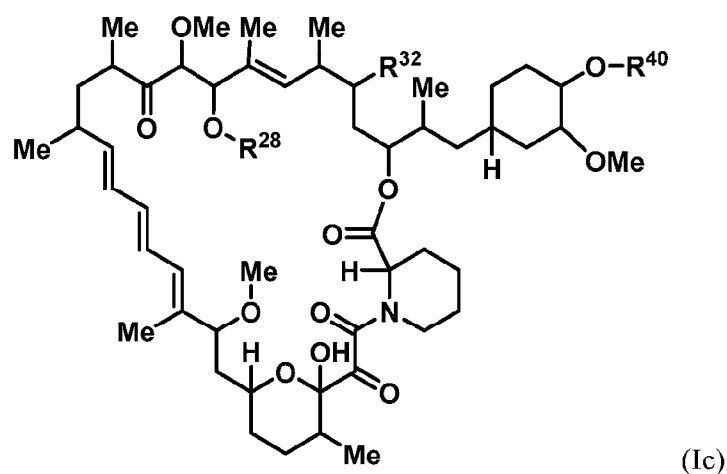


CLAIMS

1. A compound of Formula Ic:



or a pharmaceutically acceptable salt or tautomer thereof, wherein:

R^{32} is $-H$, $=O$, $-OR^3$, $-N_3$, or $-O-C(=Z^1)-R^{32a}$;

R^{28} is $-H$, $(C_1-C_6)alkyl$, or $-C(=Z^1)-R^{28a}$;

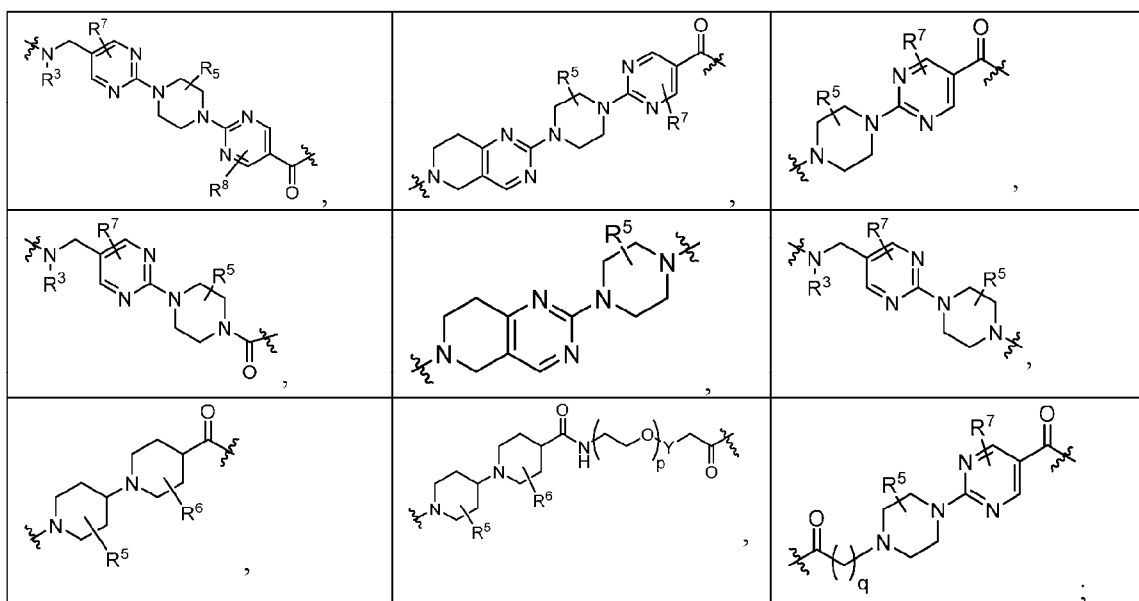
R^{40} is $-H$ or $-C(=Z^1)-R^{40a}$;

wherein when R^{28} and R^{40} are H , then R^{32} is not $=O$;

each Z^1 is independently O or S ;

