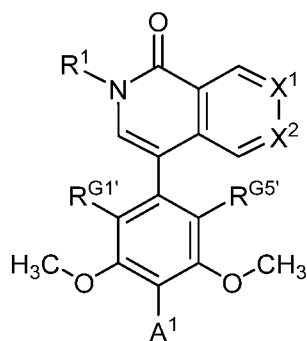
or a pharmaceutically acceptable salt thereof.

108. The compound of any one of claims 2 to 102, wherein A has the structure of **Formula IIIh**:

**Formula IIIh,**

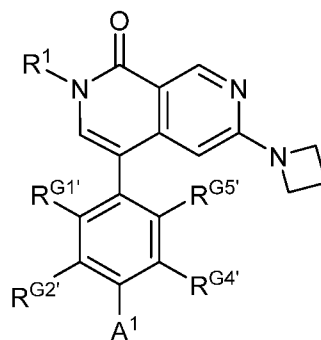
or a pharmaceutically acceptable salt thereof.

109. The compound of any one of claims 2 to 102, wherein A has the structure of **Formula IIIj**:

**Formula IIIj,**

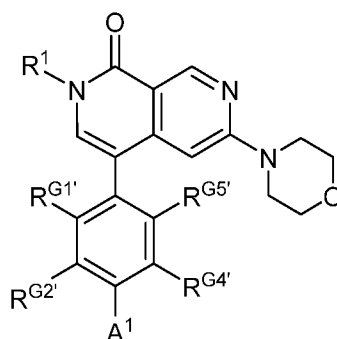
or a pharmaceutically acceptable salt thereof.

110. The compound of any one of claims 2 to 102, wherein A has the structure of **Formula IIIn**:

**Formula IIIIn,**

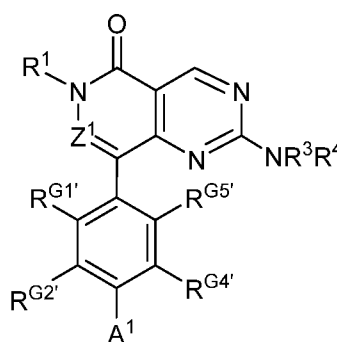
or a pharmaceutically acceptable salt thereof.

111. The compound of any one of claims 2 to 102, wherein A has the structure of **Formula IIIo**:

**Formula IIIo,**

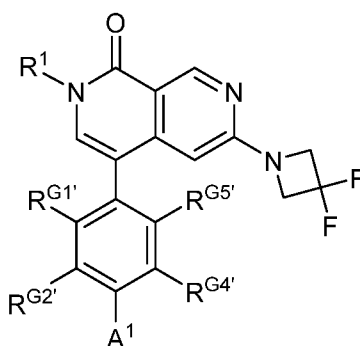
or a pharmaceutically acceptable salt thereof.

112. The compound of any one of claims 2 to 102, wherein A has the structure of **Formula IIIs**:

**Formula IIIs,**

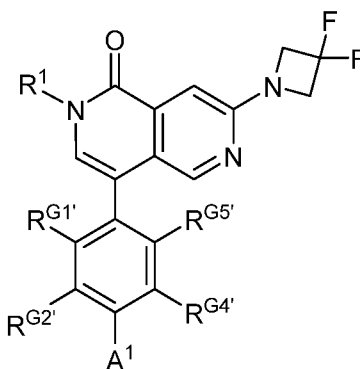
or a pharmaceutically acceptable salt thereof.

113. The compound of any one of claims 2 to 102, wherein A has the structure of **Formula IIIu**:

**Formula IIIu,**

or a pharmaceutically acceptable salt thereof.

114. The compound of any one of claims 2 to 102, wherein A has the structure of **Formula IIIv**:

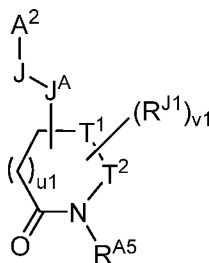
**Formula IIIv,**

or a pharmaceutically acceptable salt thereof.

115. The compound of any one of claims 2 to 114, wherein the degradation moiety is a ubiquitin ligase binding moiety.

116. The compound of claim 115, wherein the ubiquitin ligase binding moiety comprises Cereblon ligands, IAP (Inhibitors of Apoptosis) ligands, mouse double minute 2 homolog (MDM2), or von Hippel-Lindau (VHL) ligands, or derivatives or analogs thereof.

117. The compound of claim 115 or 116, wherein the degradation moiety comprises the structure of **Formula Y**:

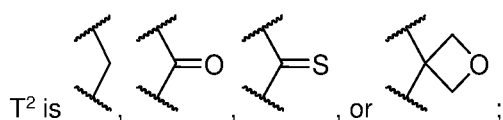
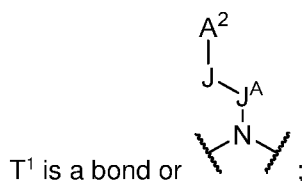
**Formula Y,**

wherein

A^2 is a bond between the degradation moiety and the linker;

v_1 is 0, 1, 2, 3, 4, or 5;

u_1 is 1, 2, or 3;

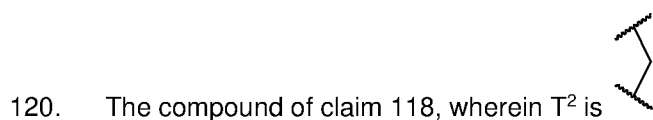
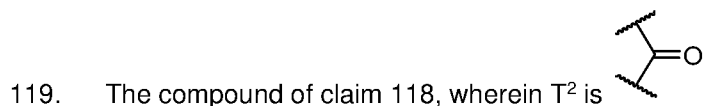
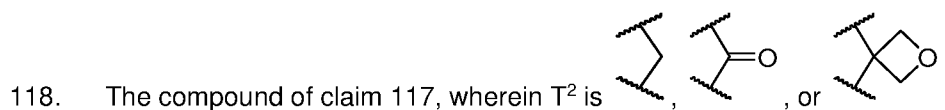


R^{5A} is H, optionally substituted C_1 - C_6 alkyl, or optionally substituted C_1 - C_6 heteroalkyl;

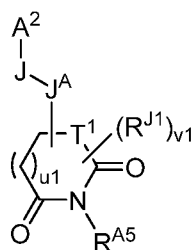
each R^{J1} is, independently, halogen, optionally substituted C_1 - C_6 alkyl, or optionally substituted C_1 - C_6 heteroalkyl;

J^A is absent, O, optionally substituted amino, optionally substituted C_1 - C_6 alkyl, or optionally substituted C_1 - C_6 heteroalkyl; and

J is absent, optionally substituted C_3 - C_{10} carbocyclylene, optionally substituted C_6 - C_{10} arylene, optionally substituted C_2 - C_9 heterocyclylene, or optionally substituted C_2 - C_9 heteroarylene, or a pharmaceutically acceptable salt thereof.



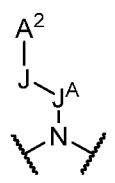
121. The compound of any one of claims 117 to 120, wherein the structure of **Formula Y** has the structure of **Formula Y1**:



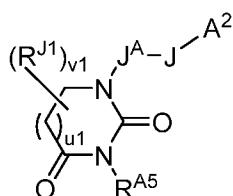
Formula Y1,

or a pharmaceutically acceptable salt thereof.

122. The compound of claim 121, wherein T¹ is a bond.

123. the compound of claim 121, wherein T¹ is .

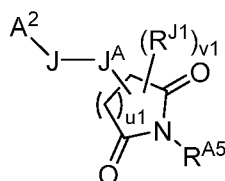
124. The compound of any one of claims 117 to 123, wherein the structure of **Formula Y** has the structure of **Formula Y2**:



Formula Y2,

or a pharmaceutically acceptable salt thereof.

125. The compound of any one of claims 117 to 123, wherein the structure of **Formula Y** has the structure of **Formula Z**:

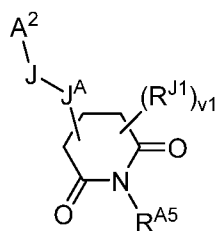


Formula Z,

or a pharmaceutically acceptable salt thereof.

126. The compound of any one of claims 117 to 125, wherein u₁ is 2.

127. The compound of claim 126, wherein the structure of **Formula Z** has the structure of **Formula AA0**:

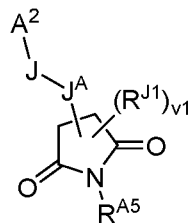


Formula AA0,

or a pharmaceutically acceptable salt thereof.

128. The compound of any one of claims 117 to 125, wherein u₁ is 1.

129. The compound of claim 128, wherein the structure of **Formula Z** has the structure of **Formula AB**:

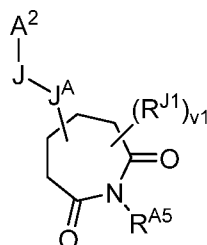


Formula AB,

or a pharmaceutically acceptable salt thereof.

130. The compound of any one of claims 117 to 125, wherein u1 is 3.

131. The compound of claim 130, wherein the structure of **Formula Z** has the structure of **Formula AC**:



Formula AC,

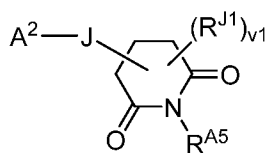
or a pharmaceutically acceptable salt thereof.

132. The compound of any one of claims 117 to 131, wherein J^A is absent.

133. The compound of any one of claims 117 to 131, wherein J^A is optionally substituted C₁-C₆ alkyl.

134. The compound of claim 133, wherein J^A is

135. The compound of claim 132, wherein the structure of **Formula AA0** has the structure of **Formula AA**:



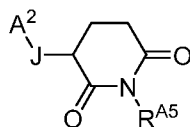
Formula AA,

or a pharmaceutically acceptable salt thereof.

136. The compound of any one of claims 117 to 135, wherein v1 is 0, 1, 2, or 3.

137. The compound of claim 136, wherein v1 is 0.

138. The compound of claim 137, wherein the structure of **Formula AA** has the structure of **Formula AA1**:



Formula AA1,

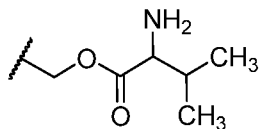
or a pharmaceutically acceptable salt thereof.

139. The compound of any one of claims 117 to 138, wherein R^{A5} is H or optionally substituted C₁-C₆ alkyl.

140. The compound of claim 139, wherein R^{A5} is H.

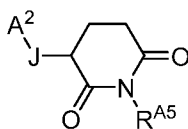
141. The compound of claim 139, wherein R^{A5} is methyl.

142. The compound of any one of claims 117 to 138, wherein R^{A5} is optionally substituted C₁-C₆ heteroalkyl.



143. The compound of claim 142, wherein R^{A5} is

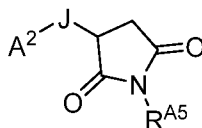
144. The compound of claim 135, wherein the structure of **Formula AA** has the structure of **Formula AA1**:



Formula AA1,

or a pharmaceutically acceptable salt thereof.

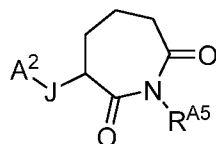
145. The compound of claim 129, wherein the structure of **Formula AB** has the structure of **Formula AB1**:



Formula AB1,

or a pharmaceutically acceptable salt thereof.

146. The compound of claim 131, wherein the structure of **Formula AC** has the structure of **Formula AC1**:

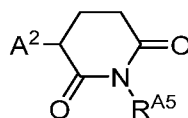


Formula AC1,

or a pharmaceutically acceptable salt thereof.

147. The compound of any one of claims 117 to 146, wherein J is absent.

148. The compound of claim 147, wherein the structure of **Formula AA1** has the structure of **Formula AA2**:

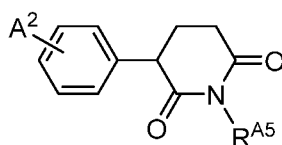


Formula AA2,

or a pharmaceutically acceptable salt thereof.

149. The compound of any one of claims 117 to 146, wherein J is optionally substituted C₃-C₁₀ carbocyclene or optionally substituted C₆-C₁₀ arylene.

150. The compound of claim 149, wherein the structure of **Formula AA** has the structure of **Formula AA4**:

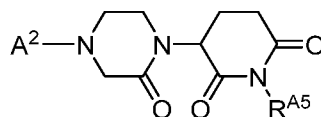


Formula AA4,

or a pharmaceutically acceptable salt thereof.

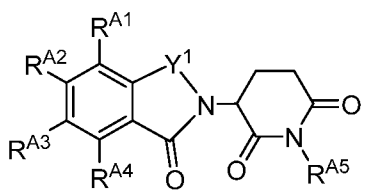
151. The compound of any one of claims 117 to 146, wherein J is optionally substituted C₂-C₉ heterocyclene or optionally substituted C₂-C₉ heteroarylene.

152. The compound of claim 151, wherein the structure of **Formula AA** has the structure of **Formula AA3**:

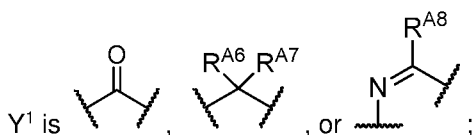
**Formula AA3,**

or a pharmaceutically acceptable salt thereof.

153. The compound of claim 151, wherein the structure of **Formula AA** has the structure of **Formula A**:

**Formula A**

wherein in



R⁵ is H, optionally substituted C₁-C₆ alkyl, or optionally substituted C₁-C₆ heteroalkyl;

R⁶ is H or optionally substituted C₁-C₆ alkyl; and R⁷ is H or optionally substituted C₁-C₆ alkyl; or

R⁶ and R⁷, together with the carbon atom to which each is bound, combine to form optionally substituted C₃-C₆ carbocyclyl or optionally substituted C₂-C₅ heterocyclyl; or R⁶ and R⁷, together with the carbon atom to which each is bound, combine to form optionally substituted C₃-C₆ carbocyclyl or optionally substituted C₂-C₅ heterocyclyl;

R⁸ is H, optionally substituted C₁-C₆ alkyl, or optionally substituted C₁-C₆ heteroalkyl;

each of R¹, R², R³, and R⁴ is, independently, H, A², halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₂-C₉ heteroaryl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, optionally substituted -O-C₃-C₆ carbocyclyl, hydroxyl, thiol, or optionally substituted amino; or R¹ and R², R² and R³, and/or R³ and

R⁴, together with the carbon atoms to which each is attached, combine to form ; and

 is optionally substituted C₆-C₁₀ aryl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heteroaryl, or C₂-C₉ heterocyclyl, any of which is optionally substituted with A²,

wherein one of R¹, R², R³, and R⁴ is A², or  is substituted with A², or a pharmaceutically acceptable salt thereof.

154. The compound of claim 153, each of R¹, R², R³, and R⁴ is, independently, H, A², halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted

C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₂-C₉ heteroaryl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, hydroxyl, thiol, or optionally substituted amino; or R^{A1} and R^{A2}, R^{A2} and R^{A3}, and/or R^{A3} and

R^{A4}, together with the carbon atoms to which each is attached, combine to form ; and

 is optionally substituted C₆-C₁₀ aryl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heteroaryl, or C₂-C₉ heterocyclyl, any of which is optionally substituted with A²,

wherein one of R^{A1}, R^{A2}, R^{A3}, and R^{A4} is A², or  is substituted with A², or a pharmaceutically acceptable salt thereof.

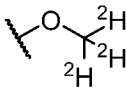
155. The compound of claim 154, wherein each of R^{A1}, R^{A2}, R^{A3}, and R^{A4} is, H, A², halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted -O-C₃-C₆ carbocyclyl, hydroxyl, optionally substituted amino; or R^{A1} and R^{A2}, R^{A2} and R^{A3}, or R^{A3} and R^{A4}, together

with the carbon atoms to which each is attached, combine to form ; and

 is optionally substituted C₂-C₉ heterocyclyl, which is optionally substituted with A²,

wherein one of R^{A1}, R^{A2}, R^{A3}, and R^{A4} is A², or  is substituted with A².

156. The compound of claim 155, wherein each of R^{A1}, R^{A2}, R^{A3}, and R^{A4} is, independently, H,

A², F, , , , or ; or R^{A1} and R^{A2}, R^{A2} and R^{A3}, or R^{A3} and R^{A4},

together with the carbon atoms to which each is attached, combine to form ; and

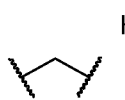
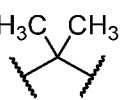
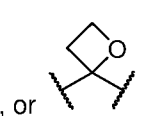
 is optionally substituted C₂-C₉ heterocyclyl, which is optionally substituted with A²,

wherein one of R^{A1}, R^{A2}, R^{A3}, and R^{A4} is A², or  is substituted with A².

157. The compound of any one of claims 153 to 156, wherein Y¹ is  or .

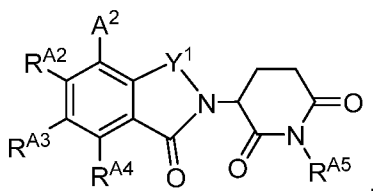
158. The compound of claim 157, wherein Y¹ is .

159. The compound of claim 157, wherein Y¹ is .

160. The compound of claim 159, wherein Y¹ is , , , , , , or .

161. The compound of claim 160, wherein Y¹ is .

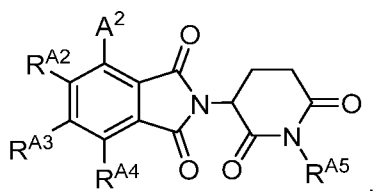
162. The compound of any one of claims 153 to 161, wherein the structure of **Formula A** has the structure of **Formula A1**:



Formula A1

or a pharmaceutically acceptable salt thereof.

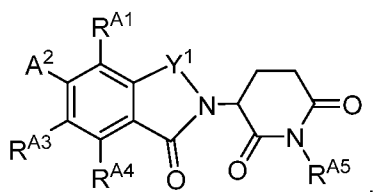
163. The compound of any one of claims 153 to 160, wherein the structure of **Formula A** has the structure of **Formula A2**:



Formula A2

or a pharmaceutically acceptable salt thereof.

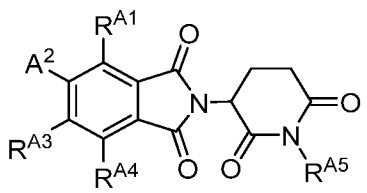
164. The compound of any one of claims 153 to 163, wherein the structure of **Formula A** has the structure of **Formula A3**:



Formula A3

or a pharmaceutically acceptable salt thereof.

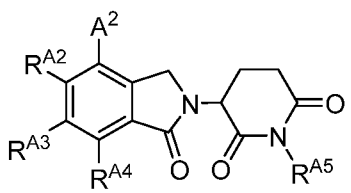
165. The compound of any one of claims 153 to 163, wherein the structure of **Formula A** has the structure of **Formula A4**:



Formula A4

or a pharmaceutically acceptable salt thereof.

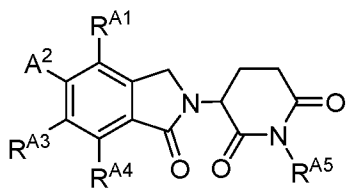
166. The compound of any one of claims 153 to 163, wherein the structure of **Formula A** has the structure of **Formula A5**:



Formula A5

or a pharmaceutically acceptable salt thereof.

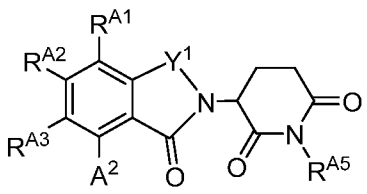
167. The compound of any one of claims 153 to 163, wherein the structure of **Formula A** has the structure of **Formula A6**:



Formula A6

or a pharmaceutically acceptable salt thereof.

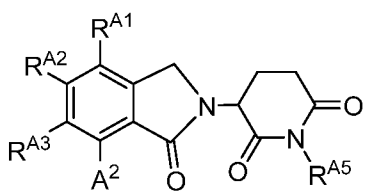
168. The compound of any one of claims 153 to 163, wherein the structure of **Formula A** has the structure of **Formula A7**:



Formula A7

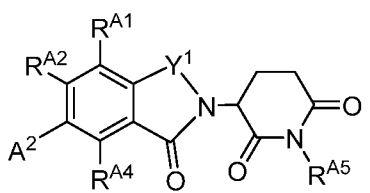
or a pharmaceutically acceptable salt thereof.

169. The compound of any one of claims 153 to 163, wherein the structure of **Formula A** has the structure of **Formula A8**:

**Formula A8**

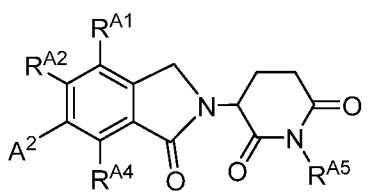
or a pharmaceutically acceptable salt thereof.

170. The compound of any one of claims 153 to 163, wherein the structure of **Formula A** has the structure of **Formula A9**:

**Formula A9**

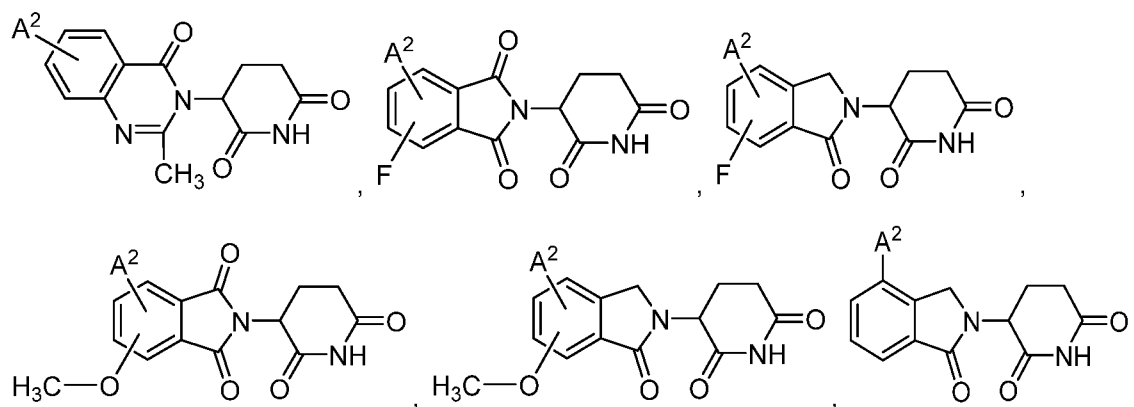
or a pharmaceutically acceptable salt thereof.

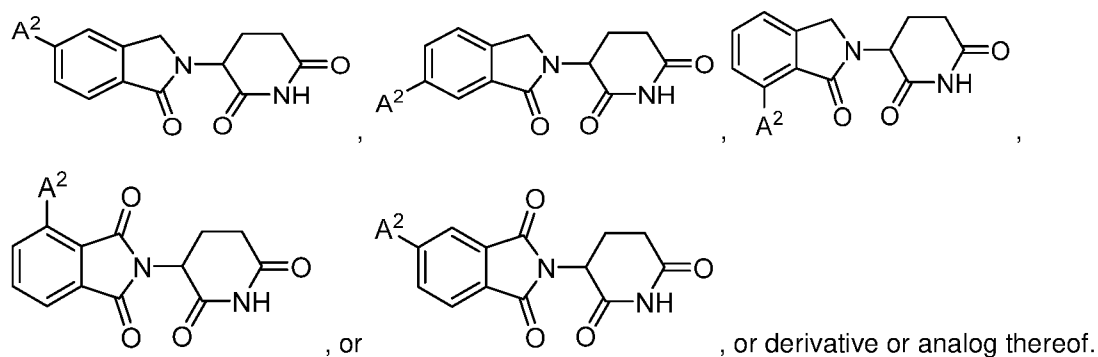
171. The compound of any one of claims 153 to 163, wherein the structure of **Formula A** has the structure of **Formula A10**:

**Formula A10**

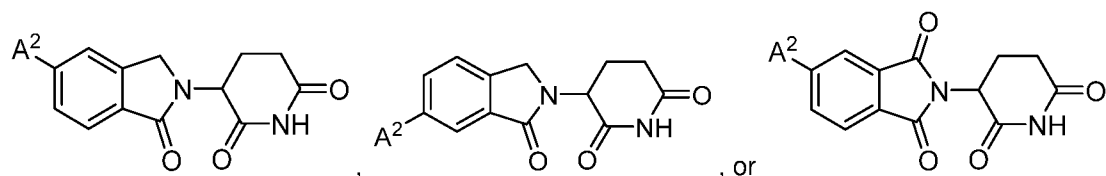
or a pharmaceutically acceptable salt thereof.

172. The compound of any one of claims 153 to 171, wherein the structure of **Formula A** is

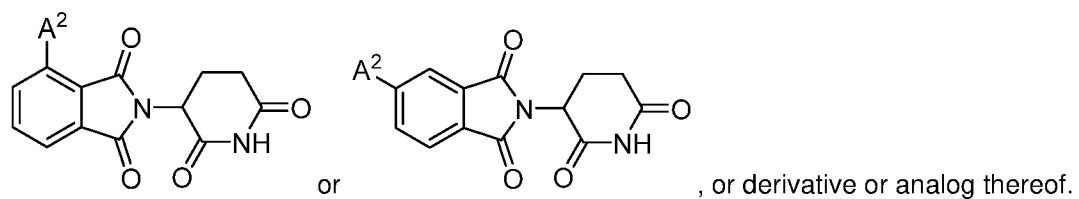




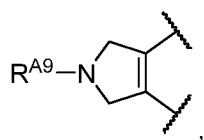
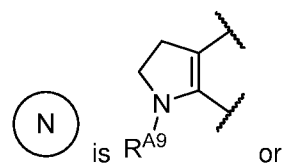
173. The compound of claim 172, wherein the structure of **Formula A** is



174. The compound of claim 173, wherein the structure of **Formula A** is

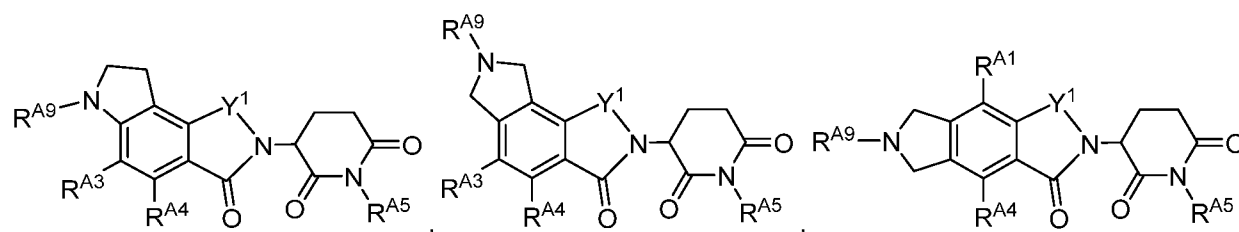


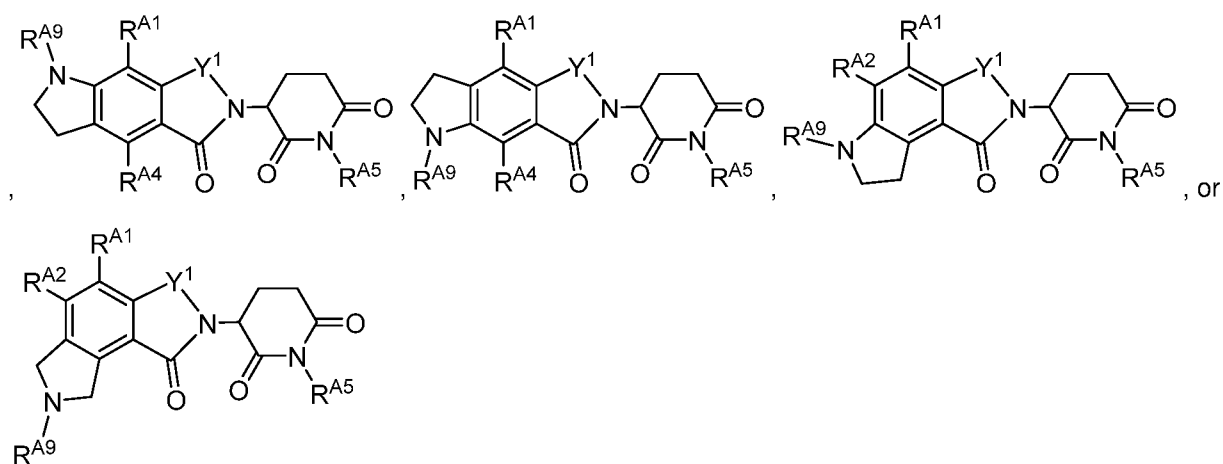
175. The compound of any one of claims 153 to 171, wherein



wherein R^A is H, A^2 , optionally substituted C_1 - C_6 alkyl, or optionally substituted C_1 - C_6 heteroalkyl.