R^{28a} , R^{32a} , and R^{40a} are independently $-A^1-L^1-A^2-B$; $-A^1-A^2-B$; $-L^2-A^1-L^1-A^2-L^3-B$; $-O-(C_1-C_6)alkyl$; or $-O-(C_6-C_{10})aryl$; wherein the aryl of $-O-(C_6-C_{10})aryl$ is unsubstituted or substituted with 1-5 substituents selected from $-NO_2$ and halogen;

A^1 and A^2 are independently absent or are independently selected from



and		

wherein the bond on the left side of A¹, as drawn, is bound to -C(=Z¹)- or L²; and
wherein the bond on the right side of the A² moiety, as drawn, is bound to B or L³;

each Q is independently 1 to 3 rings selected from arylene, cycloalkylene, heteroarylene, and heterocyclylene;

each X is independently absent or 1 to 2 rings selected from arylene, cycloalkylene, heteroarylene, and heterocyclylene;

each X¹ is independently a heteroarylene or heterocyclylene ring;

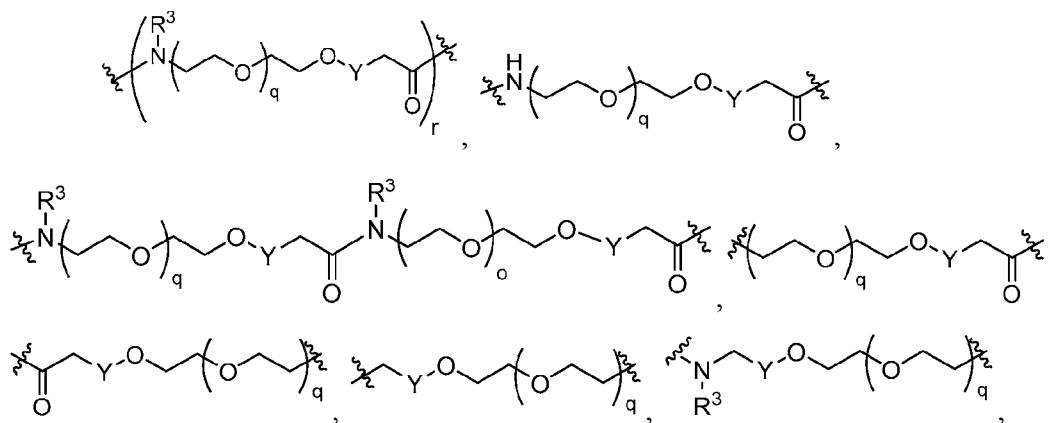
each W is independently absent or 1 to 2 rings selected from arylene, cycloalkylene, heteroarylene, and heterocyclylene;

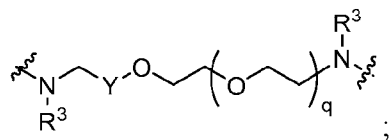
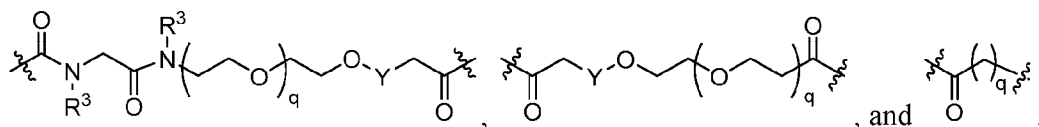
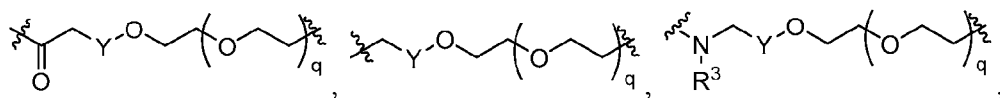
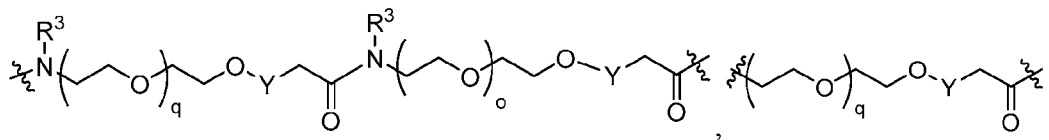
each W¹ is independently a heteroarylene or heterocyclylene ring;

each G is independently absent or a ring selected from arylene, cycloalkylene, heteroarylene, and heterocyclylene;