176. The compound of claim 175, wherein the structure of **Formula A** is

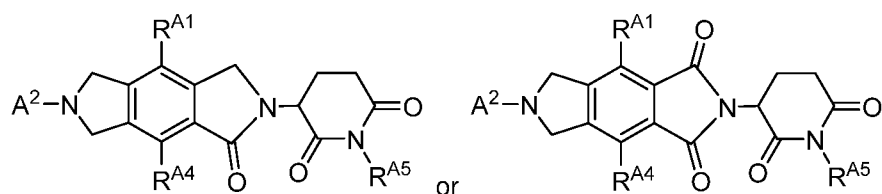




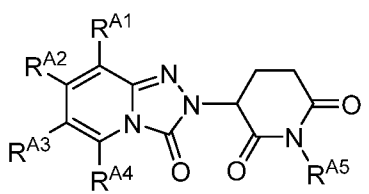
177. The compound of claim 176, wherein R^{A9} is H.

178. The compound of claim 176, wherein R^{A9} is A^2 .

179. The compound of claim 178, wherein the structure of **Formula A** is



180. The compound of claim 151, wherein the structure of **Formula AA** has the structure of **Formula B**:



Formula B

wherein

R^{A5} is H, optionally substituted C_1 - C_6 alkyl, or optionally substituted C_1 - C_6 heteroalkyl;

each of R^{A1} , R^{A2} , R^{A3} , and R^{A4} is, independently, H, A^2 , halogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_3 - C_{10} carbocyclyl, optionally substituted C_2 - C_9 heterocyclyl, optionally substituted C_6 - C_{10} aryl, optionally substituted C_2 - C_9 heteroaryl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted $-O-C_3-C_6$ carbocyclyl, hydroxyl, thiol, or optionally substituted amino; or R^{A1} and R^{A2} , R^{A2} and R^{A3} , and/or R^{A3} and

R^{A4} , together with the carbon atoms to which each is attached, combine to form ; and

 is optionally substituted C₆-C₁₀ aryl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heteroaryl, or C₂-C₉ heterocyclyl, any of which is optionally substituted with A²,

wherein one of R^{A1}, R^{A2}, R^{A3}, and R^{A4} is A², or  is substituted with A², or a pharmaceutically acceptable salt thereof.

181. The compound of claim 180, wherein each of R^{A1}, R^{A2}, R^{A3}, and R^{A4} is, H, A², halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted -O-C₃-C₆ carbocyclyl, hydroxyl, optionally substituted amino; or R^{A1} and R^{A2}, R^{A2} and R^{A3}, or R^{A3} and R^{A4}, together

with the carbon atoms to which each is attached, combine to form N ; and

 is optionally substituted C₂-C₉ heterocyclyl, which is optionally substituted with A²,

wherein one of R^{A1} , R^{A2} , R^{A3} , and R^{A4} is A^2 , or $\textcircled{N}$ is substituted with A^2 .

182. The compound of claim 181, wherein each of R^{A1} , R^{A2} , R^{A3} , and R^{A4} is, independently, H,

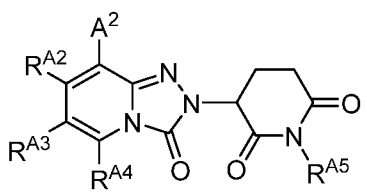
A^2 , F, , , , or ; or R^{A1} and R^{A2} , R^{A2} and R^{A3} , or R^{A3} and R^{A4}

together with the carbon atoms to which each is attached, combine to form N ; and

$\textcircled{\text{N}}$ is optionally substituted C₂-C₉ heterocyclyl, which is optionally substituted with A²,

wherein one of R^{A1} , R^{A2} , R^{A3} , and R^{A4} is A^2 , or $\textcircled{N}$ is substituted with A^2 .

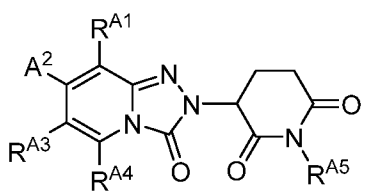
183. The compound of any one of claims 180 to 182, wherein the structure of **Formula B** has the structure of **Formula B1**:



Formula B1

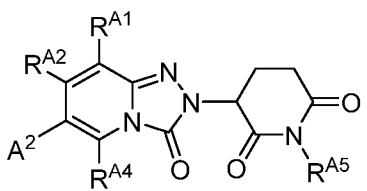
or a pharmaceutically acceptable salt thereof.

184. The compound of any one of claims 180 to 182, wherein the structure of **Formula B** has the structure of **Formula B2**:

**Formula B2**

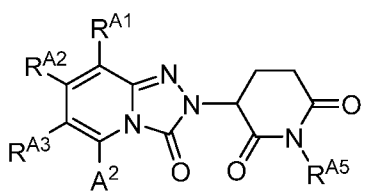
or a pharmaceutically acceptable salt thereof.

185. The compound of any one of claims 180 to 182, wherein the structure of **Formula B** has the structure of **Formula B3**:

**Formula B3**

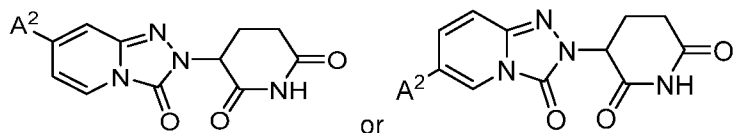
or a pharmaceutically acceptable salt thereof.

186. The compound of any one of claims 180 to 182, wherein the structure of **Formula B** has the structure of **Formula B4**:

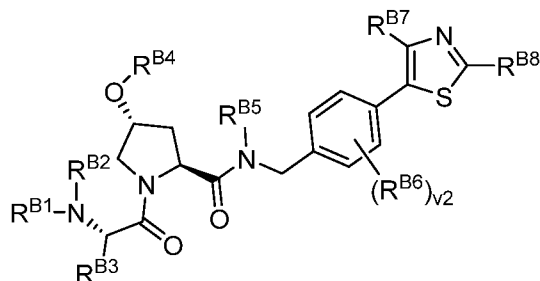
**Formula B4**

or a pharmaceutically acceptable salt thereof.

187. The compound of any one of claims 180 to 182, wherein the structure of **Formula B** is



188. The compound of any one of claims 2 to 114, wherein the degradation moiety comprises the structure of **Formula C**:



Formula C,

wherein

R^{B1} is H, A², optionally substituted C₁-C₆ alkyl, or optionally substituted C₁-C₆ heteroalkyl;

R^{B2} is H, optionally substituted C₁-C₆ alkyl, or optionally substituted C₁-C₆ heteroalkyl;

R^{B3} is A², optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₁-C₆ alkyl C₃-C₁₀ carbocyclyl, or optionally substituted C₁-C₆ alkyl C₆-C₁₀ aryl;

R^{B4} is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₁-C₆ alkyl C₃-C₁₀ carbocyclyl, or optionally substituted C₁-C₆ alkyl C₆-C₁₀ aryl;

R^{B5} is H, optionally substituted C₁-C₆ alkyl, or optionally substituted C₁-C₆ heteroalkyl;

v2 is 0, 1, 2, 3, or 4:

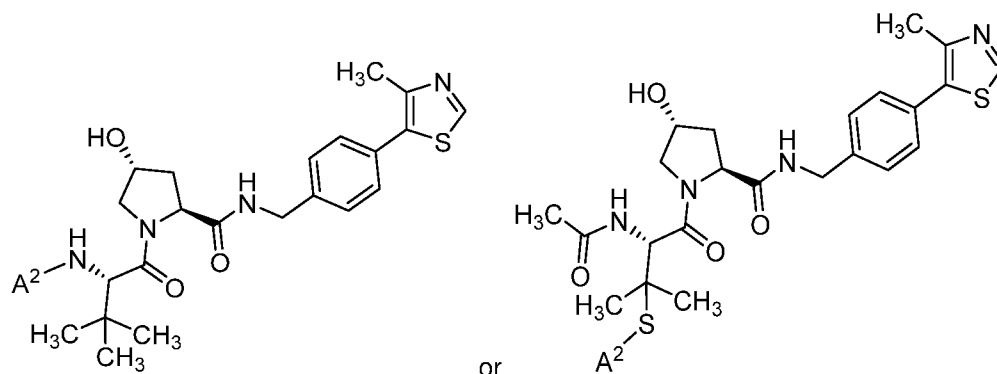
each R^{B6} is, independently, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₂-C₉ heteroaryl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, hydroxy, thiol, or optionally substituted amino; and

each of R^{B7} and R^{B8} is, independently, H, halogen, optionally substituted C₁-C₆ alkyl, or optionally substituted C₆-C₁₀ aryl,

wherein one of R^{B1} and R^{B3} is A^2 .

or a pharmaceutically acceptable salt thereof.

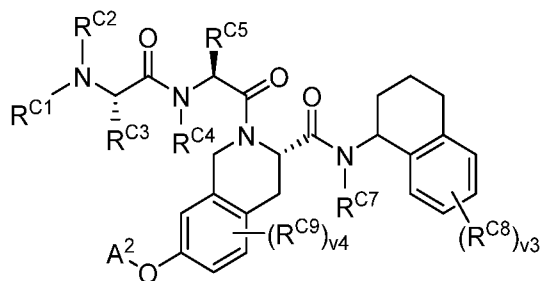
189. The compound of claim 188, wherein the structure of **Formula C** is



analog thereof.

, or derivative or

190. The compound of any one of claims 2 to 114, wherein the degradation moiety comprises the structure of **Formula D**:



Formula D,

wherein

A² is a bond between B and the linker;

each of R^{C1}, R^{C2}, and R^{C7} is, independently, H, optionally substituted C₁-C₆ alkyl, or optionally substituted C₁-C₆ heteroalkyl;

R^{C3} is optionally substituted C₁-C₆ alkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₁-C₆ alkyl C₃-C₁₀ carbocyclyl, or optionally substituted C₁-C₆ alkyl C₆-C₁₀ aryl;

R^{C5} is optionally substituted C₁-C₆ alkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₁-C₆ alkyl C₃-C₁₀ carbocyclyl, or optionally substituted C₁-C₆ alkyl C₆-C₁₀ aryl;

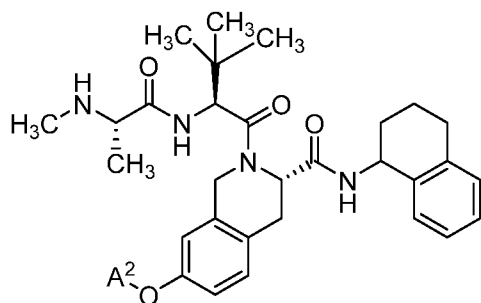
v₃ is 0, 1, 2, 3, or 4;

each R^{C8} is, independently, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₂-C₉ heteroaryl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, hydroxy, thiol, or optionally substituted amino;

v₄ is 0, 1, 2, 3, or 4; and

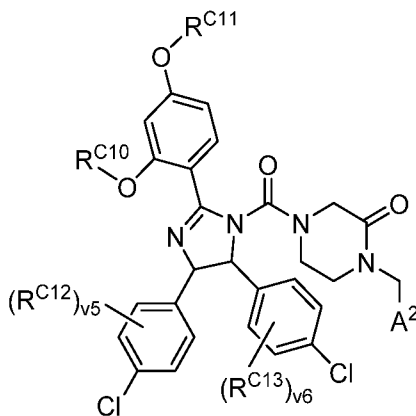
each R^{C9} is, independently, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₂-C₉ heteroaryl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, hydroxy, thiol, or optionally substituted amino, or a pharmaceutically acceptable salt thereof.

191. The compound of claim 190, wherein the structure of **Formula D** is



, or derivative or analog thereof.

192. The compound of any one of claims 2 to 114, wherein the degradation moiety comprises the structure of **Formula E**:



Formula E,

wherein

A² is a bond between B and the linker;

each of R^{C10} and R^{C11} is, independently, H, optionally substituted C₁-C₆ alkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₁-C₆ alkyl C₃-C₁₀ carbocyclyl, or optionally substituted C₁-C₆ alkyl C₆-C₁₀ aryl;

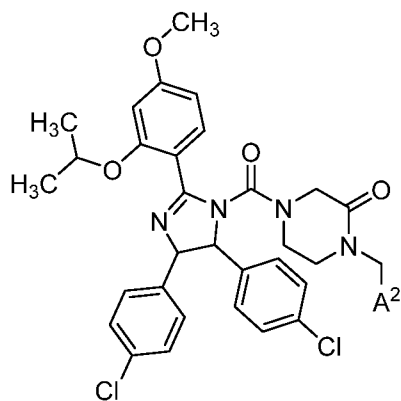
v₅ is 0, 1, 2, 3, or 4;

each R^{C12} is, independently, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₂-C₉ heteroaryl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, hydroxy, thiol, or optionally substituted amino;

v₆ is 0, 1, 2, 3, or 4; and

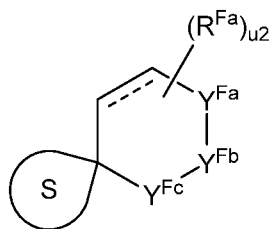
each R^{C13} is, independently, halogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₃-C₁₀ carbocyclyl, optionally substituted C₂-C₉ heterocyclyl, optionally substituted C₆-C₁₀ aryl, optionally substituted C₂-C₉ heteroaryl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, hydroxy, thiol, or optionally substituted amino, or a pharmaceutically acceptable salt thereof.

193. The compound of claim 192, wherein the structure of **Formula E** is



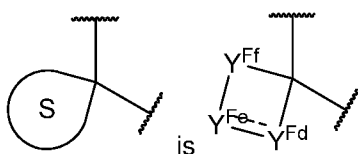
, or derivative or analog thereof.

194. The compound of any one of claims 2 to 114, wherein the degradation moiety comprises the structure of **Formula FA**:



Formula FA,

wherein



is , or a bicyclic moiety which is substituted with A^2 and substituted with one or more groups independently selected from H, R^{FF1} , and oxo;

---- is a single bond or a double bond;

u_2 is 0, 1, 2, or 3;

A^2 is a bond between the degrader and the linker;

Y^{Fa} is $CR^{Fb}R^{Fc}$, $C=O$, $C=S$, $C=CH_2$, SO_2 , $S(O)$, $P(O)Oalkyl$, $P(O)NHalkyl$, $P(O)N(alkyl)_2$, $P(O)alkyl$, $P(O)OH$, $P(O)NH_2$;

Y^{Fb} is NH , NR^{FF1} , CH_2 , CHR^{FF1} , $C(R^{FF1})_2$, O , or S ;

Y^{Fc} is $CR^{Fd}R^{Fe}$, $C=O$, $C=S$, $C=CH_2$, SO_2 , $S(O)$, $P(O)Oalkyl$, $P(O)NHalkyl$, $P(O)N(alkyl)_2$, $P(O)alkyl$, $P(O)OH$, $P(O)NH_2$;

each of R^{Fb} , R^{Fc} , R^{Fd} , and R^{Fe} is, independently, H, alkyl, aliphatic, heteroaliphatic, aryl, heteroaryl, carbocyclyl, hydroxyl, alkoxy, amino, $-NHalkyl$, or $-Nalkyl_2$;

or R^{Fb} and R^{Fc} , together with the carbon atom to which each is attached, combine to form a 3-, 4-, 5-, or 6-membered spirocarbocyclylene, or a 4-, 5-, or 6-membered spiroheterocyclylene comprising 1 or 2 heteroatoms selected from N and O;

or R^{Fd} and R^{Fe} , together with the carbon atom to which each is attached, combine to form a 3-, 4-, 5-, or 6-membered spirocarbocyclylene, or a 4-, 5-, or 6-membered spiroheterocyclylene comprising 1 or 2 heteroatoms selected from N and O; and

or R^{Fd} and R^{Fb} , together with the carbon atoms to which each is attached, combine to form a 1, 2, 3, or 4 carbon bridged ring;

each of Y^{Fd} and Y^{Ff} is, independently, CH_2 , CHR^{FF2} , $C(R^{FF2})_2$, $C(O)$, N , NH , NR^{FF3} , O , S , or $S(O)$;

Y^{Fe} is a bond or a divalent moiety attached to Y^{Fd} and Y^{Ff} that contains 1 to 5 contiguous carbon atoms that form a 3 to 8-membered ring,

wherein 1, 2, or 3 carbon atoms can be replaced with a nitrogen, oxygen, or sulfur atom;

wherein one of the ring atoms is substituted with A^2 and the others are substituted with one or more groups independently selected from H and R^{FF1} ; and

wherein the contiguous atoms of Y^{Fe} can be attached through a single or double bond;

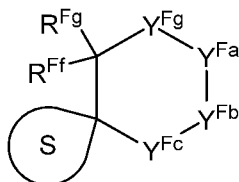
each R^{FF1} is, independently, H, alkyl, alkenyl, alkynyl, aliphatic, heteroaliphatic, carbocyclyl, halogen, hydroxyl, amino, cyano, alkoxy, aryl, heteroaryl, heterocyclyl, alkylamino, alkylhydroxyl, or haloalkyl;

each R^{FF2} is, independently, alkyl, alkene, alkyne, halogen, hydroxyl, alkoxy, azide, amino, $-\text{C}(\text{O})\text{H}$, $-\text{C}(\text{O})\text{OH}$, $-\text{C}(\text{O})$ (aliphatic, including alkyl), $-\text{C}(\text{O})\text{O}$ (aliphatic, including alkyl), $-\text{NH}$ (aliphatic, including alkyl), $-\text{N}$ (aliphatic including alkyl)(aliphatic including alkyl), $-\text{NHSO}_2\text{alkyl}$, $-\text{N}(\text{alkyl})\text{SO}_2\text{alkyl}$, $-\text{NHSO}_2\text{aryl}$, $-\text{N}(\text{alkyl})\text{SO}_2\text{aryl}$, $-\text{NHSO}_2\text{alkenyl}$, $-\text{N}(\text{alkyl})\text{SO}_2\text{alkenyl}$, $-\text{NHSO}_2\text{alkynyl}$, $-\text{N}(\text{alkyl})\text{SO}_2\text{alkynyl}$, aliphatic, heteroaliphatic, aryl, heteroaryl, heterocyclic, carbocyclic, cyano, nitro, nitroso, $-\text{SH}$, $-\text{Salkyl}$, or haloalkyl; and

R^{FF3} is alkyl, alkenyl, alkynyl, $-\text{C}(\text{O})\text{H}$, $-\text{C}(\text{O})\text{OH}$, $-\text{C}(\text{O})\text{alkyl}$, or $-\text{C}(\text{O})\text{Oalkyl}$,

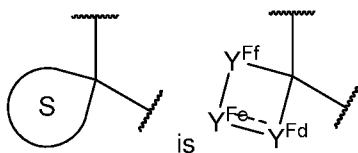
wherein if Y^{Fd} or Y^{Fe} is substituted with A^2 , then Y^{Fe} is a bond, or a pharmaceutically acceptable salt thereof.

195. The compound of any one of claims 2 to 114, wherein the degradation moiety comprises the structure of **Formula FB**:



Formula FB,

wherein



is , or a bicyclic moiety which is substituted with A^2 and substituted with one or more groups independently selected from H, R^{FF1} , and oxo;

A^2 is a bond between the degrader and the linker;

Y^{Fa} is $\text{CR}^{Fb}\text{R}^{Fc}$, $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{C}=\text{CH}_2$, SO_2 , $\text{S}(\text{O})$, $\text{P}(\text{O})\text{Oalkyl}$, $\text{P}(\text{O})\text{NHalkyl}$, $\text{P}(\text{O})\text{N}(\text{alkyl})_2$, $\text{P}(\text{O})\text{alkyl}$, $\text{P}(\text{O})\text{OH}$, $\text{P}(\text{O})\text{NH}_2$;

each of Y^{Fb} and Y^{Fg} is, independently, NH , NR^{FF1} , CH_2 , CHR^{FF1} , $\text{C}(\text{R}^{FF1})_2$, O , or S ;

Y^{Fc} is $\text{CR}^{Fd}\text{R}^{Fe}$, $\text{C}=\text{O}$, $\text{C}=\text{S}$, $\text{C}=\text{CH}_2$, SO_2 , $\text{S}(\text{O})$, $\text{P}(\text{O})\text{Oalkyl}$, $\text{P}(\text{O})\text{NHalkyl}$, $\text{P}(\text{O})\text{N}(\text{alkyl})_2$, $\text{P}(\text{O})\text{alkyl}$, $\text{P}(\text{O})\text{OH}$, $\text{P}(\text{O})\text{NH}_2$;

each of R^{Fb} , R^{Fc} , R^{Fd} , R^{Fe} , R^{Ff} , and R^{Fg} is, independently, H, alkyl, aliphatic, heteroaliphatic, aryl, heteroaryl, carbocyclyl, hydroxyl, alkoxy, amino, $-\text{NHalkyl}$, or $-\text{Nalkyl}_2$;

or R^{Fb} and R^{Fc} , together with the carbon atom to which each is attached, combine to form a 3-, 4-, 5-, or 6-membered spirocarbocyclene, or a 4-, 5-, or 6-membered spiroheterocyclene comprising 1 or 2 heteroatoms selected from N and O;

or R^{Fd} and R^{Fe} , together with the carbon atom to which each is attached, combine to form a 3-, 4-, 5-, or 6-membered spirocarbocyclene, or a 4-, 5-, or 6-membered spiroheterocyclene comprising 1 or 2 heteroatoms selected from N and O;

or R^{Ff} and R^{Fg} , together with the carbon atom to which each is attached, combine to form a 3-, 4-, 5-, or 6-membered spirocarbocyclene, or a 4-, 5-, or 6-membered spiroheterocyclene comprising 1 or 2 heteroatoms selected from N and O;

or R^{Fd} and R^{Fb} , together with the carbon atoms to which each is attached, combine to form a 1, 2, 3, or 4 carbon bridged ring;

or R^{Fd} and R^{Ff} , together with the carbon atoms to which each is attached, combine to form a 1, 2, 3, or 4 carbon bridged ring;

or R^{Fb} and R^{Fg} , together with the carbon atoms to which each is attached, combine to form a 1, 2, 3, or 4 carbon bridged ring;

each of Y^{Fd} and Y^{Ff} is, independently, CH_2 , CHR^{FF2} , $C(R^{FF2})_2$, $C(O)$, N, NH, NR^{FF3} , O, S, or $S(O)$;

Y^{Fe} is a bond or a divalent moiety attached to Y^{Fd} and Y^{Ff} that contains 1 to 5 contiguous carbon atoms that form a 3 to 8-membered ring,

wherein 1, 2, or 3 carbon atoms can be replaced with a nitrogen, oxygen, or sulfur atom;

wherein one of the ring atoms is substituted with A^2 and the others are substituted with one or more groups independently selected from H and R^{FF1} ; and

wherein the contiguous atoms of Y^{Fe} can be attached through a single or double bond;

each R^{FF1} is, independently, H, alkyl, alkenyl, alkynyl, aliphatic, heteroaliphatic, carbocyclyl, halogen, hydroxyl, amino, cyano, alkoxy, aryl, heteroaryl, heterocyclyl, alkylamino, alkylhydroxyl, or haloalkyl;

each R^{FF2} is, independently, alkyl, alkene, alkyne, halogen, hydroxyl, alkoxy, azide, amino, $-C(O)H$, $-C(O)OH$, $-C(O)$ (aliphatic, including alkyl), $-C(O)O$ (aliphatic, including alkyl), $-NH$ (aliphatic, including alkyl), $-N$ (aliphatic including alkyl)(aliphatic including alkyl), $-NHSO_2$ alkyl, $-N$ (alkyl) SO_2 alkyl, $-NHSO_2$ aryl, $-N$ (alkyl) SO_2 aryl, $-NHSO_2$ alkenyl, $-N$ (alkyl) SO_2 alkenyl, $-NHSO_2$ alkynyl, $-N$ (alkyl) SO_2 alkynyl, aliphatic, heteroaliphatic, aryl, heteroaryl, heterocyclic, carbocyclic, cyano, nitro, nitroso, $-SH$, $-S$ alkyl, or haloalkyl; and

R^{FF3} is alkyl, alkenyl, alkynyl, $-C(O)H$, $-C(O)OH$, $-C(O)$ alkyl, or $-C(O)O$ alkyl,

wherein if Y^{Fd} or Y^{Ff} is substituted with A^2 , then Y^{Fe} is a bond, or a pharmaceutically acceptable salt thereof.

196. The compound of any one of claims 2 to 114, wherein the degradation moiety comprises the structure of **Formula F1**:



Formula F1,

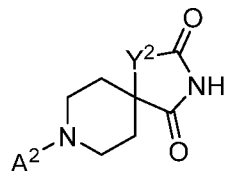
wherein

A^2 is a bond between the degrader and the linker; and

R^{F1} is absent or O,

or a pharmaceutically acceptable salt thereof.

197. The compound of any one of claims 2 to 114, wherein the degradation moiety comprises the structure of **Formula F2**:



Formula F2,

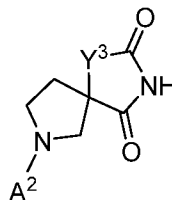
wherein

A² is a bond between the degrader and the linker; and

R^{F1} is absent or O,

or a pharmaceutically acceptable salt thereof.

198. The compound of any one of claims 2 to 114, wherein the degradation moiety comprises the structure of **Formula G**:



Formula G,

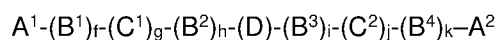
wherein

A² is a bond between the degrader and the linker; and

R^{F1} is absent or O,

or a pharmaceutically acceptable salt thereof.

199. The compound of any one of claims 2 to 198, wherein the linker has the structure of **Formula IV**:



Formula IV

wherein

A¹ is a bond between the linker and A;

A² is a bond between B and the linker;

each of B¹, B², B³, and B⁴ is, independently, optionally substituted C₁-C₂ alkyl, optionally substituted C₁-C₃ heteroalkyl, O, S, S(O)₂, or NR^N;

each R^N is, independently, H, optionally substituted C₁₋₄ alkyl, optionally substituted C₂₋₄ alkenyl, optionally substituted C₂₋₄ alkynyl, optionally substituted C₂₋₆ heterocyclyl, optionally substituted C₆₋₁₂ aryl, or optionally substituted C₁₋₇ heteroalkyl;

each of C¹ and C² is, independently, carbonyl, thiocarbonyl, sulphonyl, or phosphoryl;

each of f, g, h, i, j, and k is, independently, 0 or 1; and

D is optionally substituted C₁₋₁₀ alkyl, optionally substituted C₂₋₁₀ alkenyl, optionally substituted C₂₋₁₀ alkynyl, optionally substituted C₂₋₆ heterocyclyl, optionally substituted C₆₋₁₂ aryl, optionally

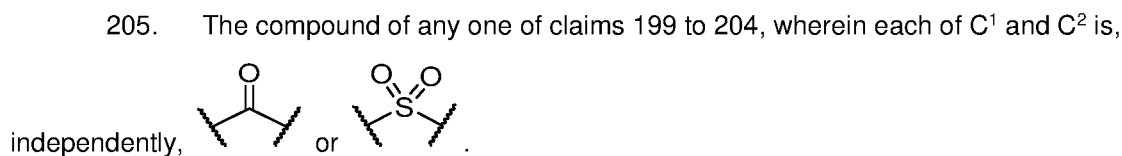
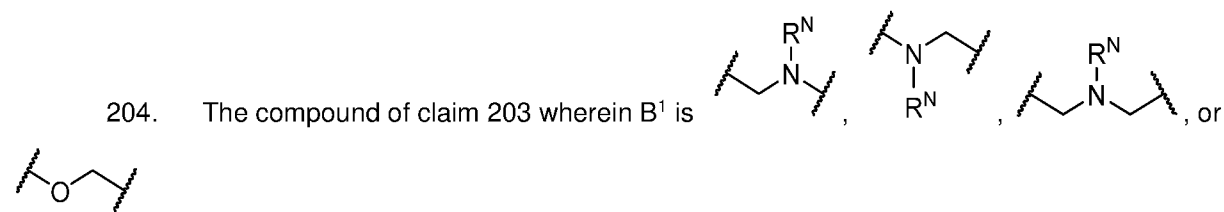
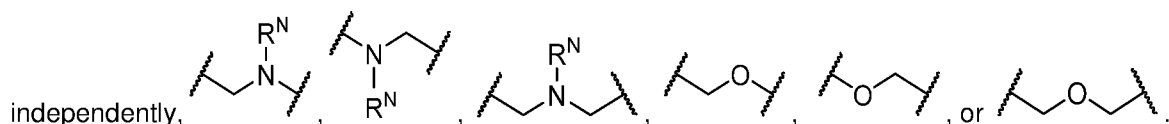
substituted C₂-C₁₀ polyethylene glycol, or optionally substituted C₁₋₁₀ heteroalkyl, or a chemical bond linking A¹-(B¹)_f-(C¹)_g-(B²)_h- to -(B³)_i-(C²)_j-(B⁴)_k-A².

200. The method of claim 199, wherein each of B¹, B², B³, and B⁴ is, independently, optionally substituted C₁-C₄ alkyl, optionally substituted C₁-C₄ heteroalkyl, or NR^N.

201. The method of claim 198 or 199, wherein each R^N is, independently, H or optionally substituted C₁-C₄ alkyl.

202. The method of any one of claims 198 to 201, wherein each R^N is, independently, H or methyl.

203. The compound of any one of claims 199 to 202, wherein each of B¹ and B⁴ is,



207. The compound of any one of claims 199 to 204, wherein B² is NR^N.

208. The compound of any one of claims 199 to 204, wherein B² is optionally substituted C₁-C₄ alkyl.

209. The compound of any one of claims 199 to 208, wherein f is 0.

210. The compound of any one of claims 199 to 208, wherein f is 1.

211. The compound of any one of claims 199 to 210, wherein g is 1.

212. The compound of any one of claims 199 to 211, wherein h is 0.

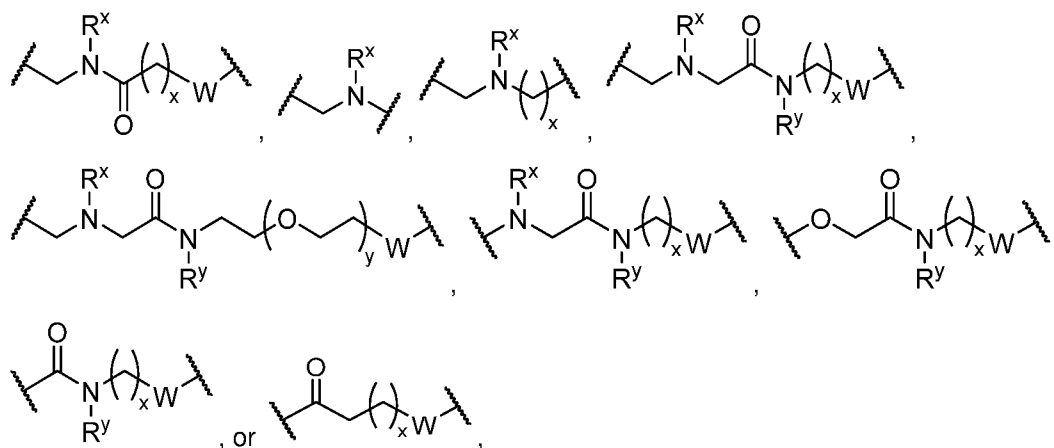
213. The compound of any one of claims 199 to 211, wherein h is 1.

214. The compound of any one of claims 199 to 213, wherein i is 0.

215. The compound of any one of claims 199 to 214, wherein j is 0.

216. The compound of any one of claims 199 to 215, wherein k is 0.

217. The compound of any one of claims 199 to 216, wherein the linker has the structure of



wherein

x is 1, 2, 3, 4, 5, 6, 7, or 8;

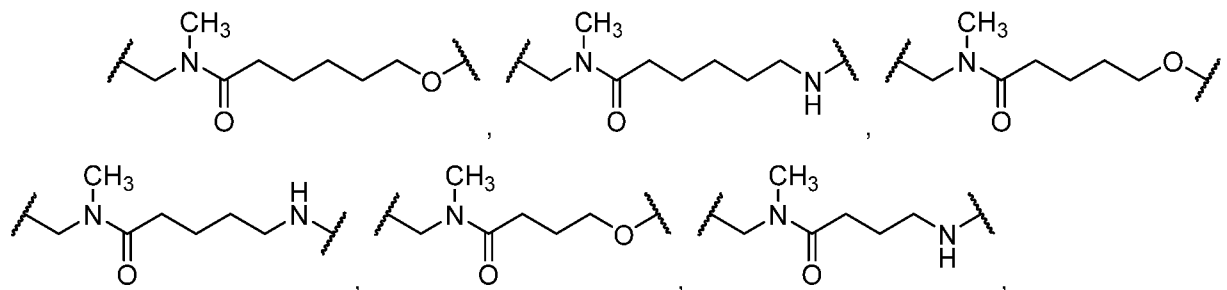
y is 1, 2, 3, or 4;

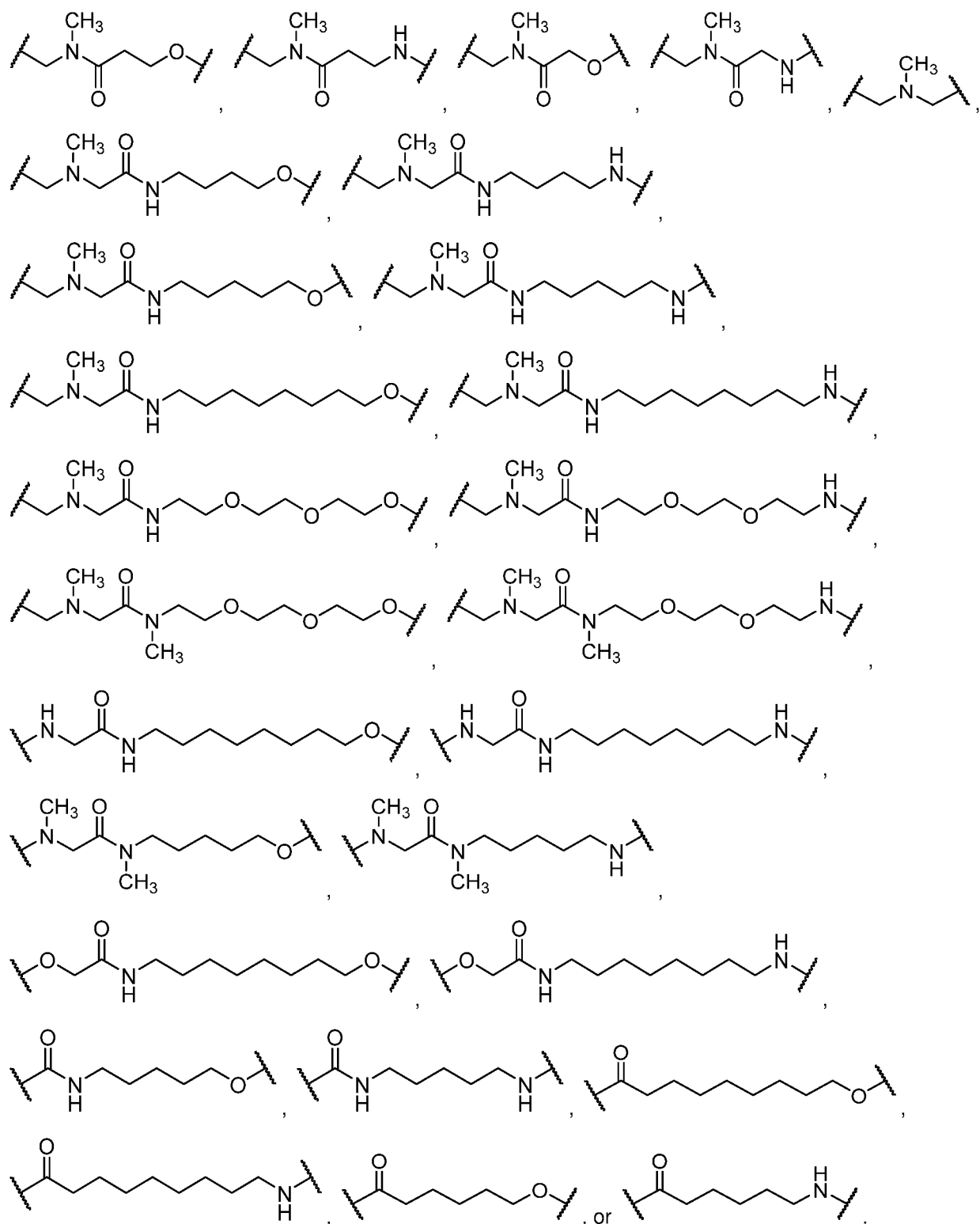
R^x is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl;

R^y is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl; and

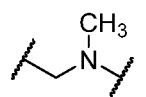
W is O or NR^w, wherein R^w is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl.

218. The compound of any one of claims 199 to 217, wherein the linker has the structure of:



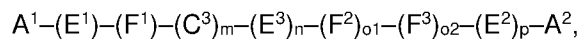


219. The compound of any one of claims 199 to 218, wherein the linker has the structure of



220. The compound of any one of claims 2 to 198, wherein the linker has the structure of

Formula V:

**Formula V**

wherein

A¹ is a bond between the linker and A;

A² is a bond between B and the linker;

each of m, n, o₁, o₂, and p is, independently, 0 or 1;

each of E¹ and E² is, independently, O, S, NR^N, optionally substituted C₁₋₁₀ alkylene, optionally substituted C₂₋₁₀ alkenylene, optionally substituted C₂₋₁₀ alkynylene, optionally substituted C_{2-C10} polyethylene glycol, or optionally substituted C₁₋₁₀ heteroalkylene;

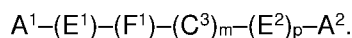
E³ is optionally substituted C_{1-C6} alkylene, optionally substituted C_{1-C6} heteroalkylene, O, S, or NR^N;

each R^N is, independently, H, optionally substituted C₁₋₄ alkyl, optionally substituted C₂₋₄ alkenyl, optionally substituted C₂₋₄ alkynyl, optionally substituted C₂₋₆ heterocyclyl, optionally substituted C₆₋₁₂ aryl, or optionally substituted C₁₋₇ heteroalkyl;

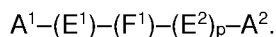
C³ is carbonyl, thiocarbonyl, sulphonyl, or phosphoryl; and

each of F¹, F², and F³ is, independently, optionally substituted C_{3-C10} carbocyclylene, optionally substituted C₂₋₁₀ heterocyclylene, optionally substituted C_{6-C10} arylene, or optionally substituted C_{2-C9} heteroarylene.

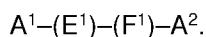
221. The compound of claim 220, wherein the linker has the structure of **Formula Va**:

**Formula Va**

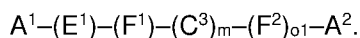
222. The compound of claim 220, wherein the linker has the structure of **Formula Vb**:

**Formula Vb**

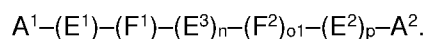
223. The compound of claim 220, wherein the linker has the structure of **Formula Vc**:

**Formula Vc**

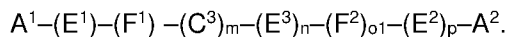
224. The compound of claim 220, wherein the linker has the structure of **Formula Vd**:

**Formula Vd**

225. The compound of claim 220, wherein the linker has the structure of **Formula Ve**:

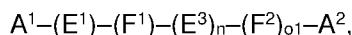
**Formula Ve**

226. The compound of claim 220, wherein the linker has the structure of **Formula Vf**:



Formula Vf

227. The compound of claim 220, wherein the linker has the structure of **Formula Vg**:



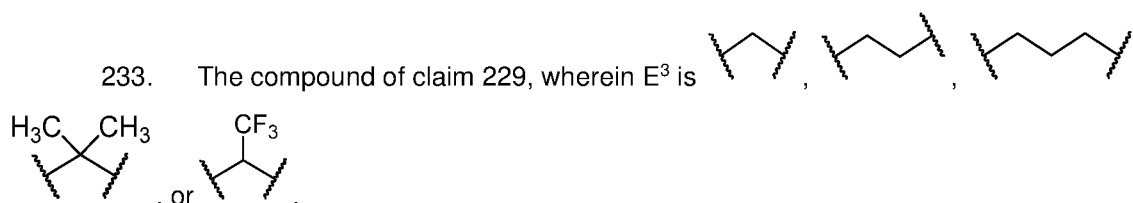
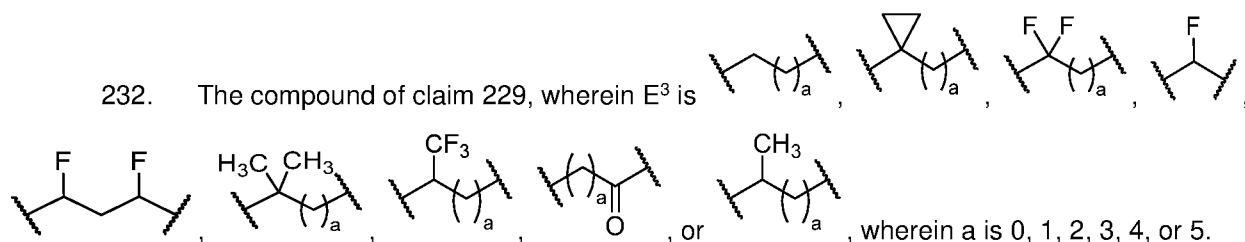
Formula Vg

228. The compound of any one of claims 220 to 227, wherein each of E^1 and E^2 is, independently, NR^N , optionally substituted C_{1-10} alkylene, optionally substituted C_2-C_{10} polyethylene glycolene, or optionally substituted C_{1-10} heteroalkylene.

229. The compound of any one of claims 220 to 228, wherein E^3 is optionally substituted C_1 - C_6 alkylene, O, S, or NR^N .

230. The compound of claim 229, wherein E^3 is optionally substituted C_1 - C_6 alkylene.

231. The compound of claim 229, wherein E^3 is optionally substituted C_1 - C_3 alkylene.



234. The compound of claim 229, wherein E^3 is O.

235. The compound of any one of claims 220 to 234, wherein each R^N is, independently, H or optionally substituted C_{1-4} alkyl.

236. The compound of claim 235, wherein each R^N is, independently, H or methyl.

237. The compound of any one of claims 220 to 236, wherein E¹ is



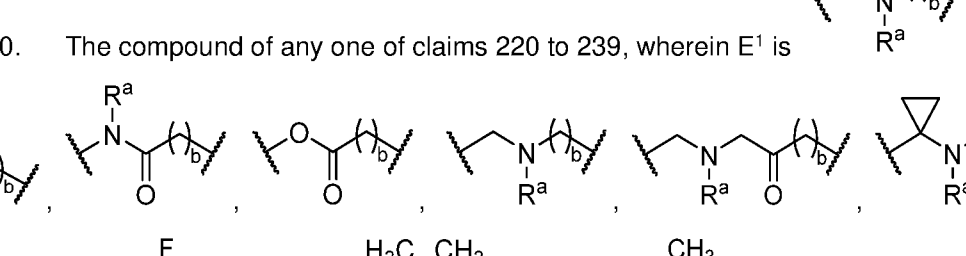
, wherein a is 0, 1, 2, 3, 4, or 5.

238. The compound of claim 237, wherein E¹ is , , , , 

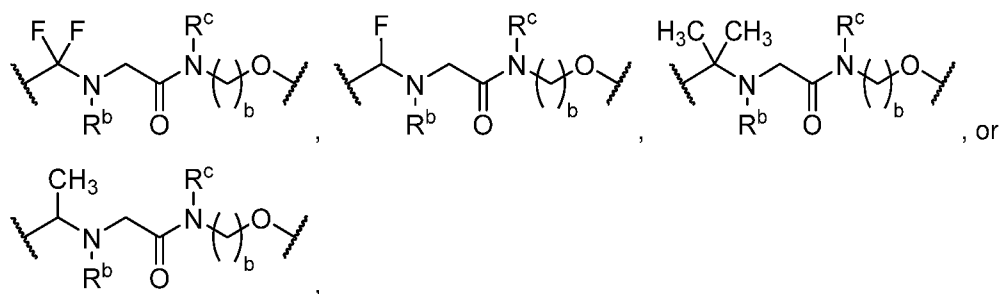
, , , , or .

239. The compound of claim 238, wherein E¹ is 

240. The compound of any one of claims 220 to 239, wherein E¹ is



The image displays 18 chemical structures for E¹, arranged in three rows of six. Each structure is a chemical fragment with wavy lines indicating attachment points. The structures include various amide, ester, and ether linkages, as well as different substituents like R^a, R^b, R^c, and various alkyl and cyclopropyl groups. Some structures include a repeating unit symbol (b) in parentheses.



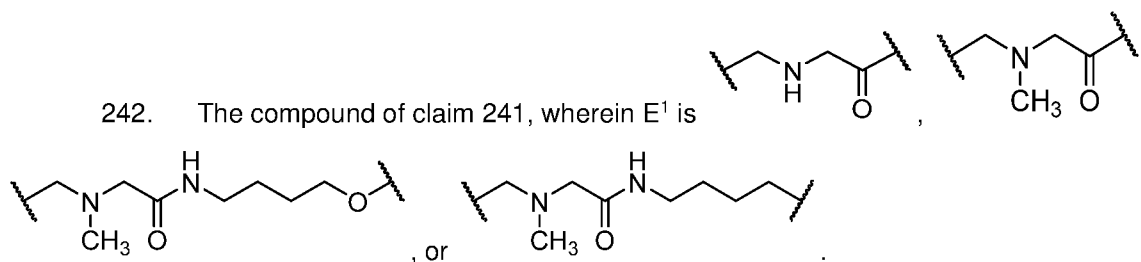
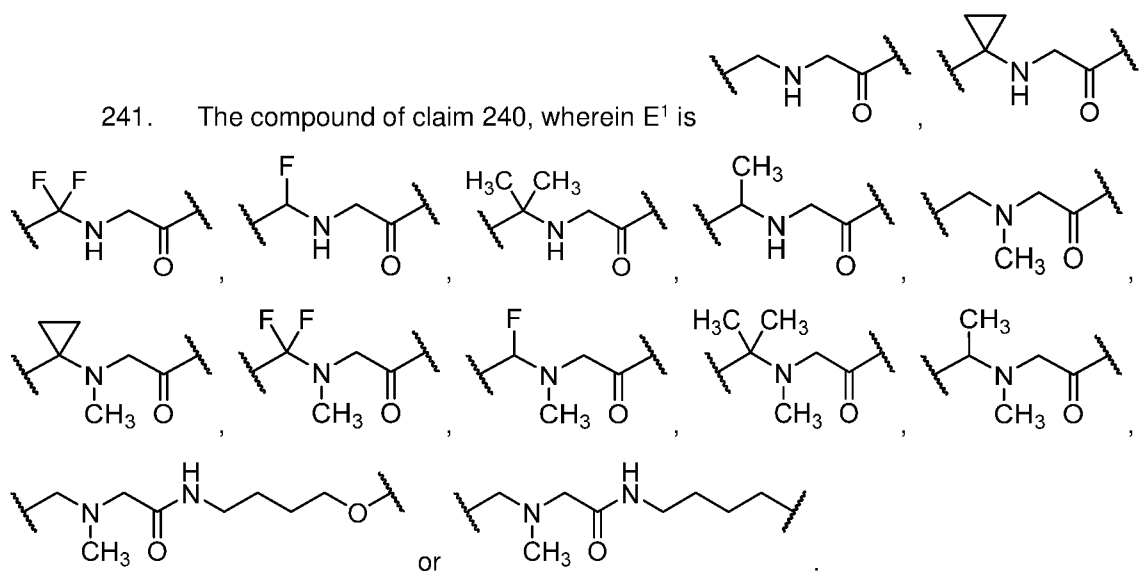
wherein

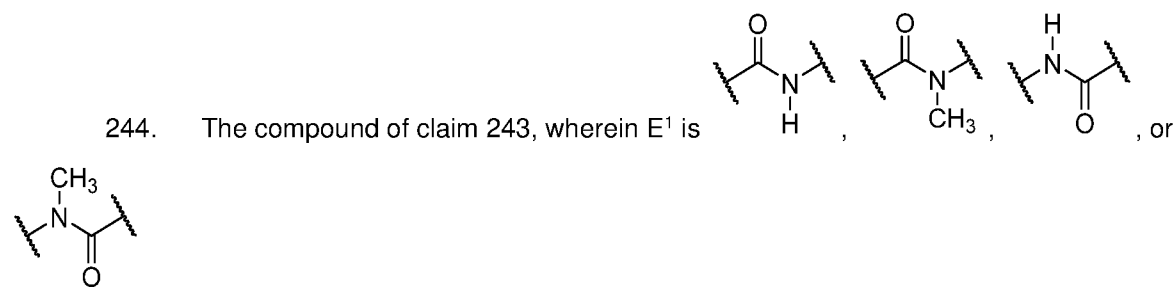
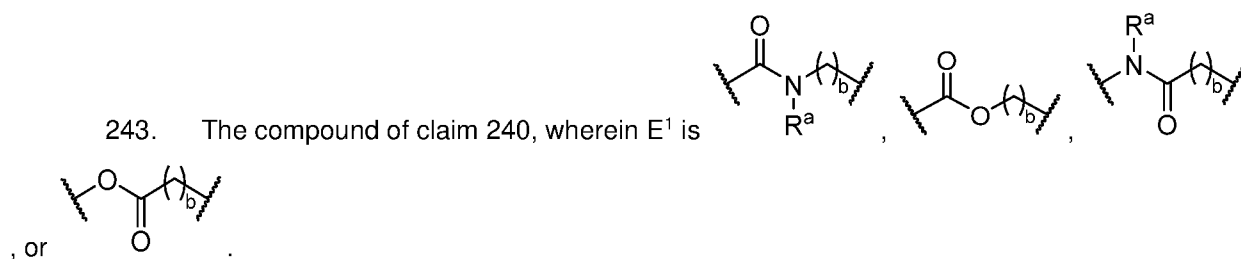
b is 0, 1, 2, 3, 4, 5, or 6;

R^a is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl;

R^b is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl; and

R^c is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl.

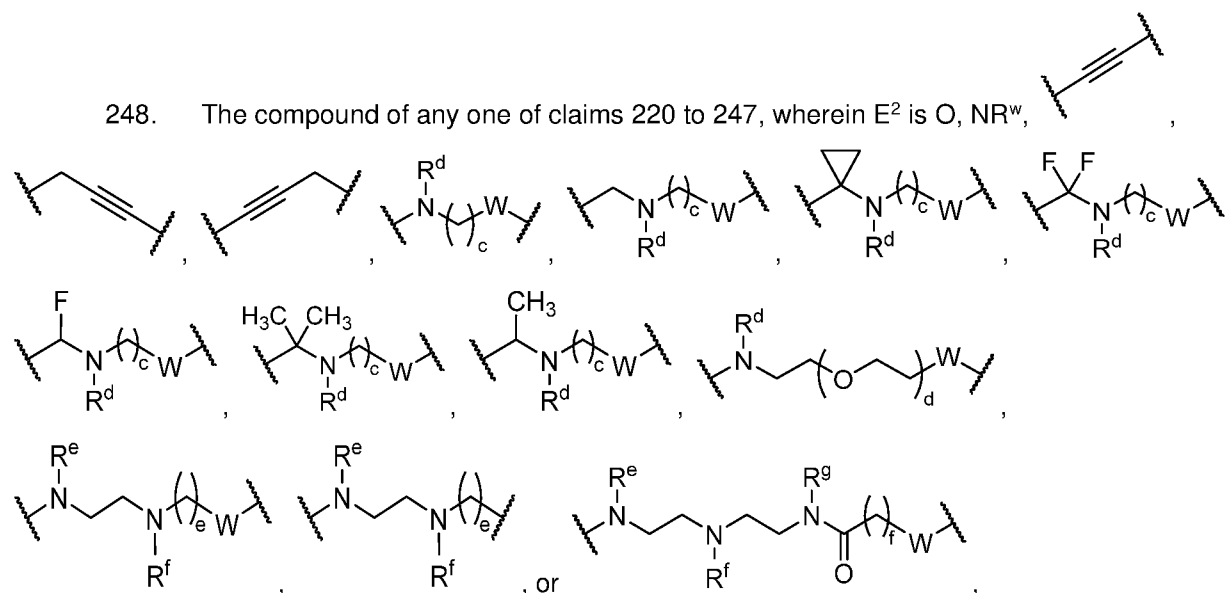




245. The compound of any one of claims 240 to 244, wherein R^a is H or methyl.

246. The compound of claim 245, wherein R^a is H.

247. The compound of claim 245, wherein R^a is methyl.



wherein

c is 0, 1, 2, 3, 4, 5, 6, 7, or 8;

d is 0, 1, 2, or 3;

e is 0, 1, 2, 3, 4, 5, or 6;

f is 0, 1, 2, 3, or 4;

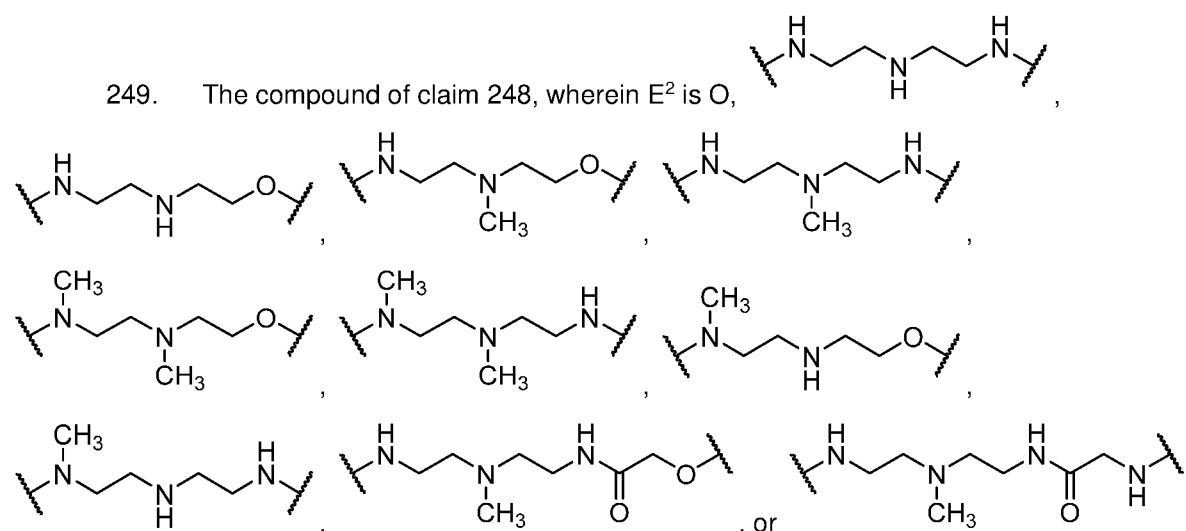
R^d is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl;

R^e is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl;

R^f is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl;

R^g is H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, or optionally substituted C₃-C₆ carbocyclyl; and

W is O or NR^w, wherein R^w is H or optionally substituted C₁-C₆ alkyl.



250. The compound of any one of claims 220 to 249, wherein each of F¹, F², or F³ is, independently, optionally substituted C₃-C₁₀ carbocyclylene.