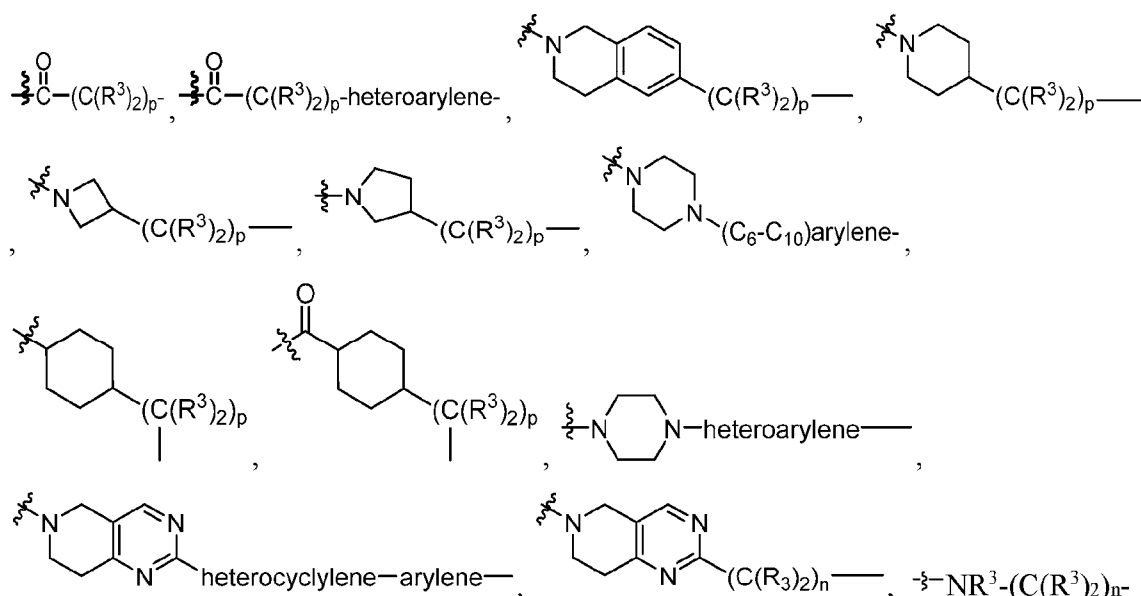
each G¹ and G² are independently heteroarylene or heterocyclylene ring;

each L¹ is independently selected from




$$\left(\text{N}(\text{R}^3) \left(\text{CH}_2 \text{CH}_2 \text{O} \right)_q \text{CH}_2 \text{O} \text{Y} \text{CH}_2 \text{C}(=\text{O}) \right)_r$$

$$-\text{NR}^3-(\text{C}(\text{R}^3)_2)_n\text{-heteroarylene-}, -\text{NR}^3-(\text{C}(\text{R}^3)_2)_n\text{-heteroarylene-(C}(\text{R}^3)_2)_n\text{-}$$

$\text{---}^3\text{---}(\text{C}_6\text{--C}_{10})\text{arylene-}$, $\text{---}^3\text{---NR}^3\text{---}(\text{C}(\text{R}^3)_2)_n\text{---NR}^3\text{C(O)-}$, $\text{---}^3\text{---NR}^3\text{---}(\text{C}(\text{R}^3)_2)_n\text{---heteroarylene-}$,
heterocyclylene- $(\text{C}_6\text{--C}_{10})\text{arylene-}$, $\text{---}^3\text{---heteroarylene-heterocyclylene-}(\text{C}_6\text{--C}_{10})\text{arylene-}$,



$\text{S(O)}_2\text{---arylene-C(O)-}$, and $\text{---}^3\text{---NR}^3\text{---}(\text{C}(\text{R}^3)_2)_n\text{---S(O)}_2\text{---arylene-}(\text{C}(\text{R}^3)_2)_n\text{---}$, wherein the $\text{---}^3\text{---}$ bond on the left side of B^1 , as drawn, is bound to A^2 , L^3 , or L^1 ; and wherein the heteroarylene, heterocyclylene, and arylene are each independently optionally substituted with alkyl, hydroxyalkyl, haloalkyl, alkoxy, halogen, or hydroxyl;

each R^3 is independently H or $(\text{C}_1\text{--C}_6)\text{alkyl}$;

each R^4 is independently H, $(\text{C}_1\text{--C}_6)\text{alkyl}$, halogen, 5-12 membered heteroaryl, 5-12 membered heterocyclyl, $(\text{C}_6\text{--C}_{10})\text{aryl}$, wherein the heteroaryl, heterocyclyl, and aryl are optionally substituted with $\text{---N(R}^3)_2$, ---OR^3 , halogen, $(\text{C}_1\text{--C}_6)\text{alkyl}$, $\text{---}(\text{C}_1\text{--C}_6)\text{alkylene-heteroaryl}$, $\text{---}(\text{C}_1\text{--C}_6)\text{alkylene-CN}$, $\text{---C(O)NR}^3\text{---heteroaryl}$, or $\text{---C(O)NR}^3\text{---heterocyclyl}$;

each R^5 is independently H, $(\text{C}_1\text{--C}_6)\text{alkyl}$, ---C(O)OR^3 , or $\text{---N(R}^3)_2$, wherein the alkyl of $(\text{C}_1\text{--C}_6)\text{alkyl}$ is optionally substituted with $\text{---N(R}^3)_2$ or ---OR^3 ;

each R^6 is independently H, $(\text{C}_1\text{--C}_6)\text{alkyl}$, ---C(O)OR^3 , or $\text{---N(R}^3)_2$, wherein the alkyl of $(\text{C}_1\text{--C}_6)\text{alkyl}$ is optionally substituted with $\text{---N(R}^3)_2$ or ---OR^3 ;

each R^7 is independently H, $(\text{C}_1\text{--C}_6)\text{alkyl}$, ---C(O)OR^3 , or $\text{---N(R}^3)_2$, wherein the alkyl of $(\text{C}_1\text{--C}_6)\text{alkyl}$ is optionally substituted with $\text{---N(R}^3)_2$ or ---OR^3 ;

each R^8 is independently H, $(\text{C}_1\text{--C}_6)\text{alkyl}$, ---C(O)OR^3 , or $\text{---N(R}^3)_2$, wherein the alkyl of $(\text{C}_1\text{--C}_6)\text{alkyl}$ is optionally substituted with $\text{---N(R}^3)_2$ or ---OR^3 ;

each Y is independently $\text{C}(\text{R}^3)_2$ or a bond;

each n is independently an integer from one to 12;

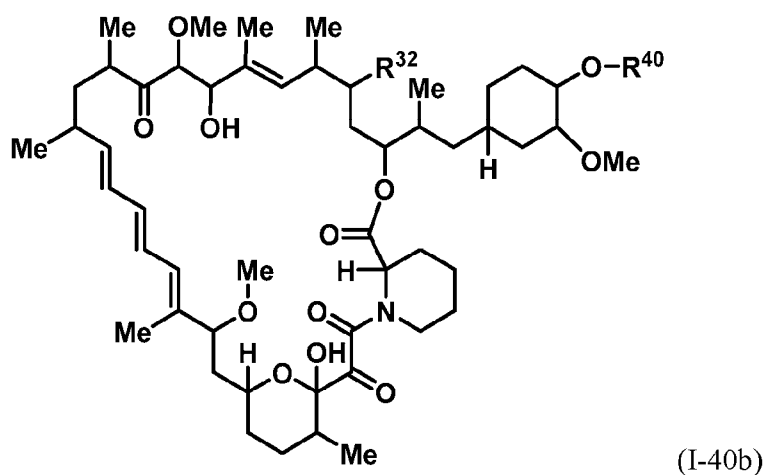
each o is independently an integer from zero to 30;