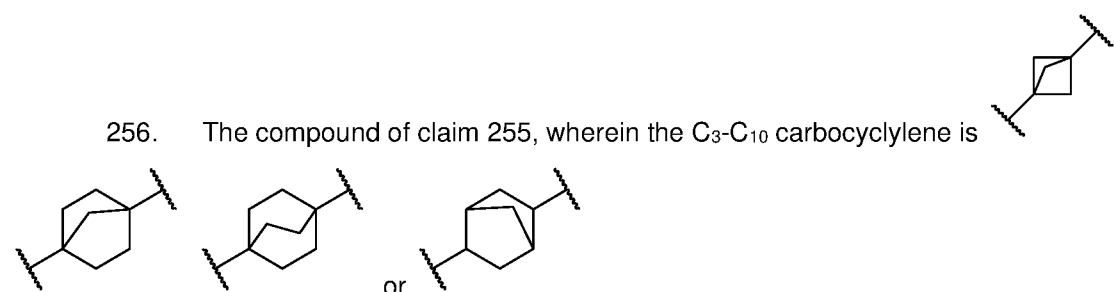
251. The compound of claim 250, wherein the C₃-C₁₀ carbocyclylene is monocyclic.

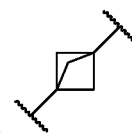
252. The compound of claim 250, wherein the C₃-C₁₀ carbocyclylene is polycyclic.

253. The compound of claim 252, wherein the C₃-C₁₀ carbocyclylene is fused.

254. The compound of claim 252, wherein the C₃-C₁₀ carbocyclylene is spirocyclic.

255. The compound of claim 252, wherein the C₃-C₁₀ carbocyclylene is bridged.

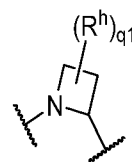




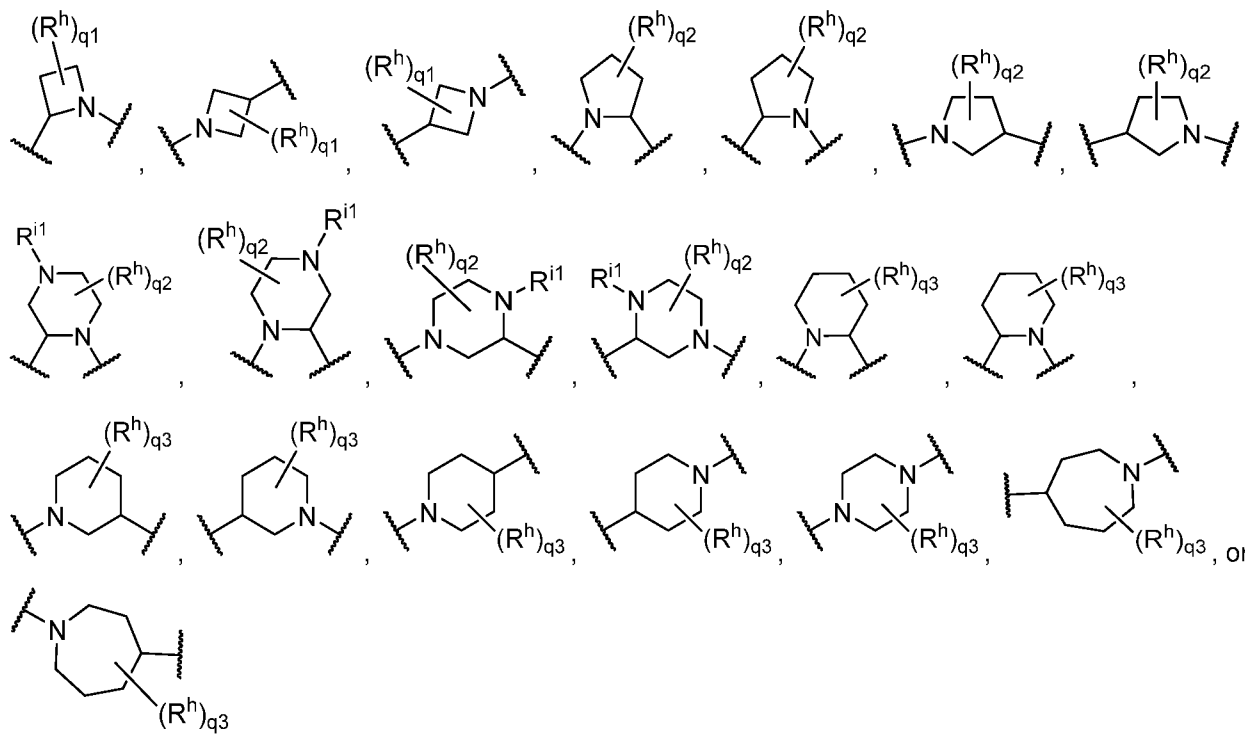
257. The compound of claim 256, wherein the C₃-C₁₀ carbocyclylene is

258. The compound of any one of claims 220 to 249, wherein each of F¹, F², or F³ is, independently, optionally substituted C₂-C₆ heterocyclylene.

259. The compound of claim 258, wherein the C₂-C₆ heterocyclylene is monocyclic.



260. The compound of claim 259, wherein the C₂-C₆ heterocyclylene is



wherein

q₁ is 0, 1, 2, 3, or 4;

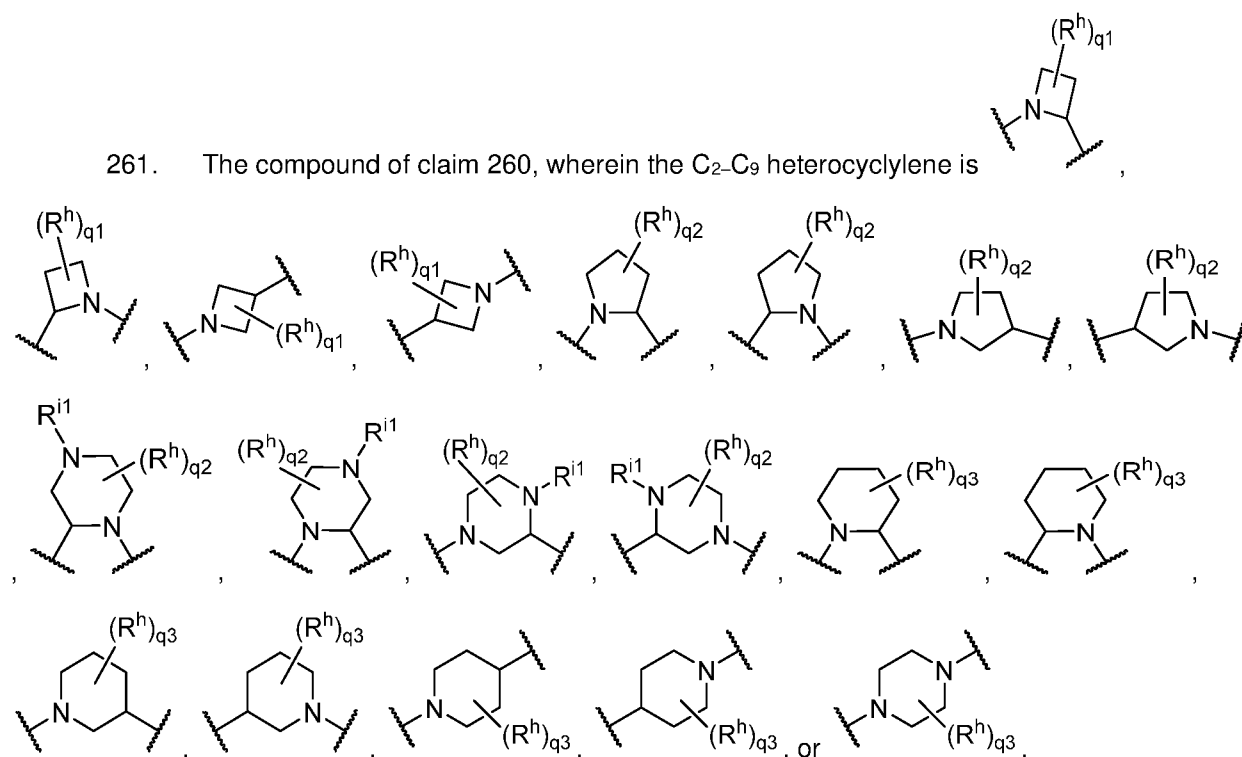
q₂ is 0, 1, 2, 3, 4, 5, or 6;

q₃ is 0, 1, 2, 3, 4, 5, 6, 7, or 8;

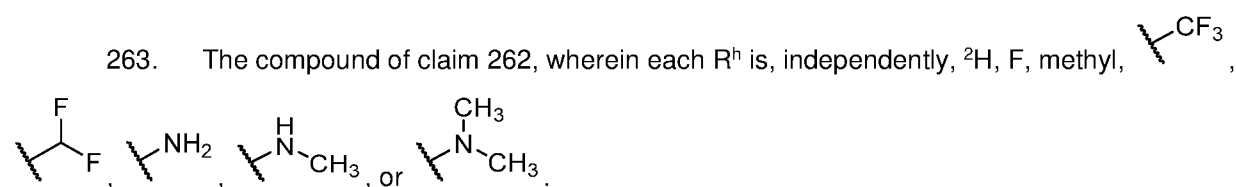
each R^h is, independently, ²H, halogen, optionally substituted C₁-C₆ alkyl, ORⁱ², or NRⁱ³Rⁱ⁴; or two R^h groups, together with the carbon atom to which each is attached, combine to form optionally substituted C₃-C₁₀ carbocyclyl or optionally substituted C₂-C₉ heterocyclyl; or two R^h groups, together with the carbon atoms to which each is attached, combine to form optionally substituted C₃-C₁₀ carbocyclyl or optionally substituted C₂-C₉ heterocyclyl;

Rⁱ¹ is H or optionally substituted C₁-C₆ alkyl;

R^{i2} is H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, or optionally substituted C_3 - C_6 carbocyclyl;



262. The compound of claim 260 or 261, wherein each R^h is, independently, ^2H , halogen, cyano, optionally substituted C_1 - C_6 alkyl, OR^{i2} , or $NR^{i3}R^{i4}$.



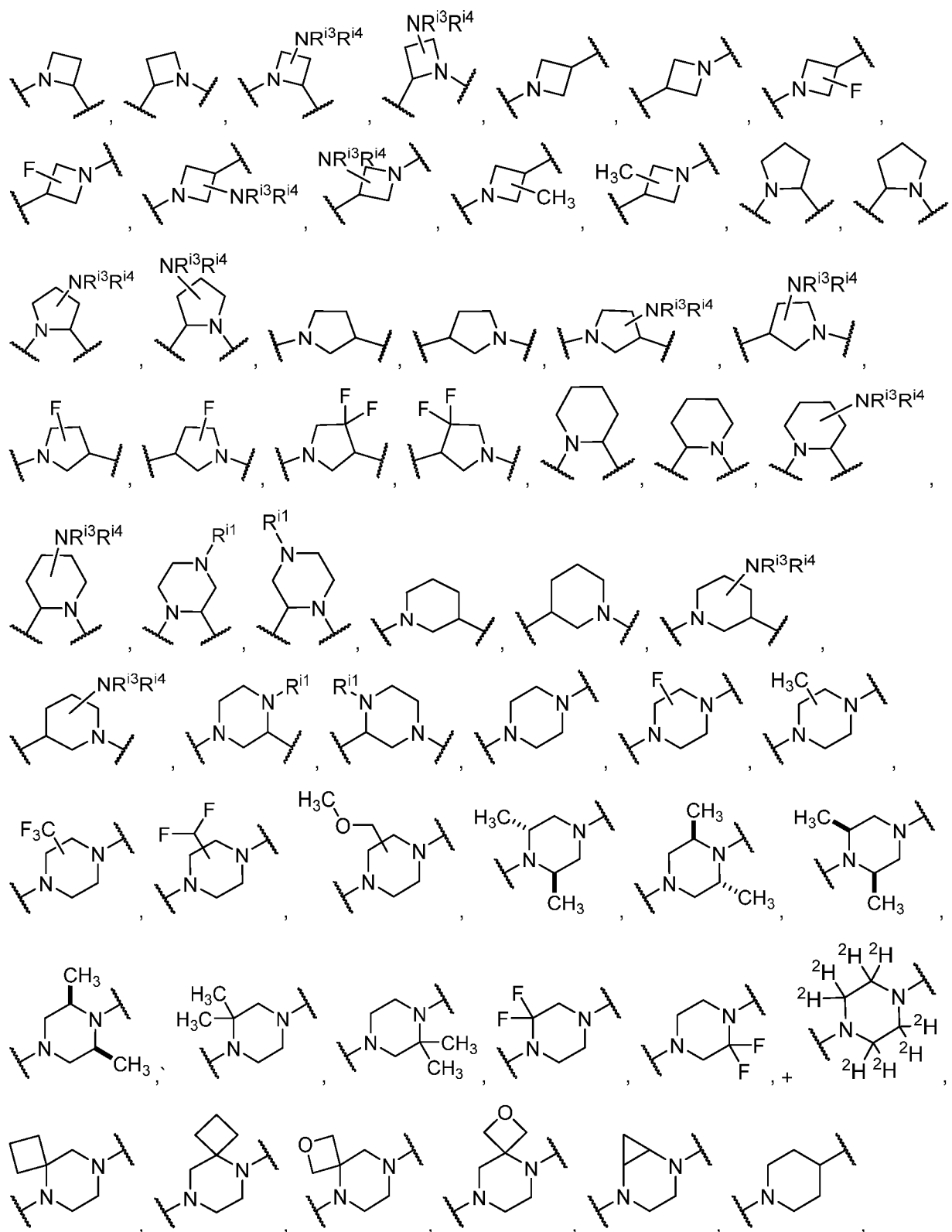
264. The compound of claim 263, wherein each R^h is, independently, F, methyl, or $NR^{i3}R^{i4}$.

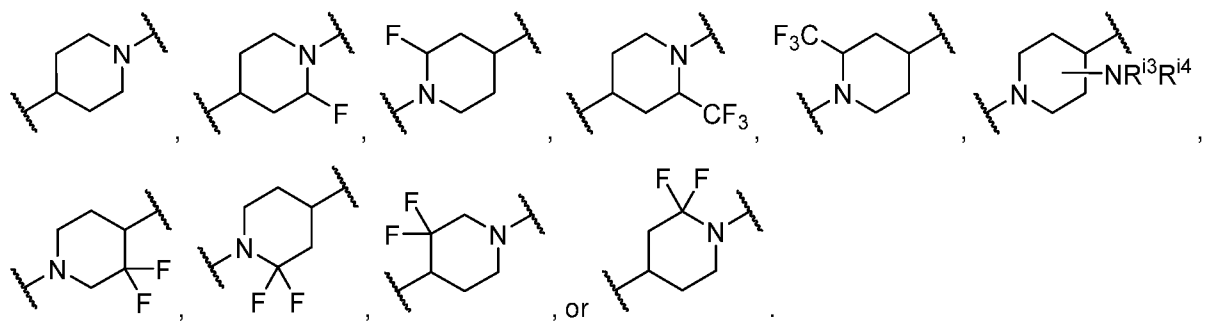
265. The compound of any one of claims 260 to 264, wherein q_1 is 0, 1, or 2.

266. The compound of any one of claims 260 to 265, wherein q_2 is 0, 1, or 2.

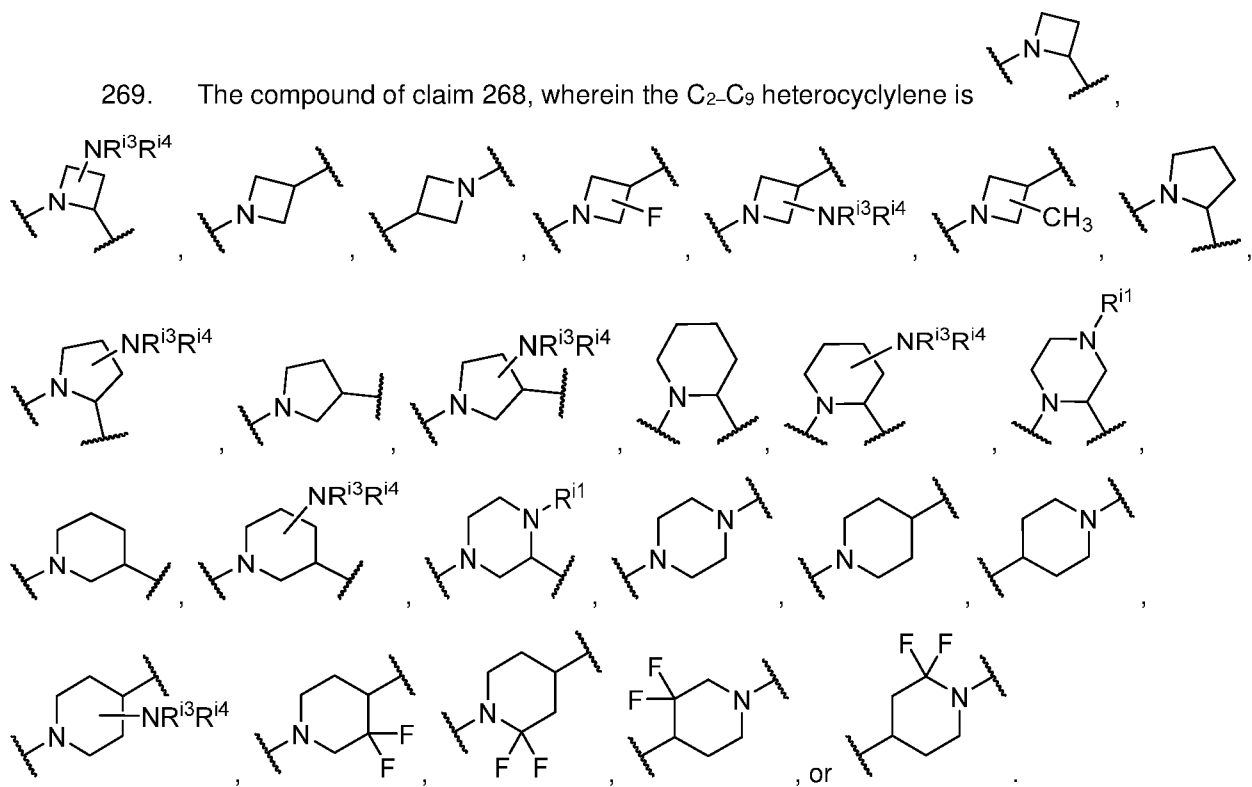
267. The compound of any one of claims 260 to 264, wherein q_3 is 0, 1, or 2.

268. The compound of any one of claims 260 to 267, wherein the C₂-C₉ heterocyclylene is

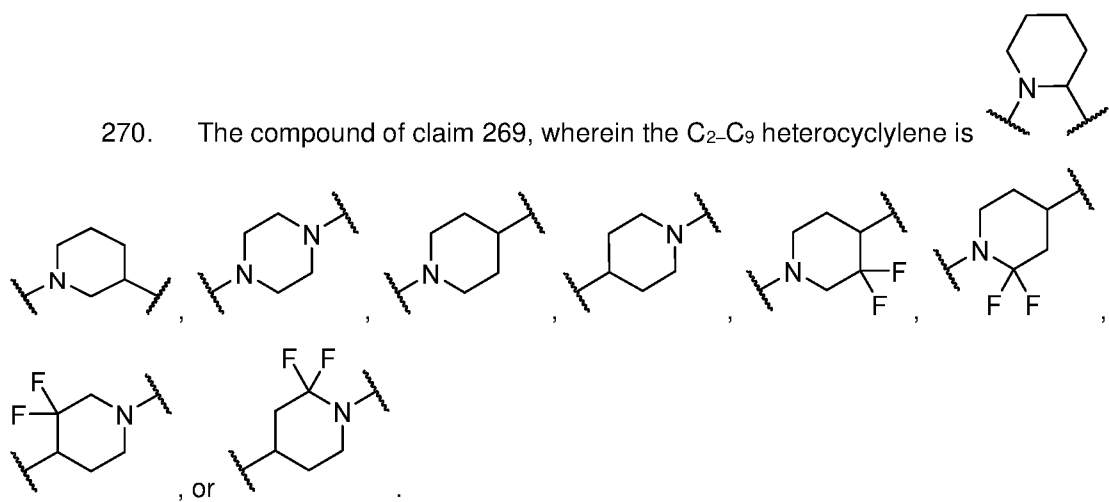




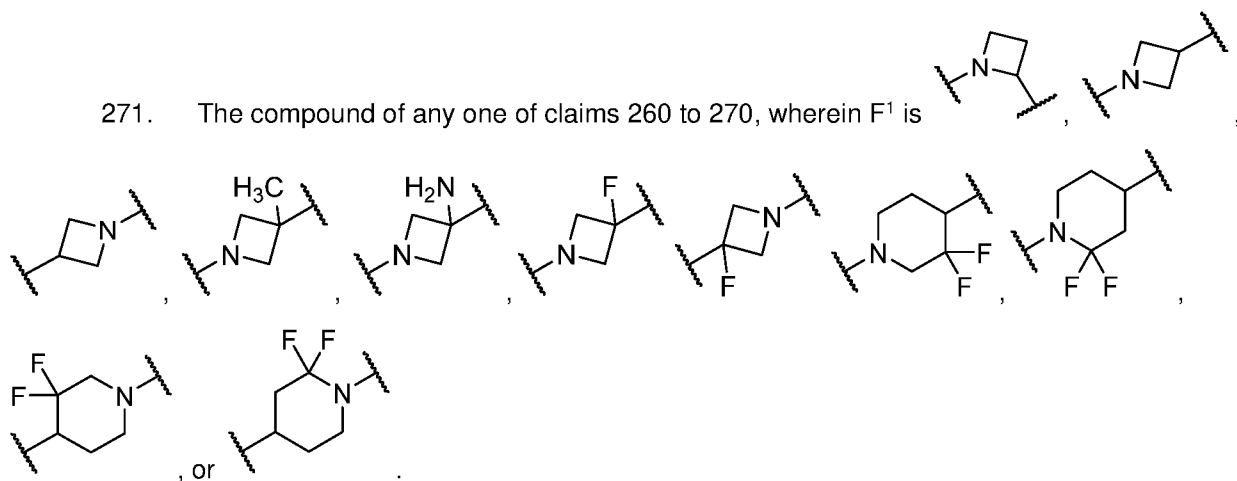
269. The compound of claim 268, wherein the $\text{C}_2\text{-C}_9$ heterocyclylene is



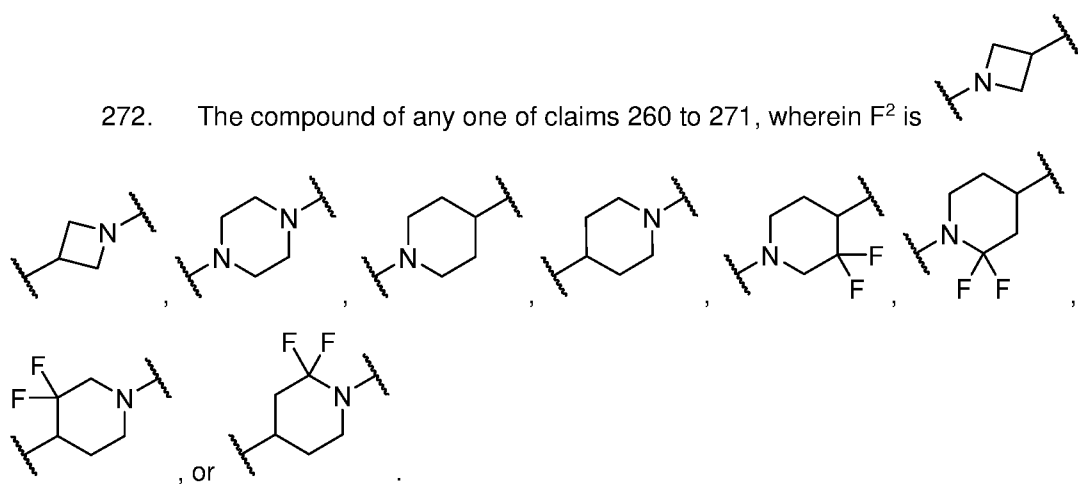
270. The compound of claim 269, wherein the $\text{C}_2\text{-C}_9$ heterocyclylene is



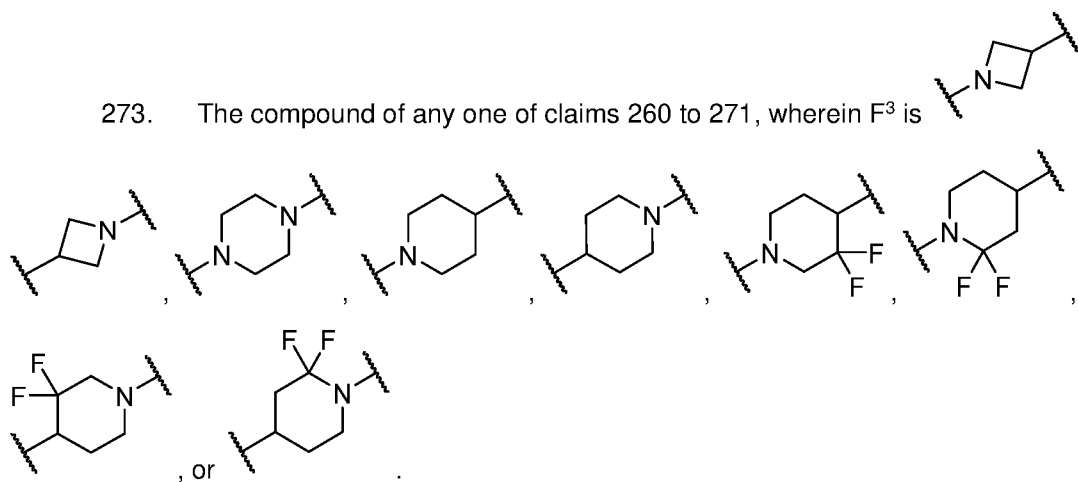
271. The compound of any one of claims 260 to 270, wherein F^1 is



272. The compound of any one of claims 260 to 271, wherein F^2 is



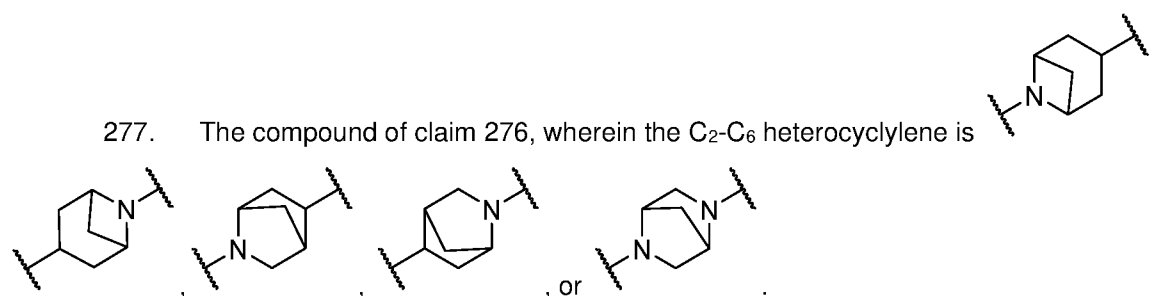
273. The compound of any one of claims 260 to 271, wherein F^3 is



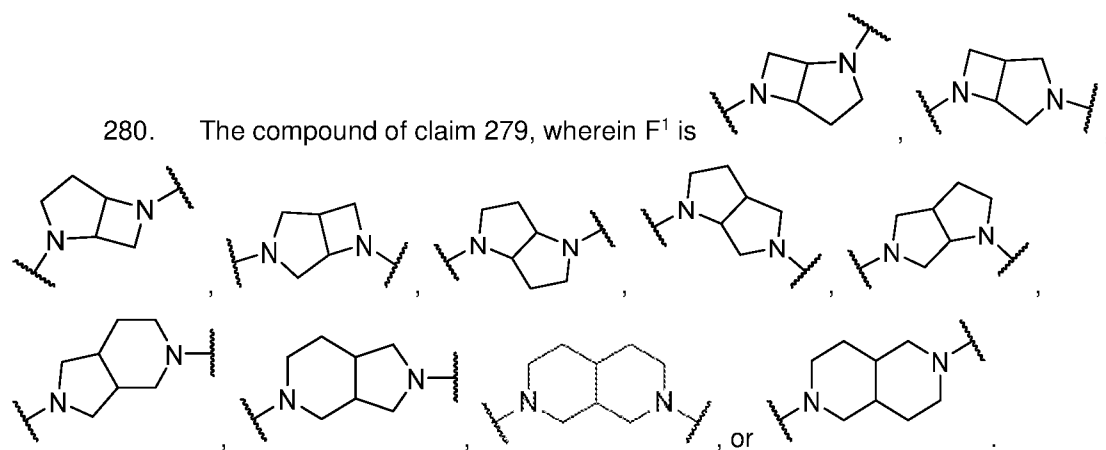
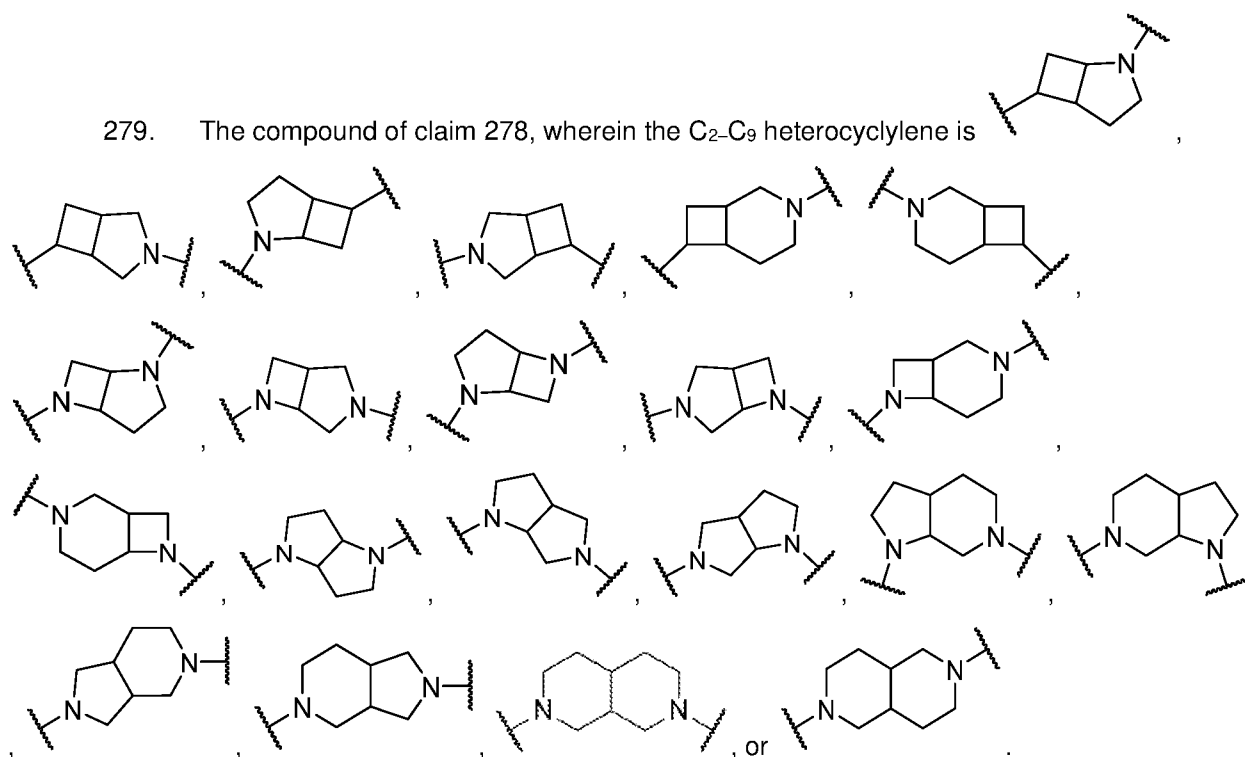
274. The compound of claim 258, wherein the C_2 - C_6 heterocyclylene is polycyclic.

275. The compound of claim 274, wherein the C_2 - C_6 heterocyclylene is bicyclic.

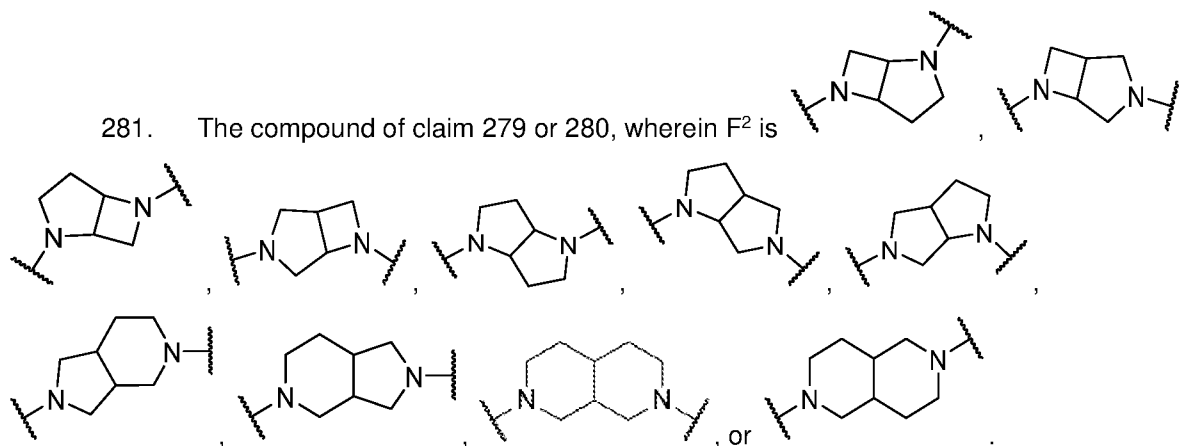
276. The compound of claim 274 or 275, wherein the C_2 - C_6 heterocyclylene is bridged.



278. The compound of claim 274 or 275, wherein the C₂-C₆ heterocyclylene is fused.

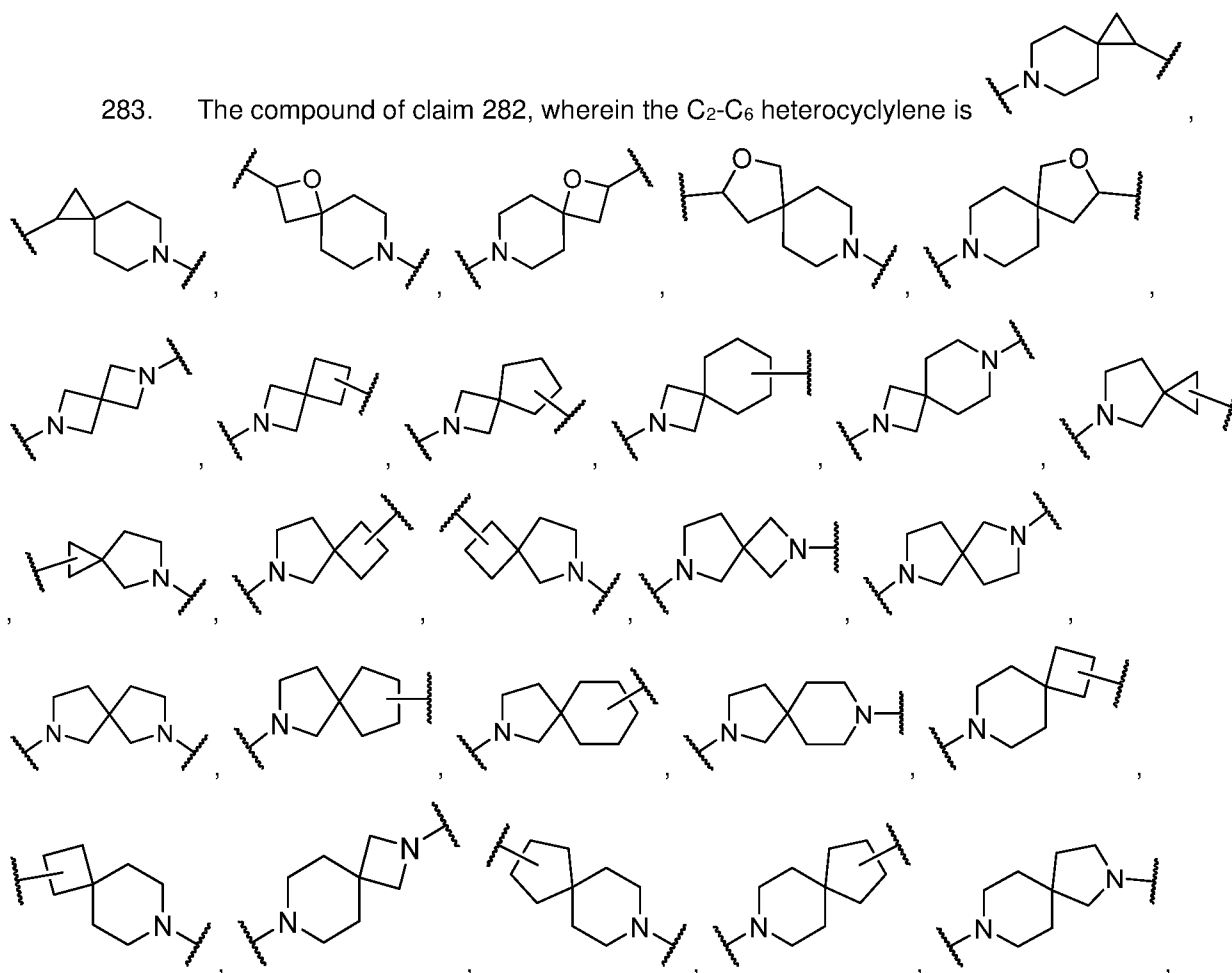


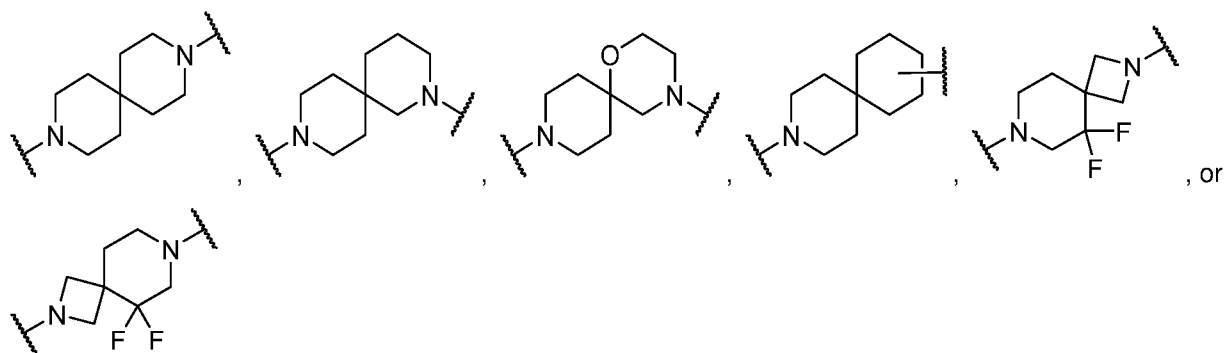
281. The compound of claim 279 or 280, wherein F² is



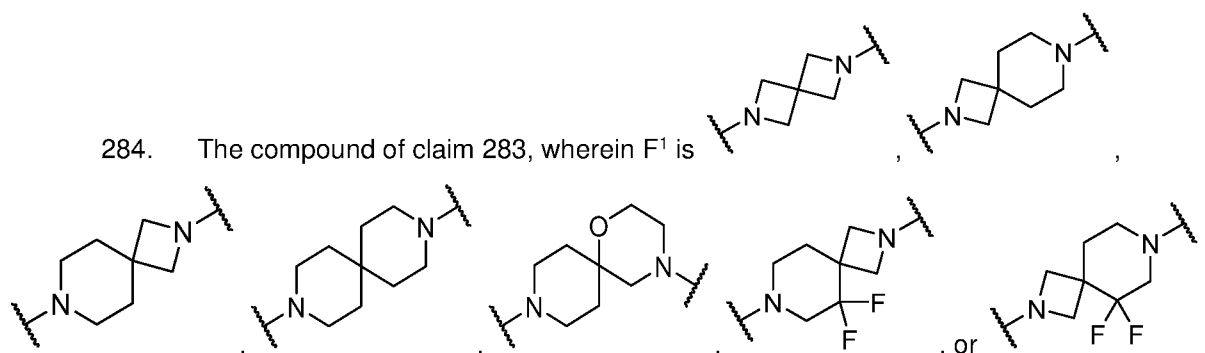
282. The compound of claim 274 or 275, wherein the C₂-C₆ heterocyclene is spirocyclic.

283. The compound of claim 282, wherein the C₂-C₆ heterocyclene is

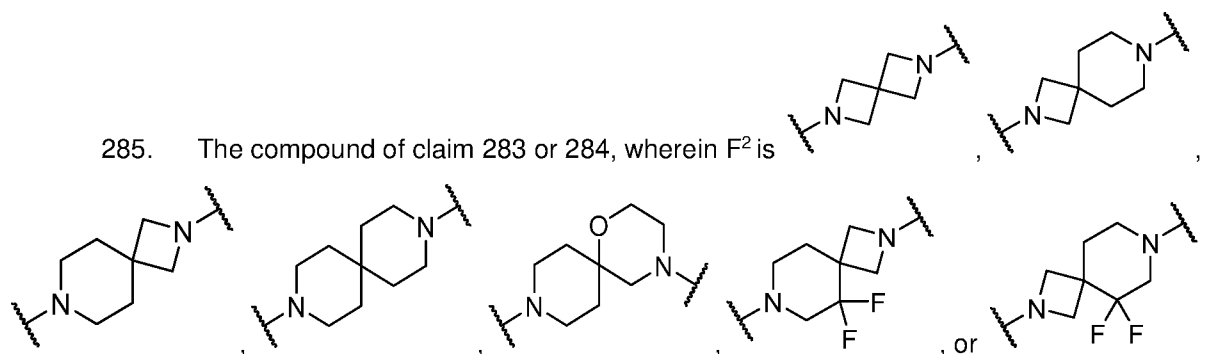




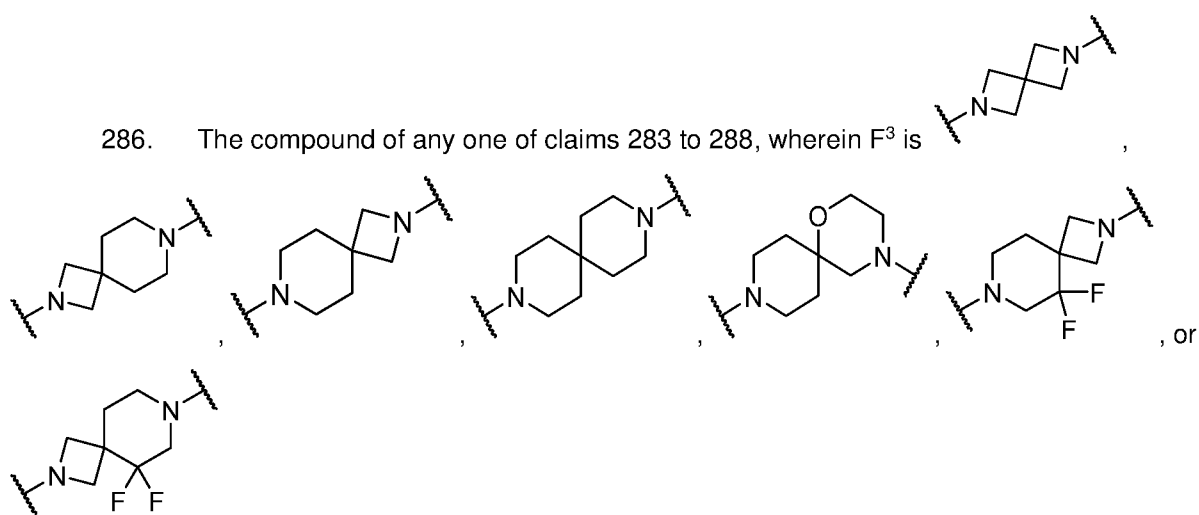
284. The compound of claim 283, wherein F^1 is



285. The compound of claim 283 or 284, wherein F^2 is

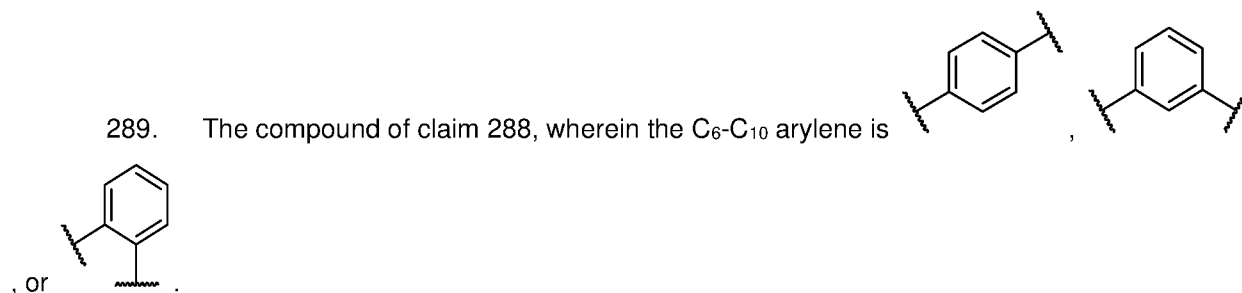


286. The compound of any one of claims 283 to 288, wherein F^3 is

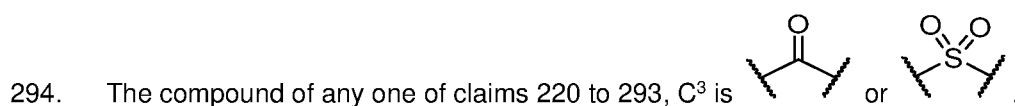
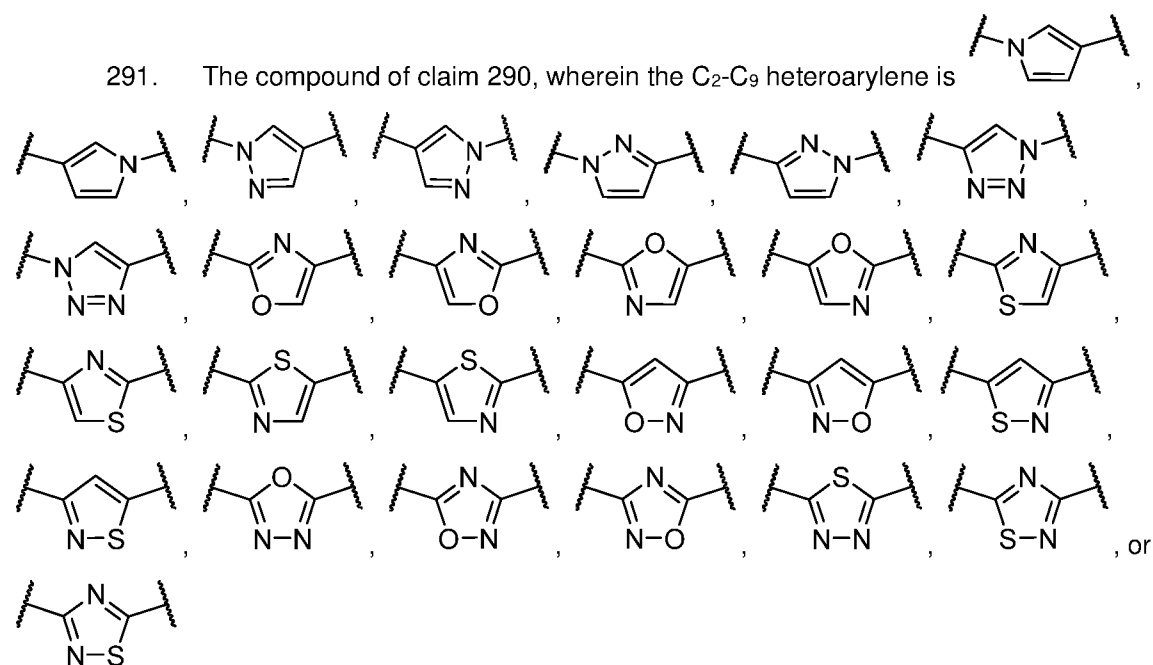


287. The compound of any one of claims 258 to 286 wherein the C_2 - C_9 heterocyclylene comprises a quaternary amine.

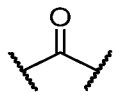
288. The compound of any one of claims 220 to 249, wherein each of F¹, F², or F³ is, independently, optionally substituted C₆-C₁₀ arylene.



290. The compound of any one of claims 220 to 249, wherein each of F¹, F², or F³ is, independently, optionally substituted C₂-C₉ heteroarylene.



295. The compound of claim 294, wherein C³ is



296. The compound of any one of claims 220 to 295, wherein m is 1.

297. The compound of any one of claims 220 to 295, wherein m is 0.

298. The compound of any one of claims 220 to 297, wherein p is 1.

299. The compound of any one of claims 220 to 297, wherein p is 0.

300. The compound of any one of claims 220 to 299, wherein o₁ is 1.

301. The compound of any one of claims 220 to 299, wherein o₁ is 0.

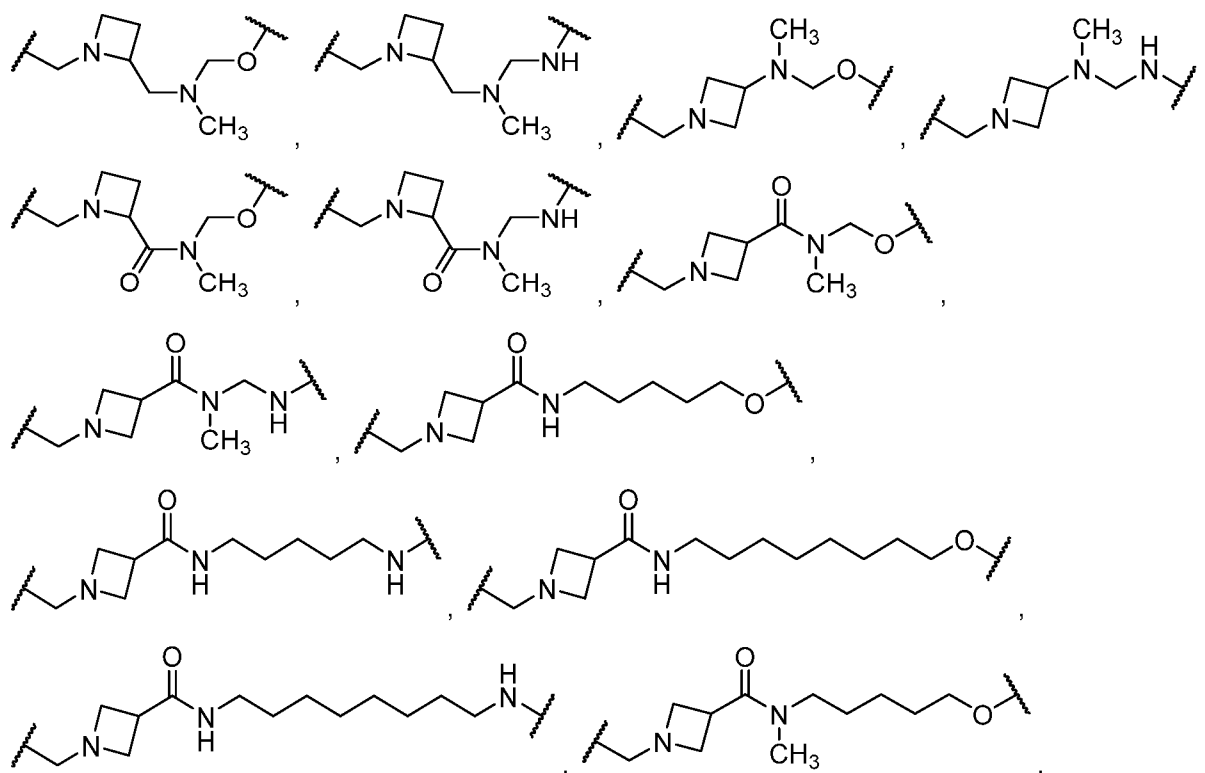
302. The compound of any one of claims 220 to 301, wherein o₂ is 1.

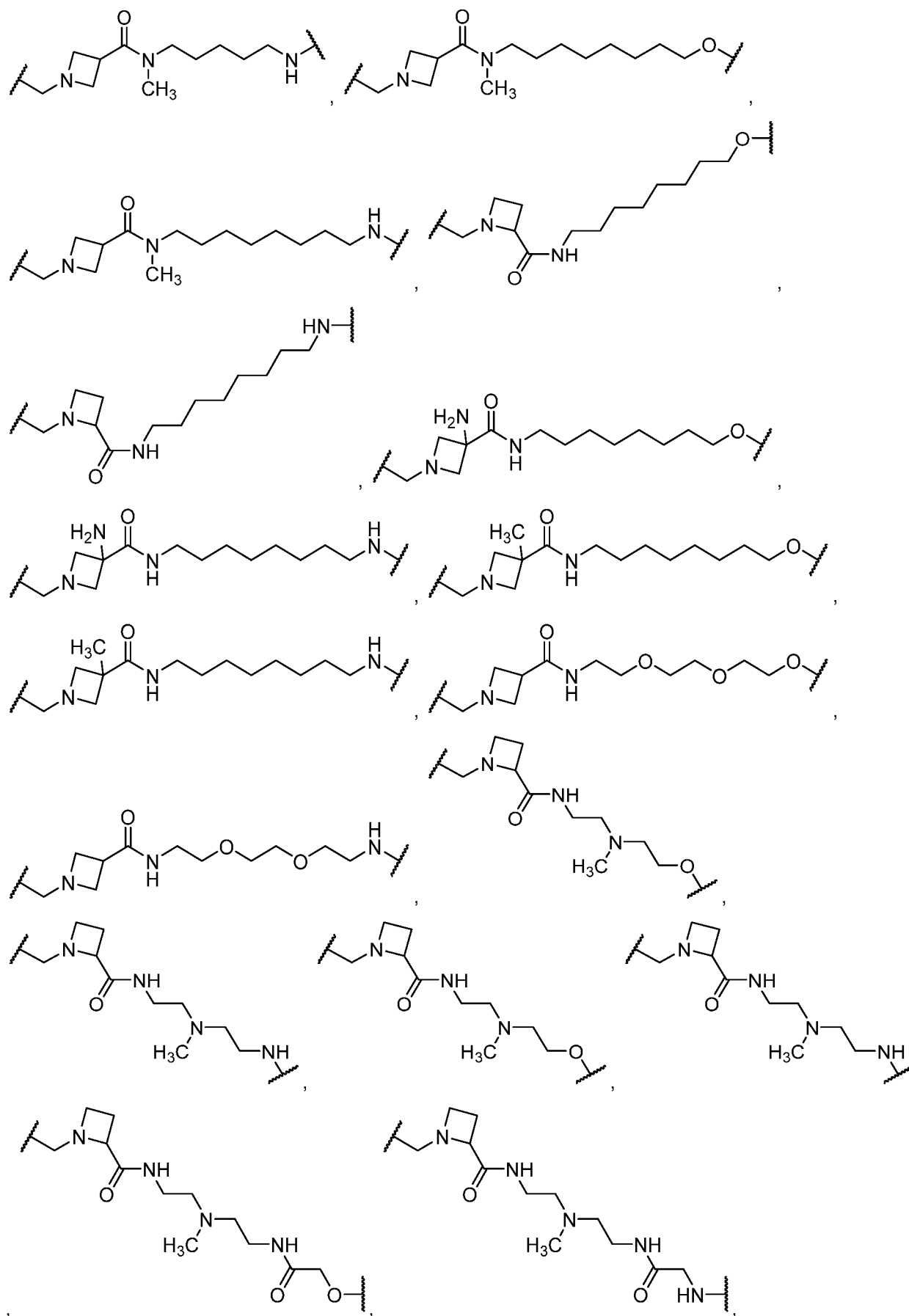
303. The compound of any one of claims 220 to 301, wherein o₂ is 0.

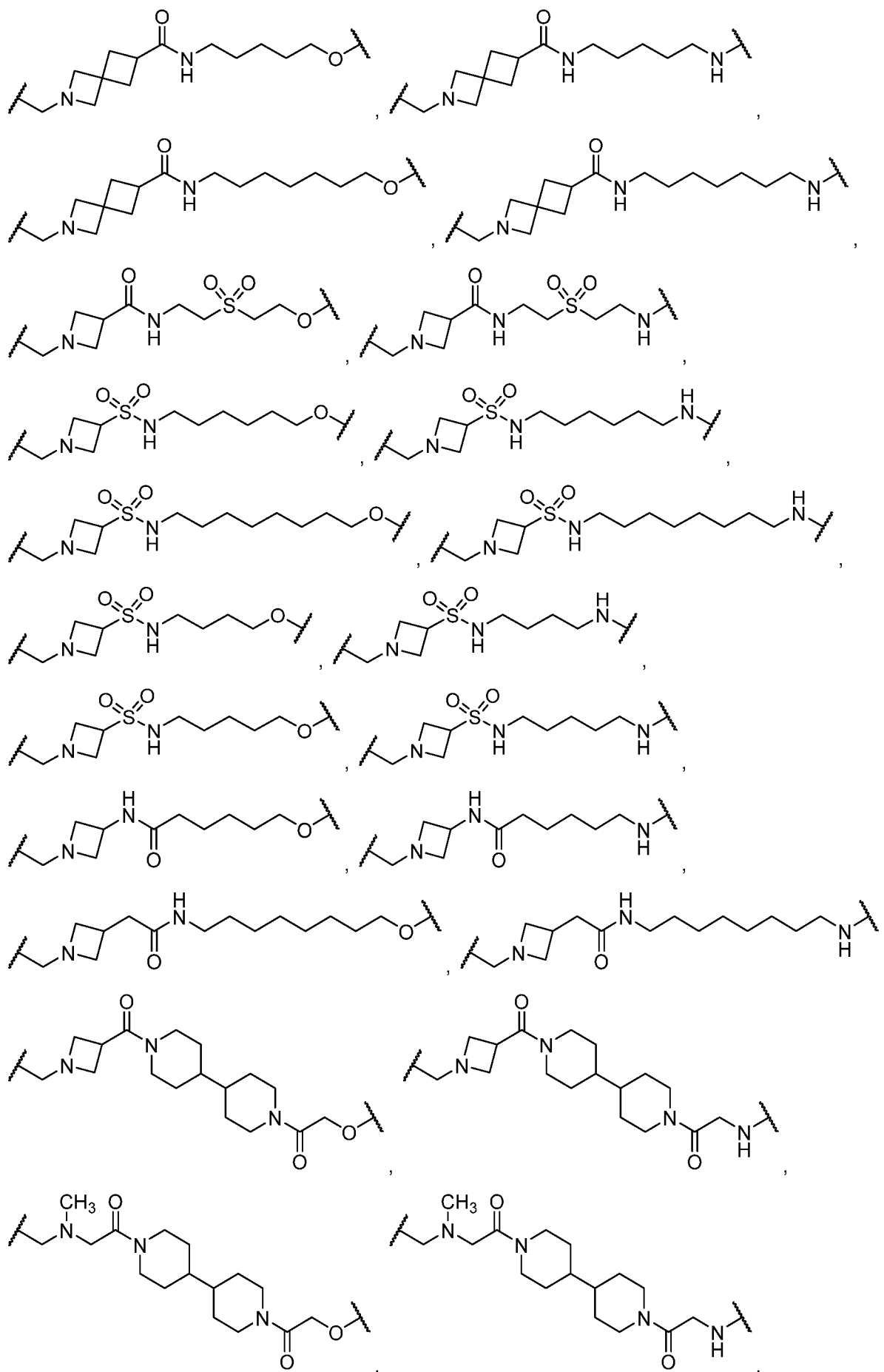
304. The compound of any one of claims 220 to 303, wherein n is 1.

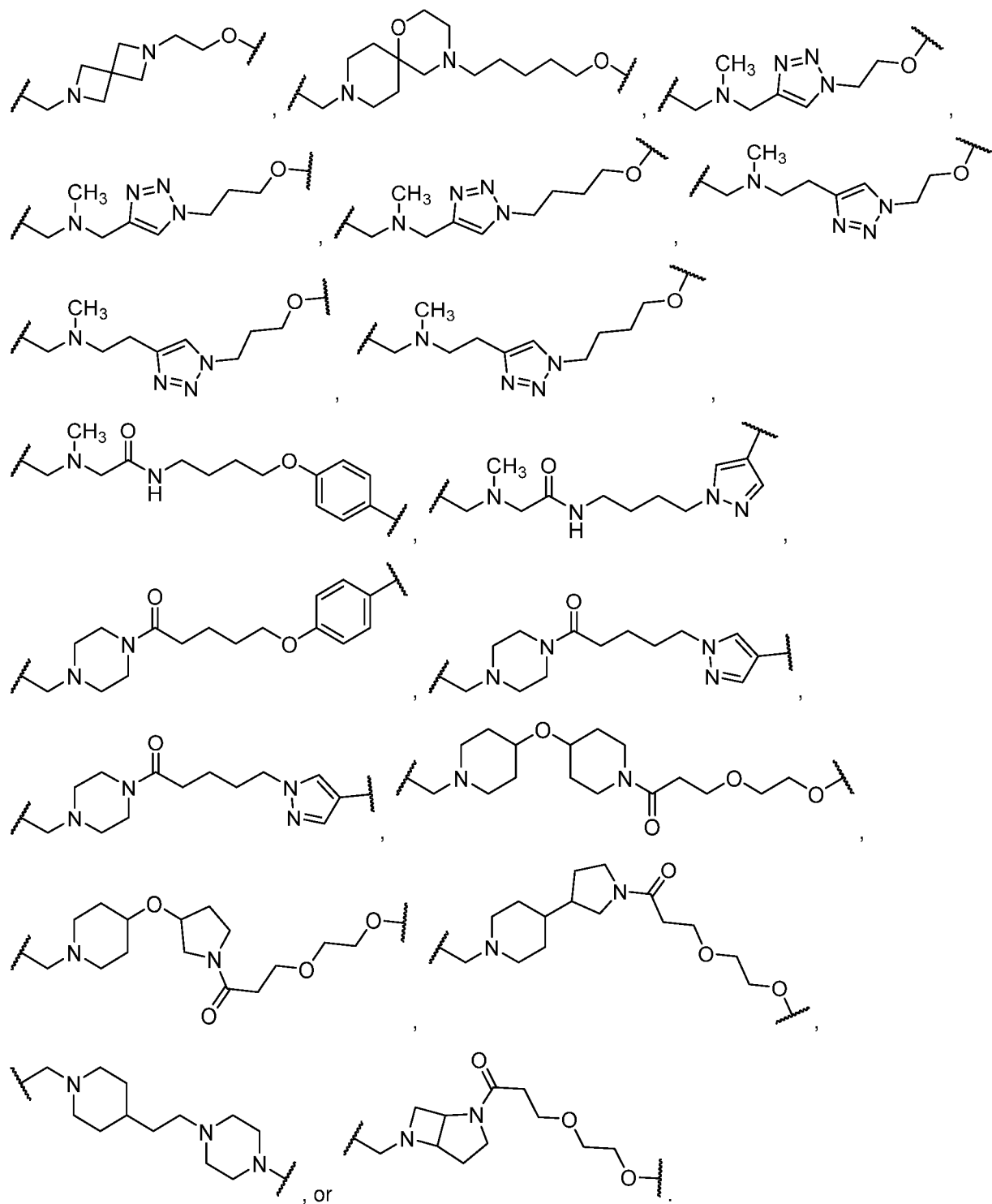
305. The compound of any one of claims 220 to 303, wherein n is 0.

306. The compound of any one of claims 220 to 305, wherein the linker has the structure of

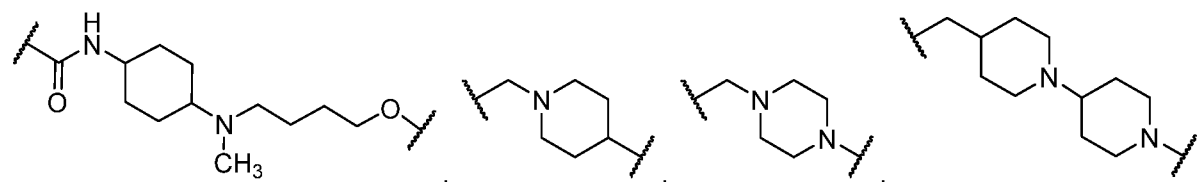


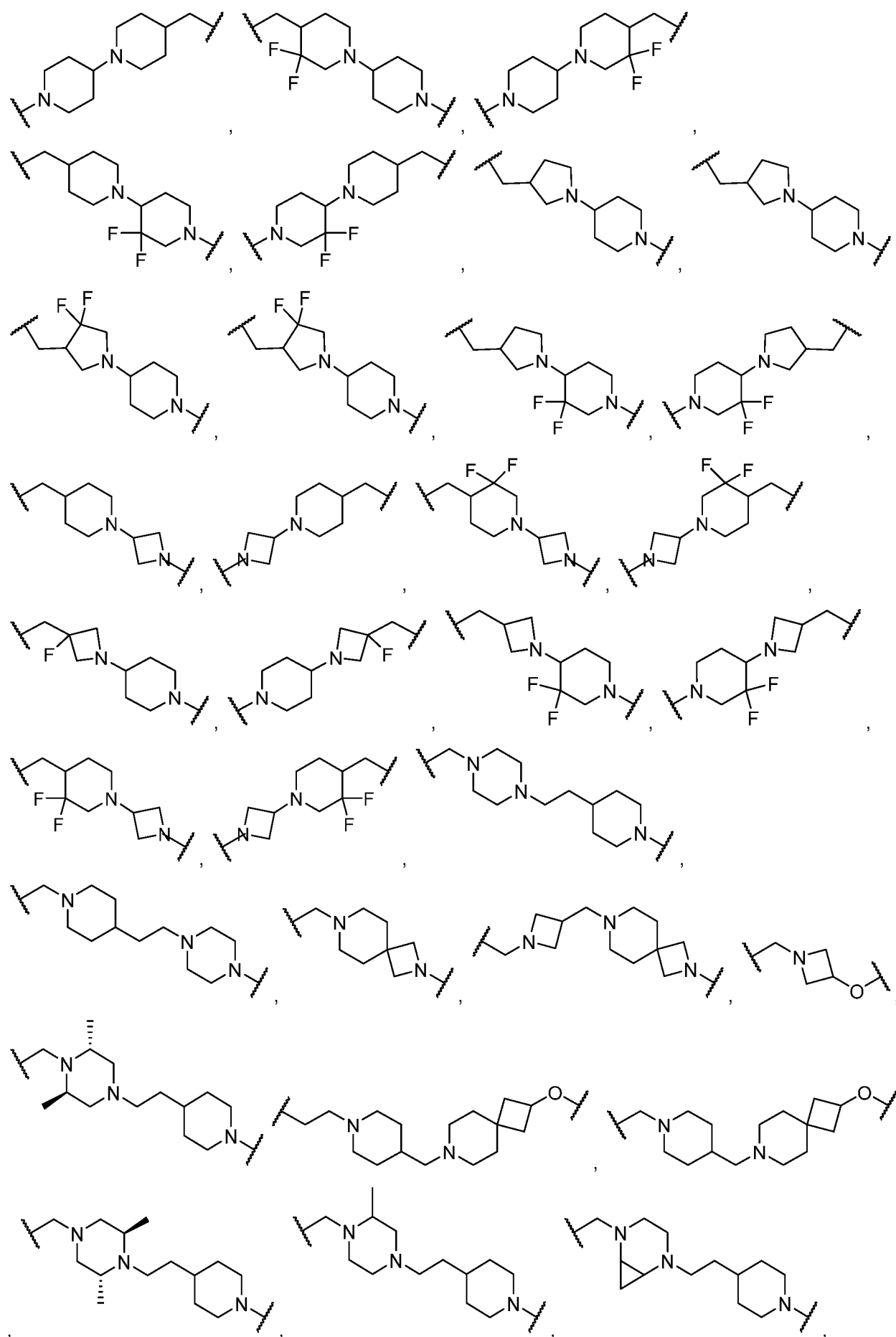


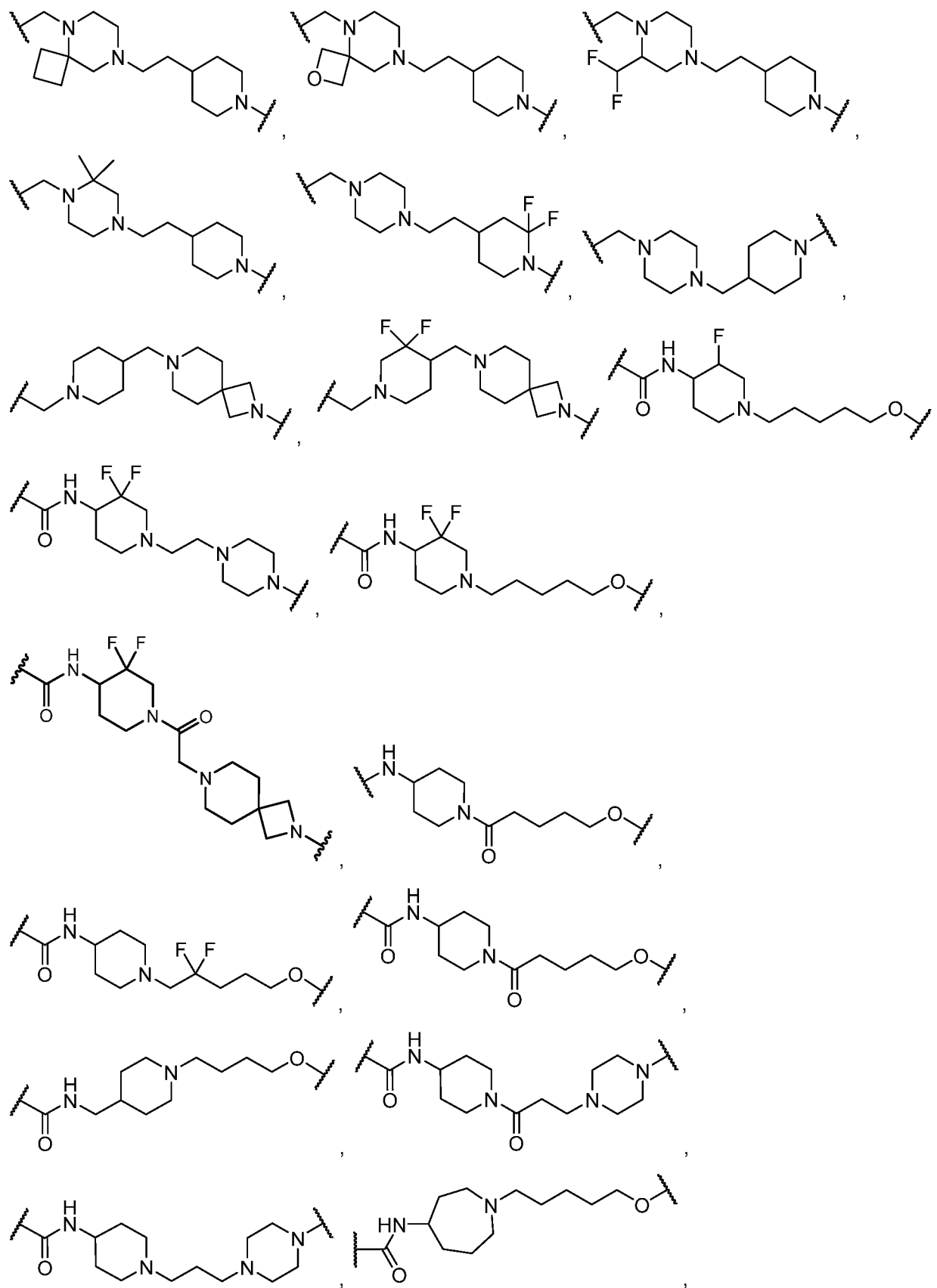


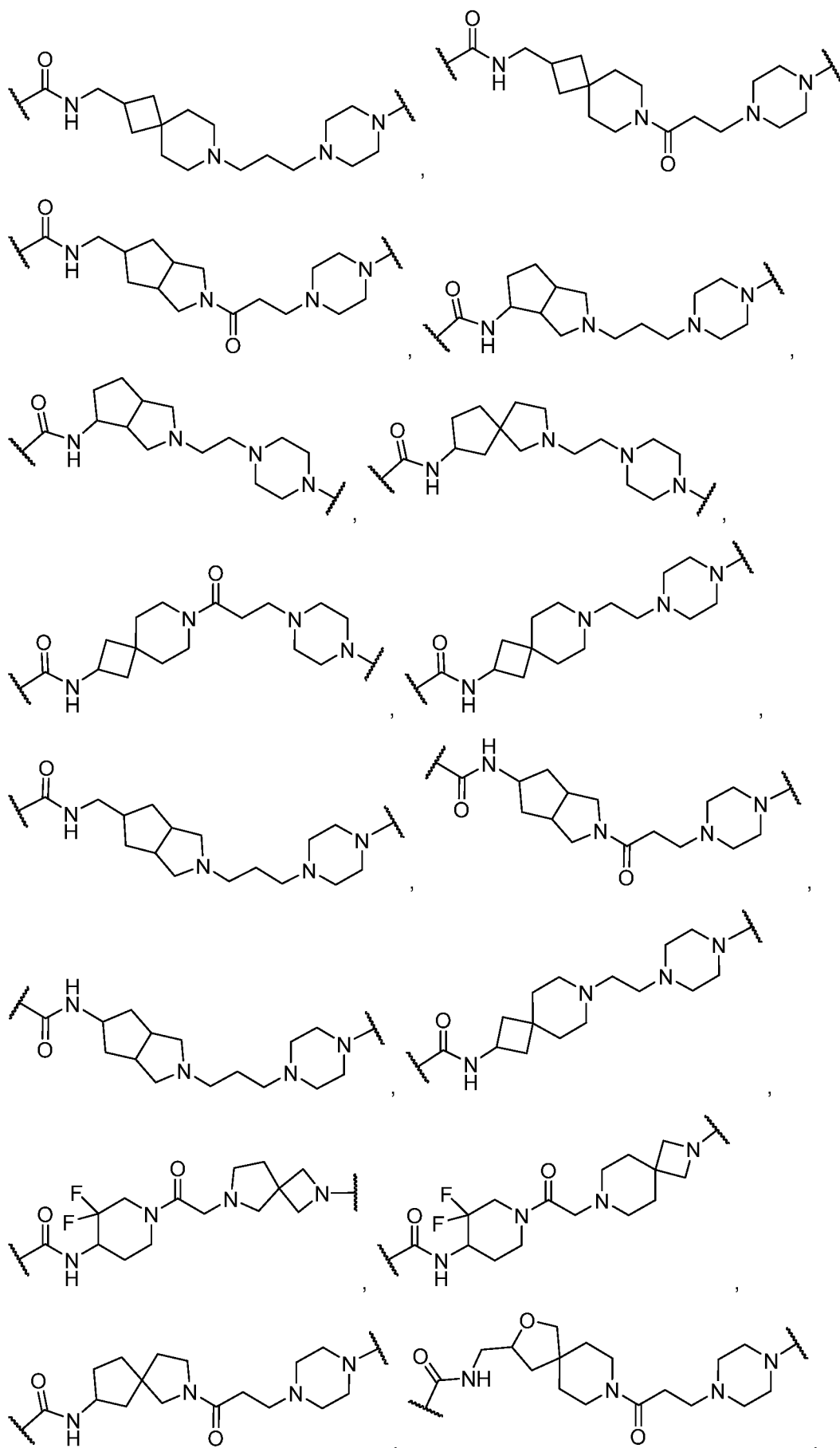


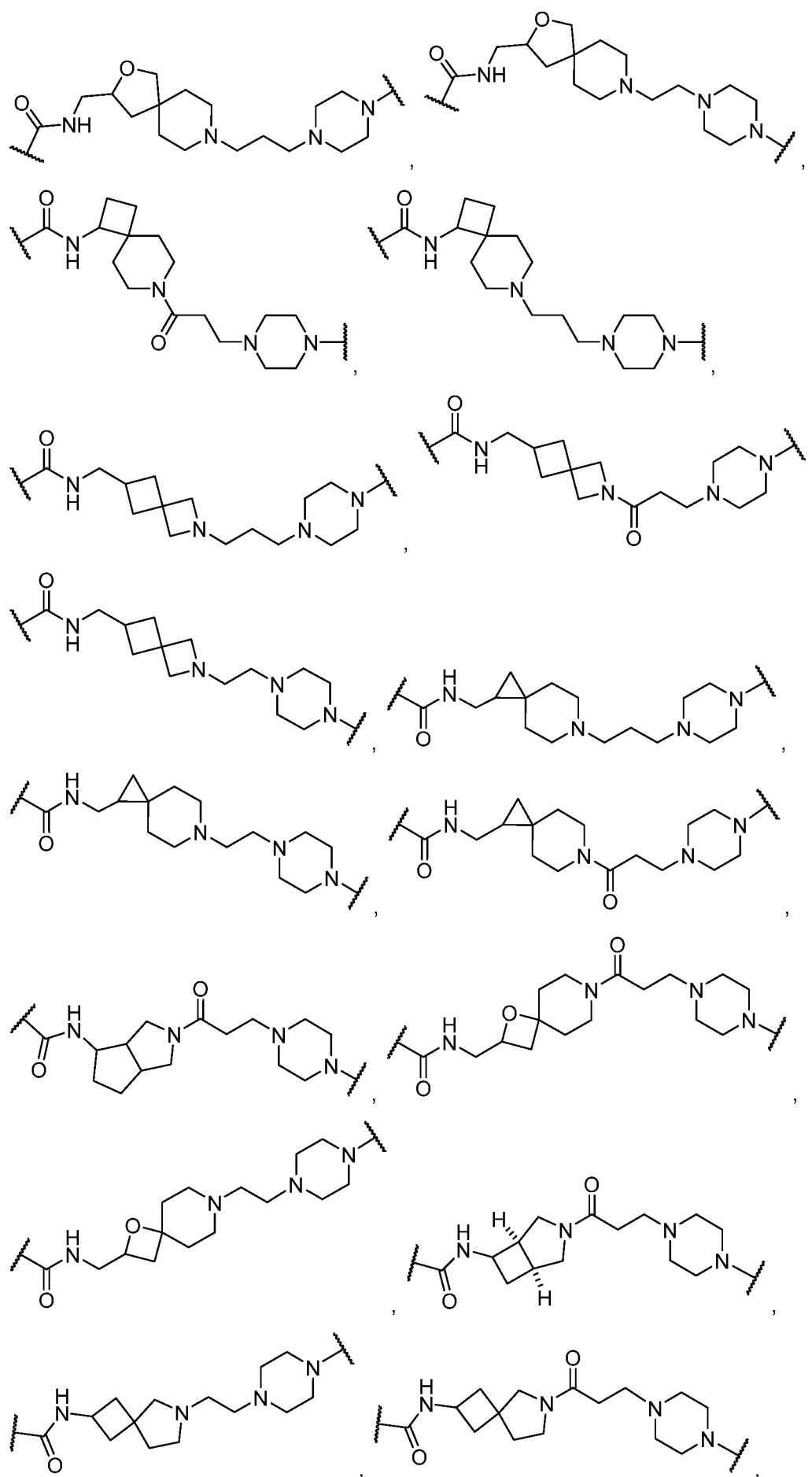
307. The compound of any one of claims 220 to 305, wherein the linker has the structure of

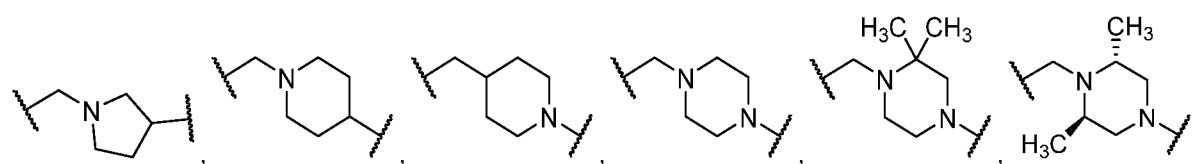
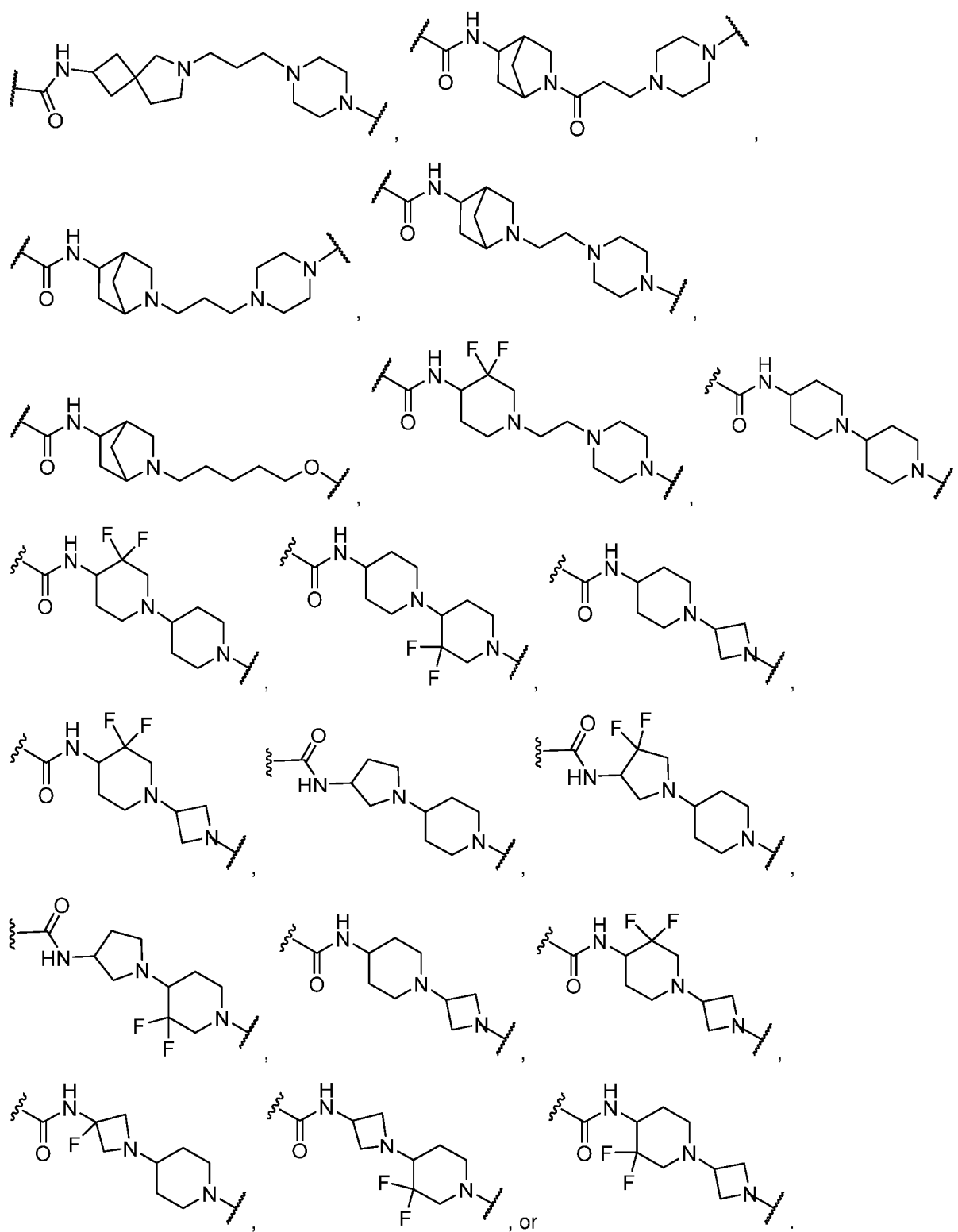


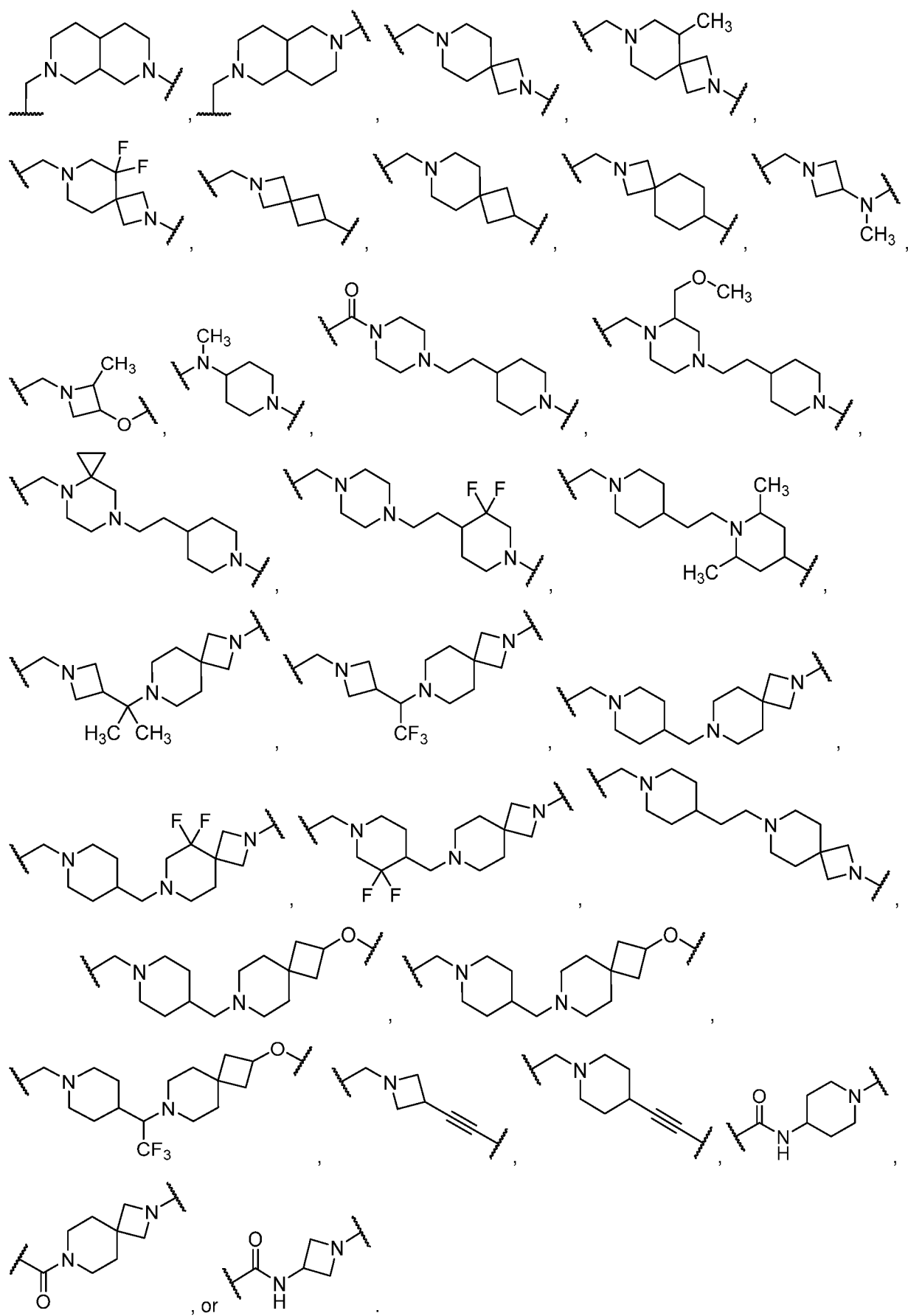






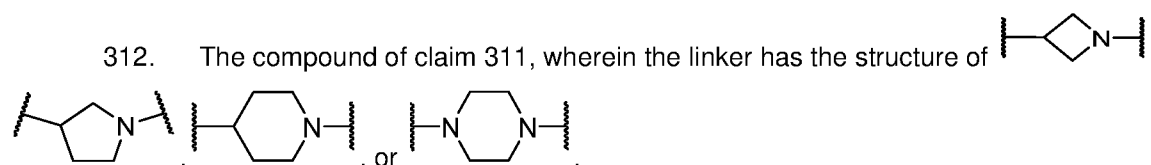
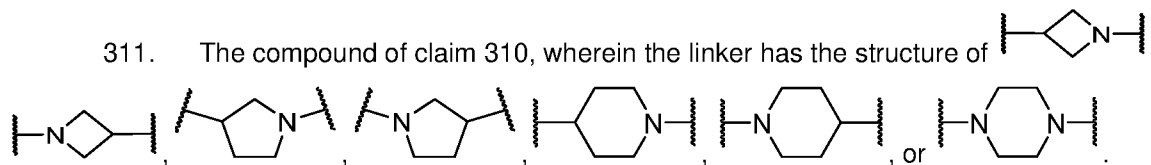






309. The compound of any one of claims 2 to 198, wherein the linker is optionally substituted C₃-C₁₀ carbocyclylene, optionally substituted C₂-₁₀ heterocyclylene, optionally substituted C₆-C₁₀ arylene, or optionally substituted C₂-C₉ heteroarylene.

310. The compound of claim 309, wherein the linker is optionally substituted C₂-₁₀ heterocyclylene



313. The compound of any one of claims 2 to 198, wherein the linker is absent.

314. The compound of claim 1, wherein the compound has the structure of any one of compounds B1-B6 in Table 1, or a pharmaceutically acceptable salt thereof.

315. The compound of any one of claims 2 to 313, wherein the compound has the structure of any one of compounds D1-D15 in Table 2A, or a pharmaceutically acceptable salt thereof.

316. The compound of any one of claims 2 to 313, wherein the compound has the structure of any one of compounds D16-D90 in Table 2B, or a pharmaceutically acceptable salt thereof.

317. The compound of any one of claims 2 to 313, wherein the compound has the structure of any one of compounds D91-D220 in Table 2C, or a pharmaceutically acceptable salt thereof.

318. A pharmaceutical composition comprising the compound of any one of claims 1 to 317 and a pharmaceutically acceptable excipient.

319. A method of inhibiting the level of BRD9 in a cell, the method involving contacting the cell with an effective amount of a compound of any one of claims 1 to 317, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 318.

320. A method of inhibiting the activity of BRD9 in a cell, the method involving contacting the cell with an effective amount of a compound of any one of claims 1 to 317, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 318.

321. The method of claim 319 or 320, wherein the cell is a cancer cell.

322. The method of claim 321, wherein the cancer is a malignant, rhabdoid tumor, a CD8+ T-cell lymphoma, endometrial carcinoma, ovarian carcinoma, bladder cancer, stomach cancer, pancreatic cancer, esophageal cancer, prostate cancer, renal cell carcinoma, melanoma, colorectal cancer, a sarcoma, non-small cell lung cancer, stomach cancer, or breast cancer.

323. The method of claim 322, wherein the cancer is a sarcoma.

324. The method of claim 323, wherein the sarcoma is a soft tissue sarcoma, synovial sarcoma, Ewing's sarcoma, osteosarcoma, rhabdomyosarcoma, adult fibrosarcoma, alveolar soft-part sarcoma, angiosarcoma, clear cell sarcoma, desmoplastic small round cell tumor, epithelioid sarcoma, fibromyxoid sarcoma, gastrointestinal stromal tumor, Kaposi sarcoma, liposarcoma, leiomyosarcoma, malignant mesenchymoma malignant peripheral nerve sheath tumors, myxofibrosarcoma, or low-grade rhabdomyosarcoma.

325. The method of claim 324, wherein the sarcoma is synovial sarcoma.

326. A method of treating a BAF complex-related disorder in a subject in need thereof, the method involving administering to the subject an effective amount of a compound of any one of claims 1 to 317, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 318.

327. A method of treating an SS18-SSX fusion protein-related disorder in a subject in need thereof, the method involving administering to the subject an effective amount of a compound of any one of claims 1 to 317, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 318.

328. A method of treating a BRD9-related disorder in a subject in need thereof, the method involving administering to the subject an effective amount of a compound of any one of claims 1 to 315, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 318.

329. The method of any one of claims 326 to 328, wherein the disorder is cancer.

330. A method of treating a cancer in a subject in need thereof, the method including administering to the subject an effective amount of a compound of any one of claims 1 to 317, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 318.

331. The method of claim 329 or 330, wherein the cancer is a malignant, rhabdoid tumor, a CD8+ T-cell lymphoma, endometrial carcinoma, ovarian carcinoma, bladder cancer, stomach cancer,

pancreatic cancer, esophageal cancer, prostate cancer, renal cell carcinoma, melanoma, colorectal cancer, a sarcoma, non-small cell lung cancer, stomach cancer, or breast cancer.

332. The method of claim 331, wherein the cancer is a sarcoma.

333. The method of claim 332, wherein the sarcoma is a soft tissue sarcoma, synovial sarcoma, Ewing's sarcoma, osteosarcoma, rhabdomyosarcoma, adult fibrosarcoma, alveolar soft-part sarcoma, angiosarcoma, clear cell sarcoma, desmoplastic small round cell tumor, epithelioid sarcoma, fibromyxoid sarcoma, gastrointestinal stromal tumor, Kaposi sarcoma, liposarcoma, leiomyosarcoma, malignant mesenchymoma malignant peripheral nerve sheath tumors, myxofibrosarcoma, or low-grade rhabdomyosarcoma.

334. The method of claim 333, wherein the sarcoma is synovial sarcoma.

335. The method of any one of claims 326 to 328, wherein the disorder is infection.

336. A method of treating infection in a subject in need thereof, the method comprising administering to the subject an effective amount of a compound of any one of claims 1 to 317, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 318.

337. The method of claim 335 or 336, wherein the infection is a viral infection.

338. The method of claim 337, wherein the viral infection is an infection with a virus of the Retroviridae family, Hepadnaviridae family, Flaviviridae family, Adenoviridae family, Herpesviridae family, Papillomaviridae family, Parvoviridae family, Polyomaviridae family, Paramyxoviridae family, or Togaviridae family.

339. The method of claim 337 or 338, wherein the viral infection is Coffin Siris, Neurofibromatosis, or Multiple Meningioma.

FIG. 1

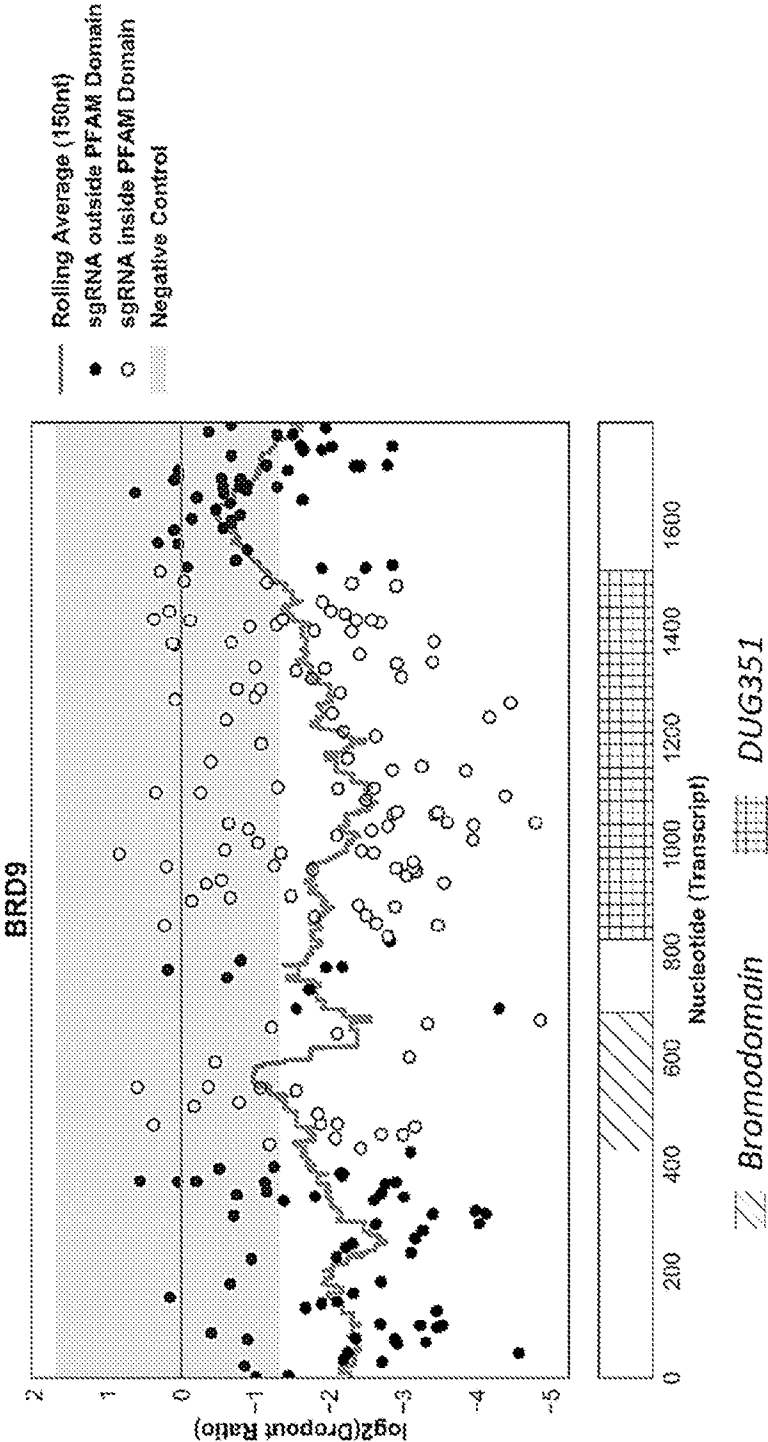
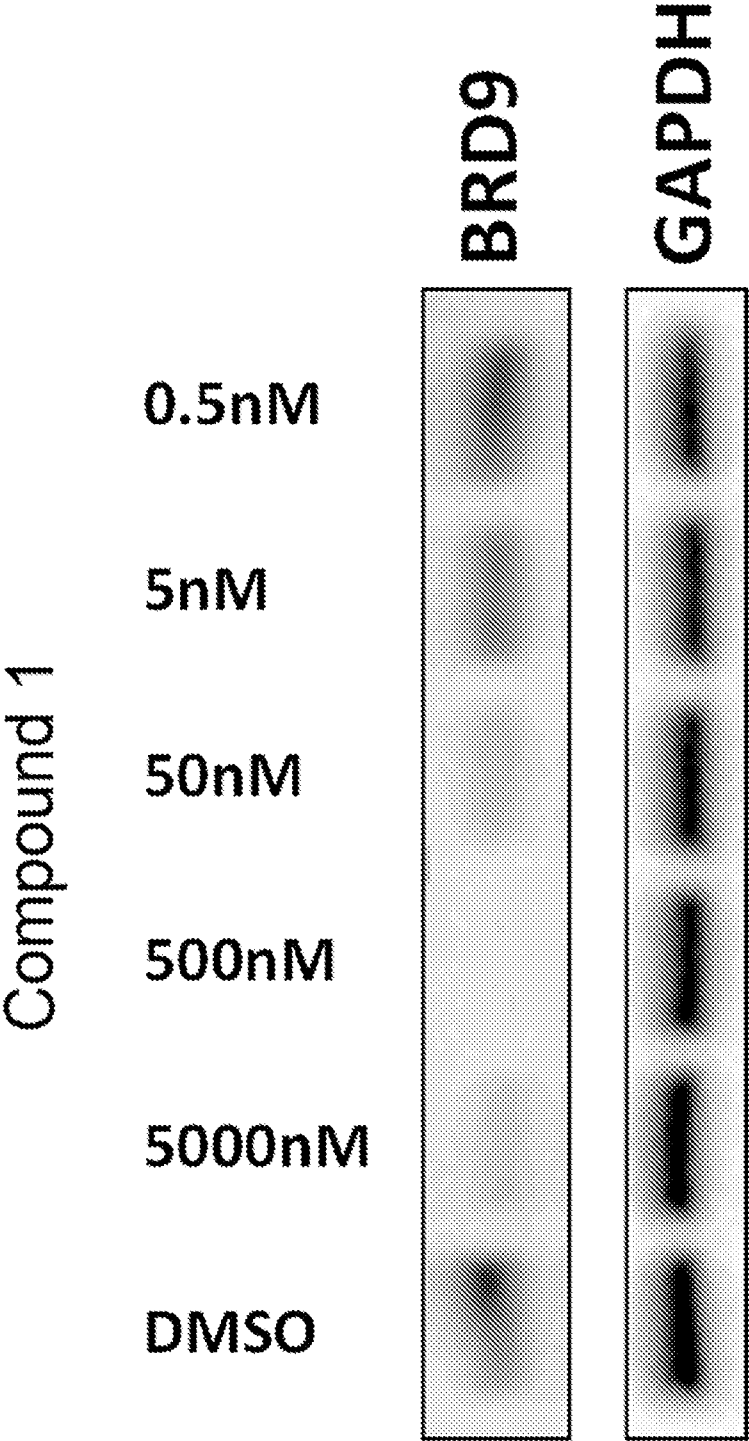


FIG. 2



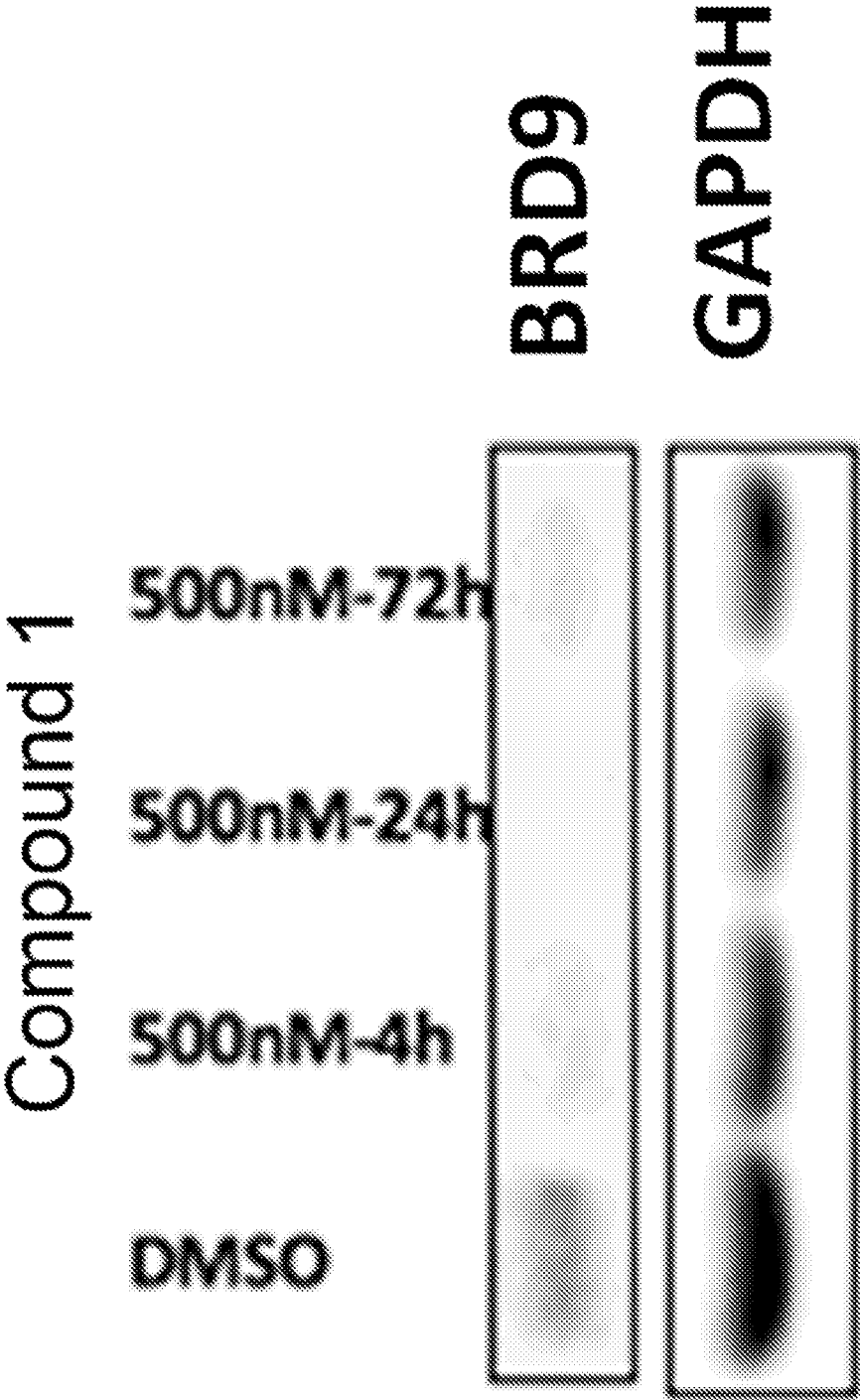


FIG. 3

FIG. 4

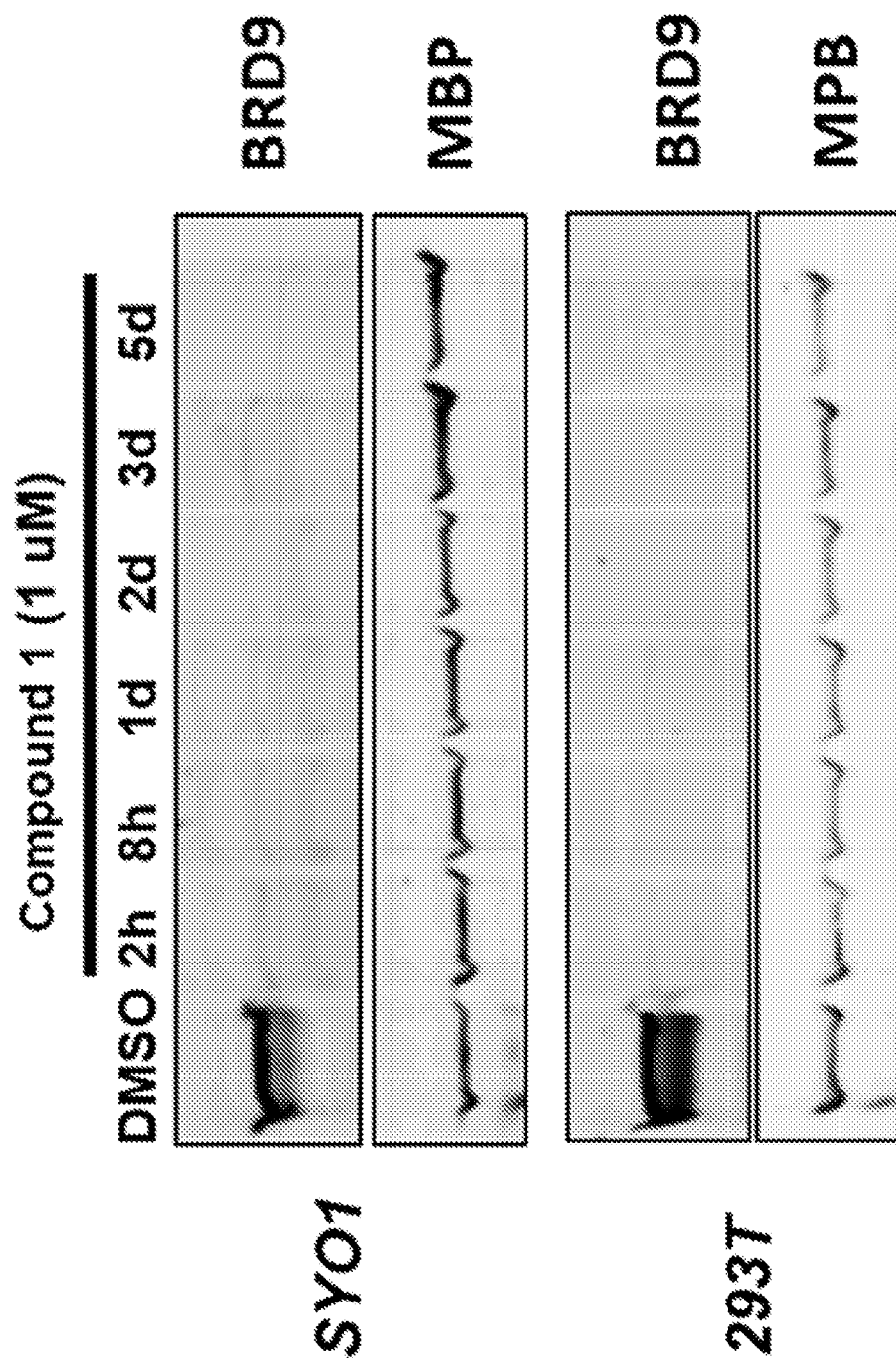
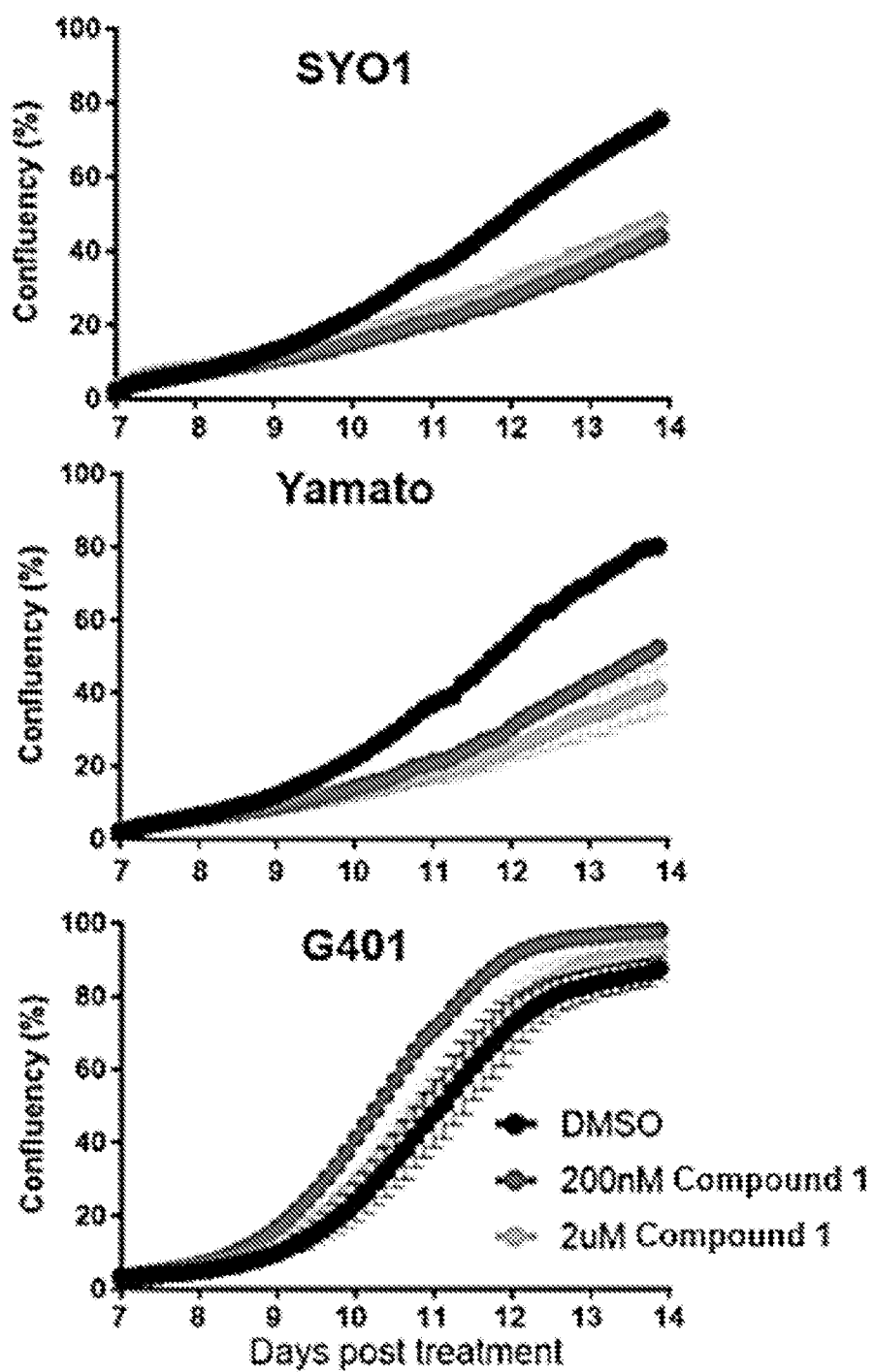


FIG. 5



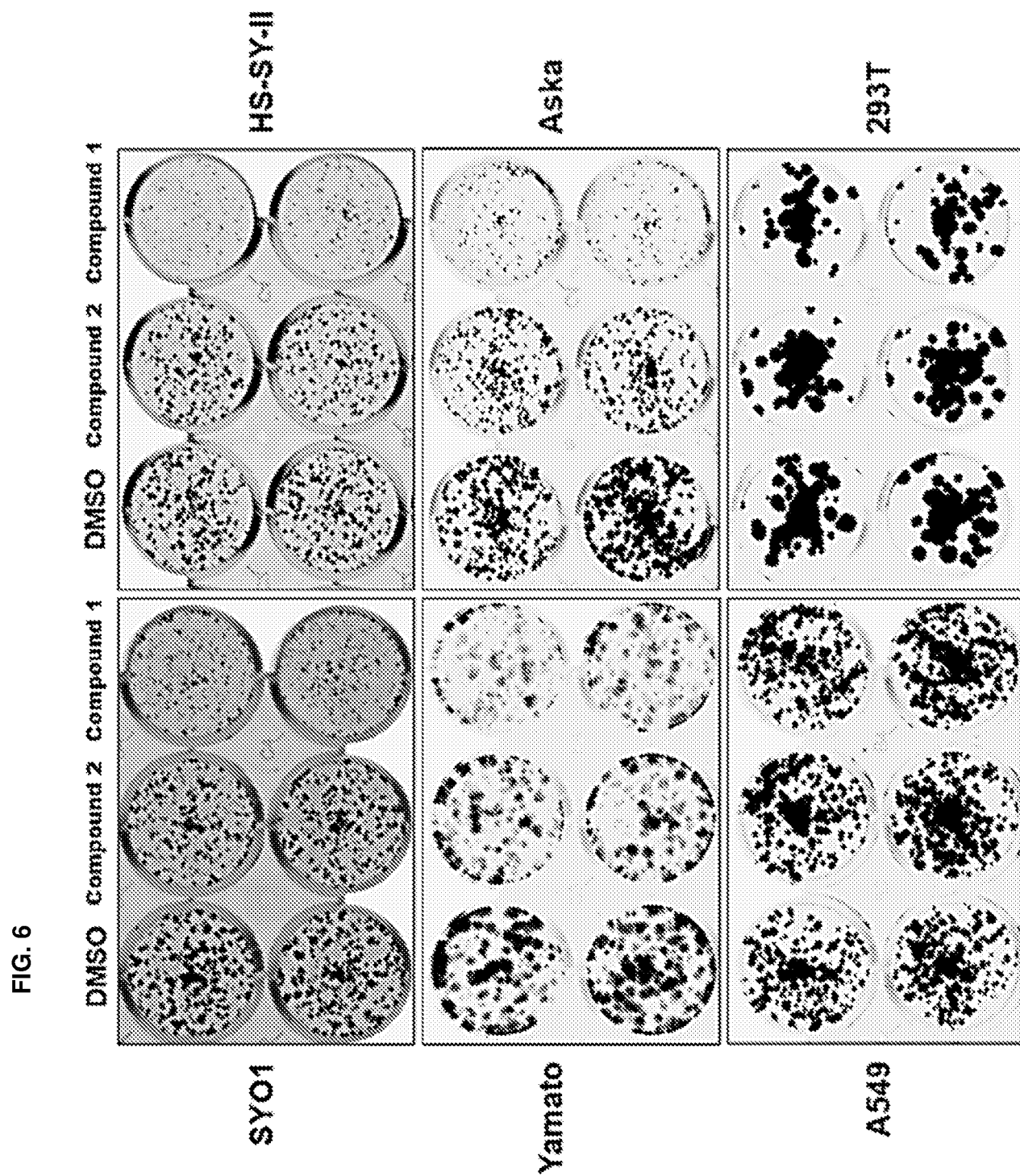


FIG. 7

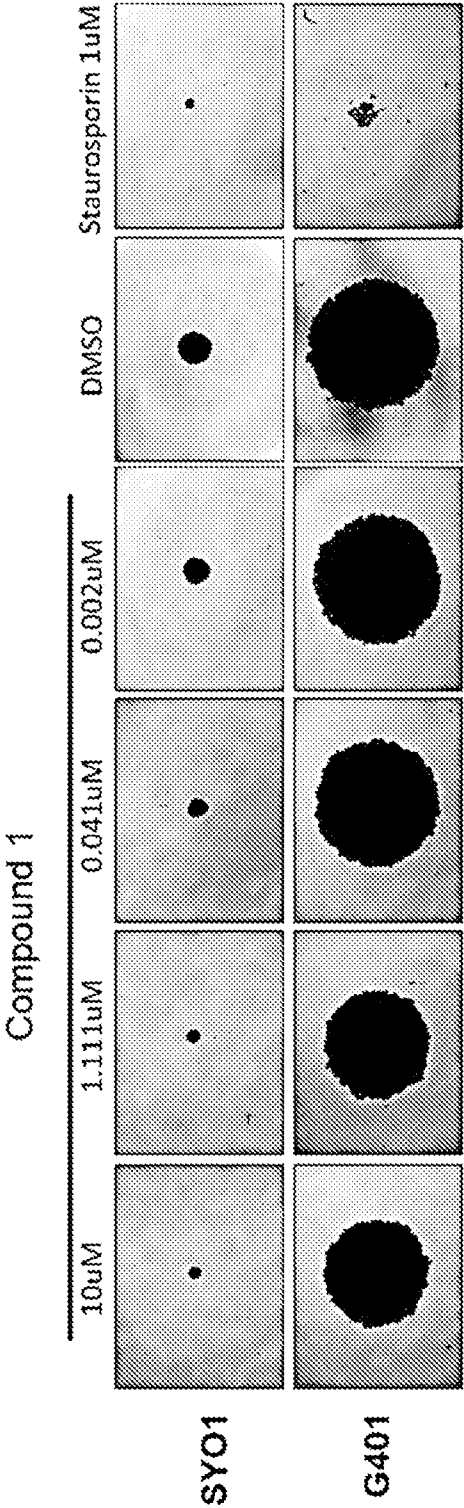
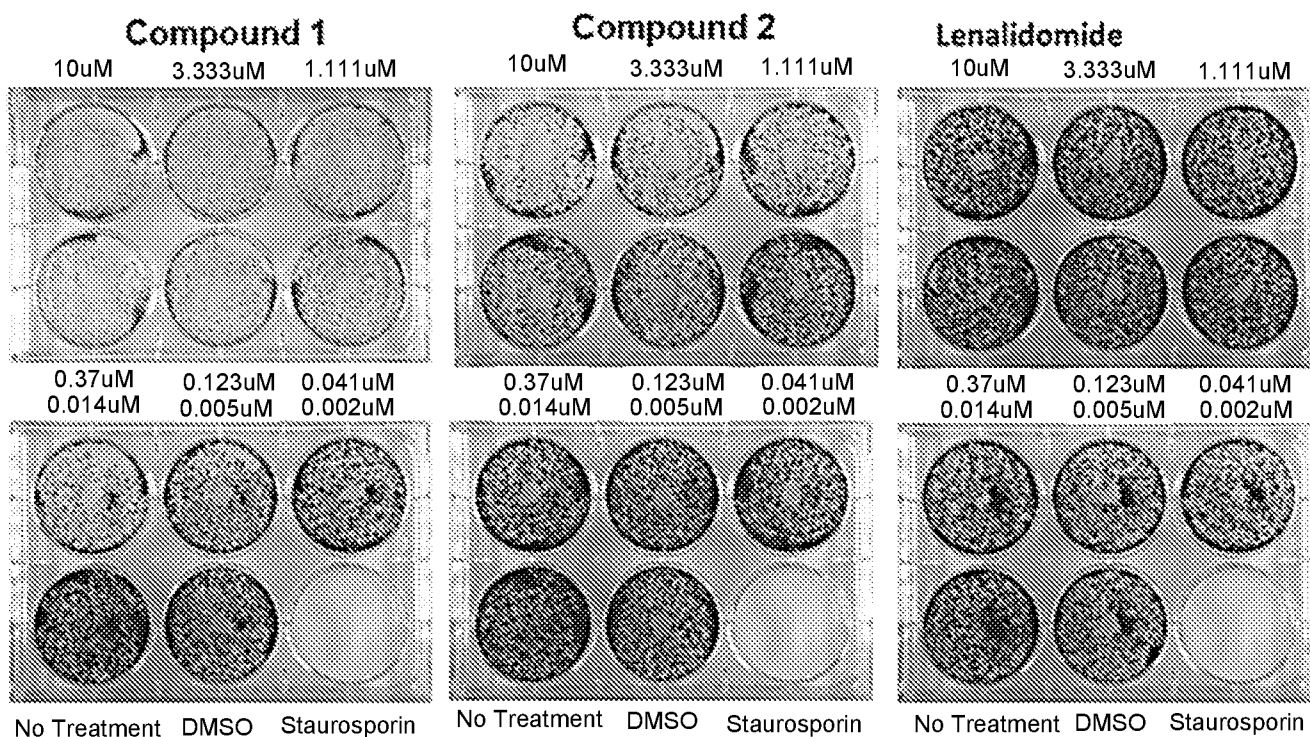
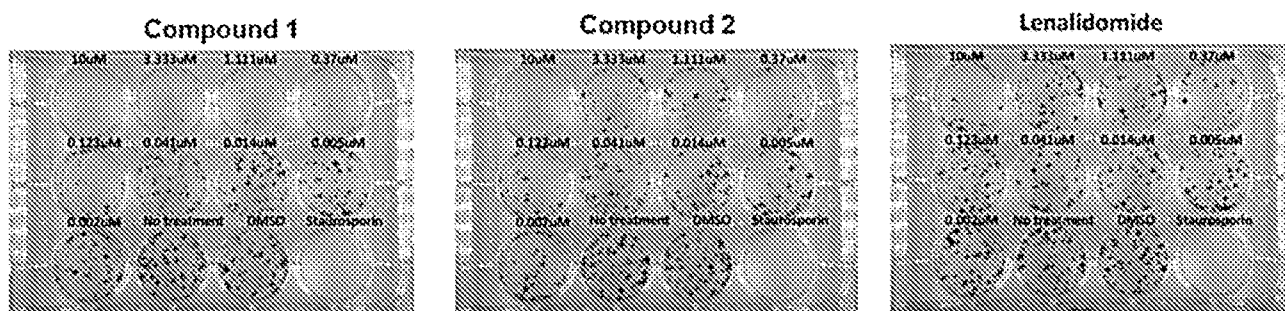


FIG. 8

SYO1



HS-SY-II



ASKA

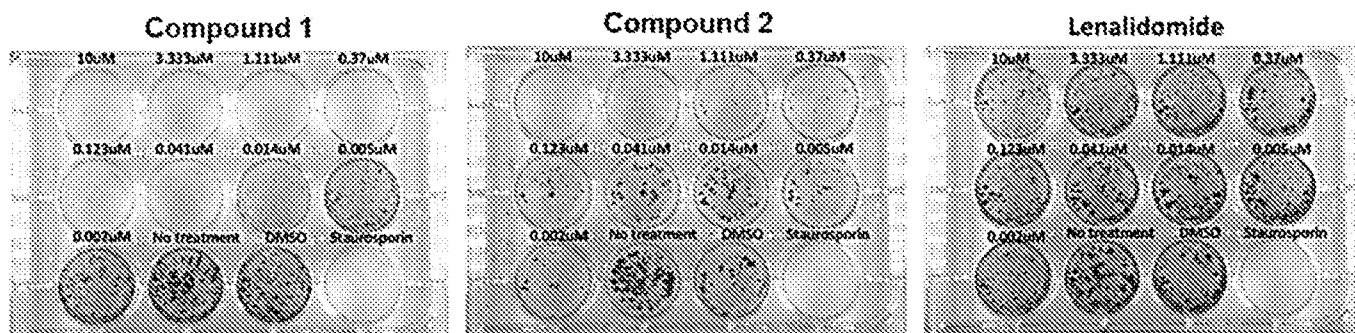
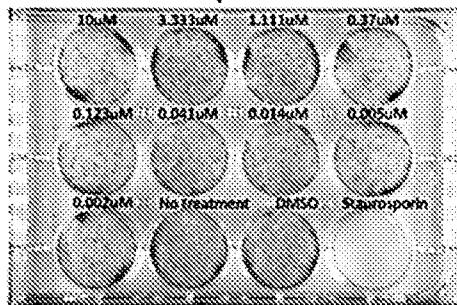


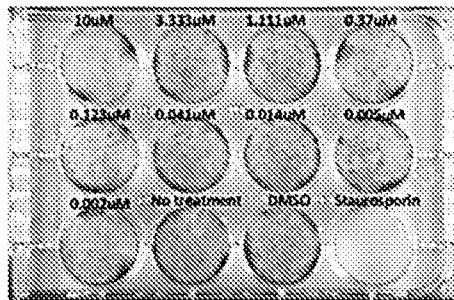
FIG. 9

RD

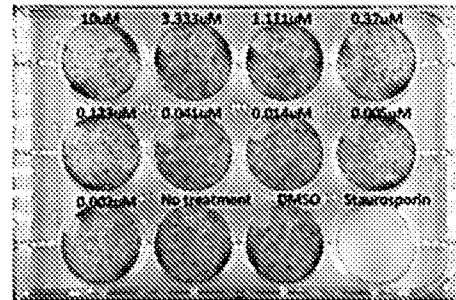
Compound 1



Compound 2

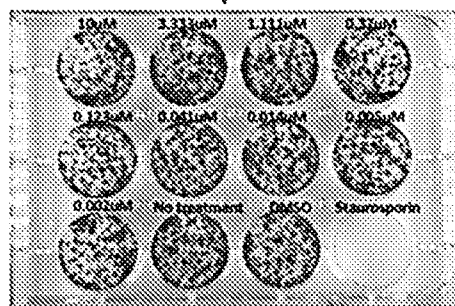


Lenalidomide

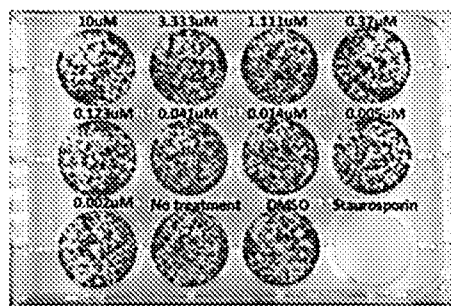


HCT116

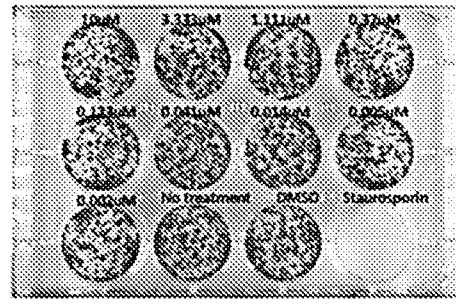
Compound 1



Compound 2

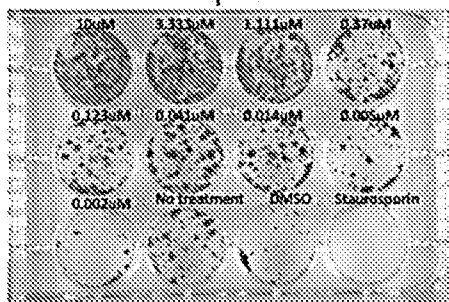


Lenalidomide

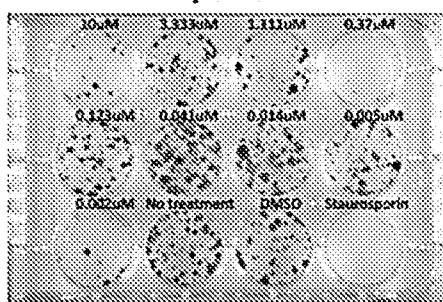


Calu6

Compound 1



Compound 2



Lenalidomide

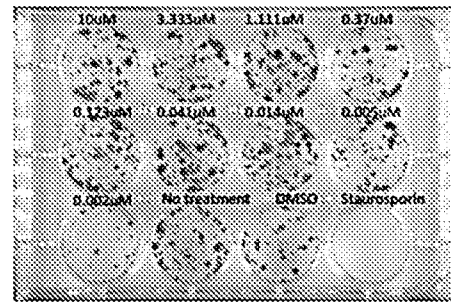


FIG. 10

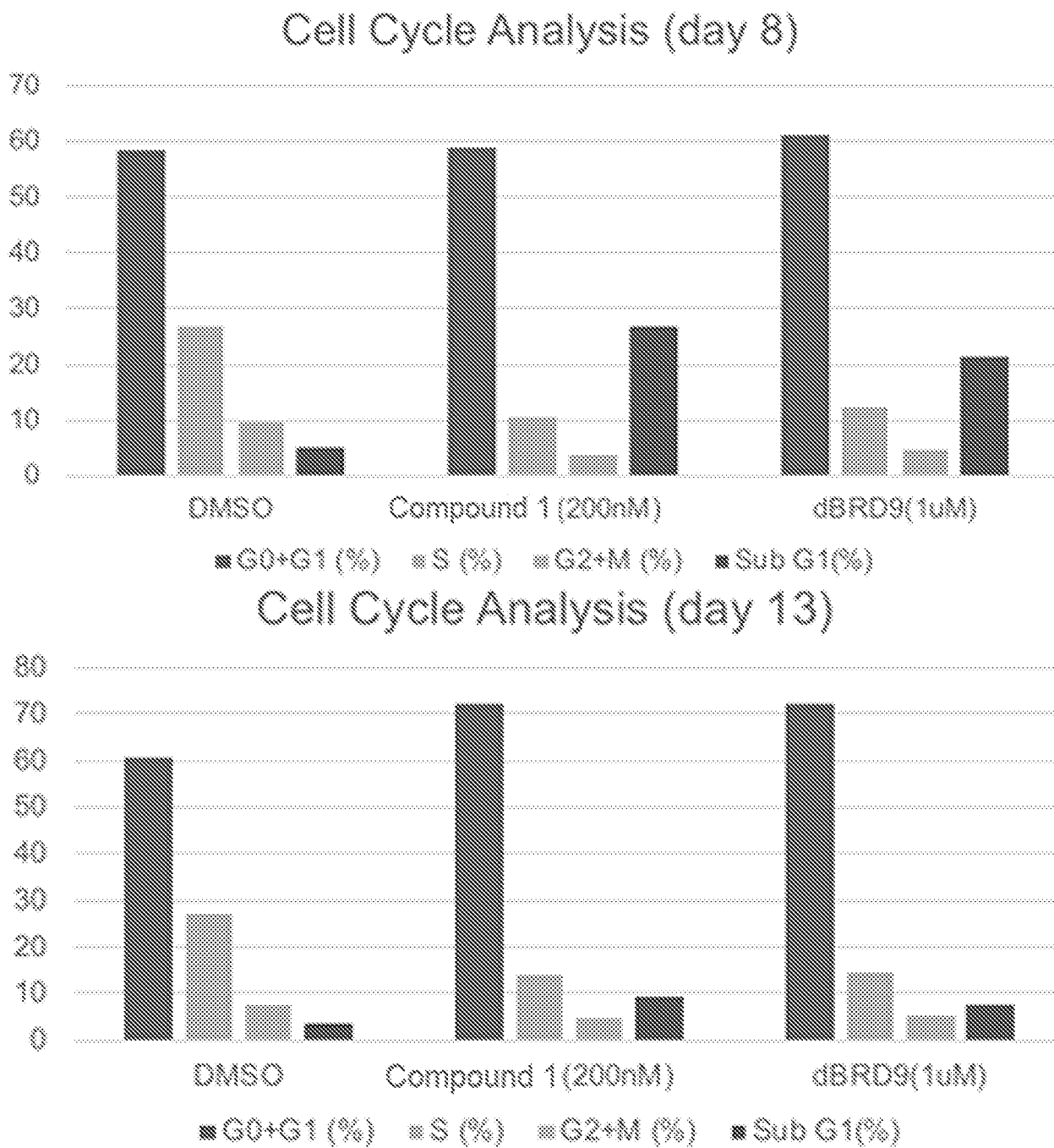


FIG. 11

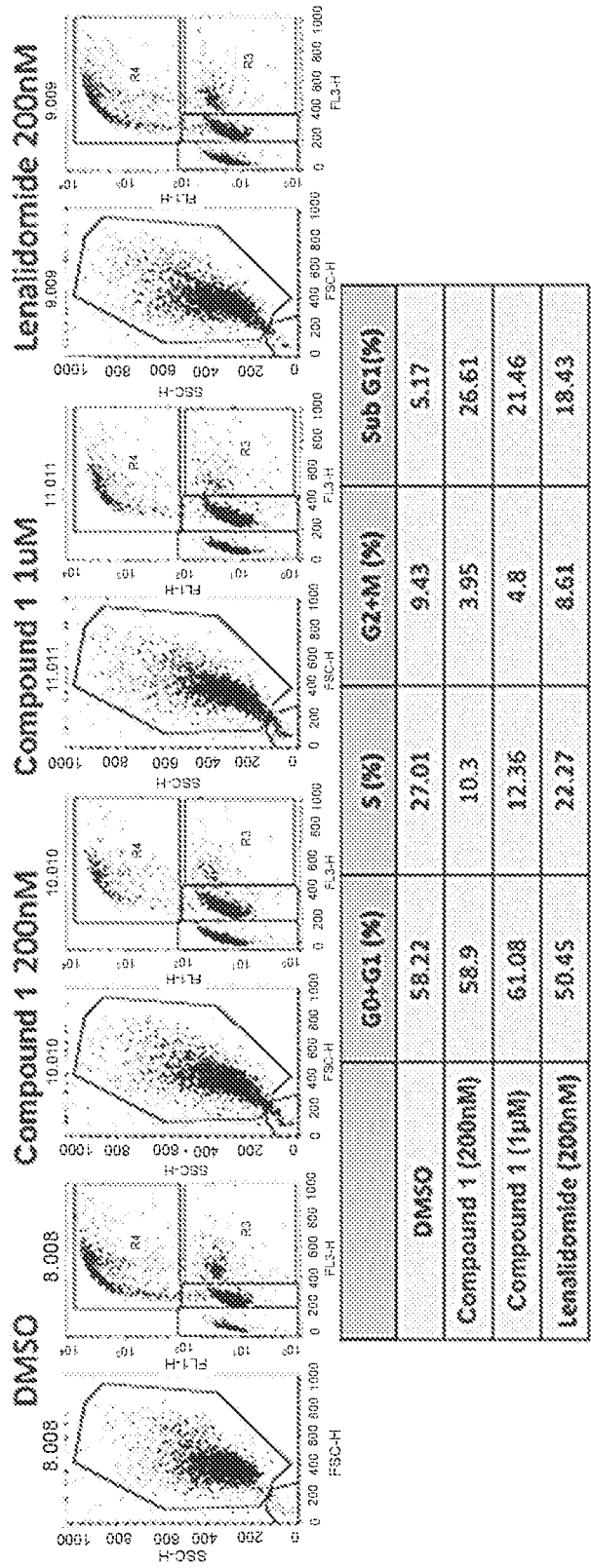
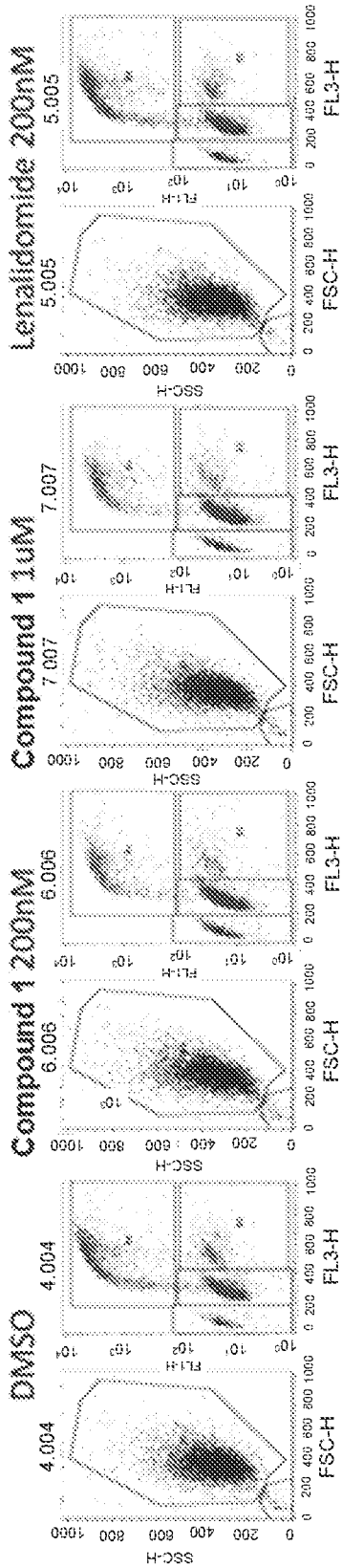
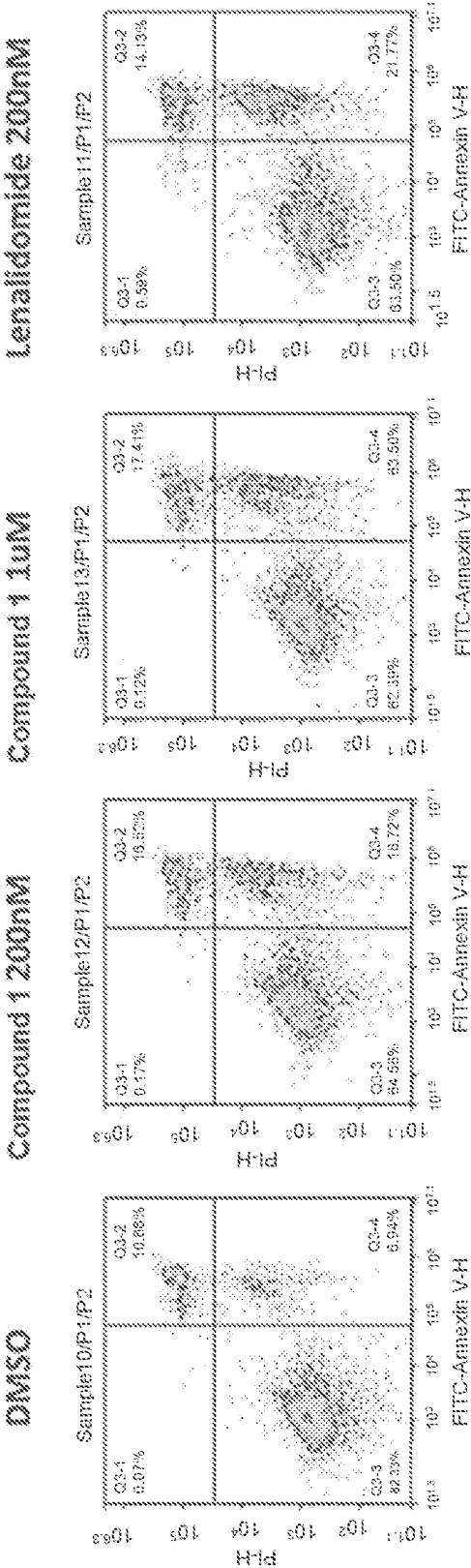


FIG. 12



	G0+G1 (%)	S (%)	G2+M (%)	Sub G1 (%)
DMSO	60.83	27.29	7.53	3.88
Compound 1 (200nM)	71.9	14.06	4.76	9.1
Compound 1 (1µM)	72.21	14.53	5.08	7.91
Lenalidomide(200nM)	58.67	27.28	6.71	7.11

FIG. 13



	DMSO	Compound 1 (200nM)	Compound 1 (1uM)	Lenalidomide(200nM)
Early Apoptosis Cell	6.94	18.72	20.08	21.77
Late Apoptosis Cell	10.66	16.52	17.41	14.13