each p is independently an integer from zero to 12;
 each q is independently an integer from zero to 30; and
 each r is independently an integer from one to 6.

2. The compound of claim 1, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{32} is =O.

3. The compound of claim 1, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{32} is -OR³.

4. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt or tautomer thereof, wherein the compound is represented by the structure of Formula (I-40b):



wherein R^{40} is $-C(=Z^1)-R^{40a}$.

5. The compound of claim 4, or a pharmaceutically acceptable salt or tautomer thereof, wherein Z^1 is O.

6. The compound of claim 4, or a pharmaceutically acceptable salt or tautomer thereof, wherein Z^1 is S.

7. The compound of any one of claims 4-6, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{40a} is $-A^1-L^1-A^2-B$, wherein A^1 and A^2 are absent.

8. The compound of any one of claims 4-6, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{40a} is $-A^1-L^1-A^2-B$, wherein A^2 is absent.

9. The compound of any one of claims 4-6, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{40a} is $-A^1-L^1-A^2-B$, wherein A^1 is absent.

10. The compound of any one of claims 4-6, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{40a} is $-A^1-L^1-A^2-B$.

11. The compound of any one of claims 4-6, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{40a} is $-A^1-A^2-B$.

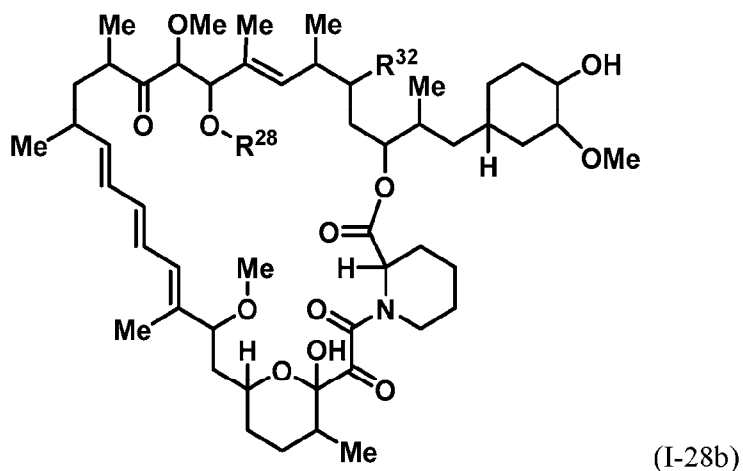
12. The compound of any one of claims 4-6, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{40a} is $-L^2-A^1-L^1-A^2-L^3-B$, wherein L^2 and A^1 are absent.

13. The compound of any one of claims 4-6, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{40a} is $-L^2-A^1-L^1-A^2-L^3-B$, wherein L^2 is absent.

14. The compound of any one of claims 4-6, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{40a} is $-L^2-A^1-L^1-A^2-L^3-B$, wherein L^3 is absent.

15. The compound of any one of claims 4-6, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{40a} is $-O-(C_1-C_6)\text{alkyl}$ or $-O-(C_6-C_{10})\text{aryl}$; wherein the aryl of $-O-(C_6-C_{10})\text{aryl}$ is unsubstituted or substituted with 1-5 substituents selected from $-\text{NO}_2$ and halogen.

16. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt or tautomer thereof, wherein the compound is represented by the structure of Formula (I-28b):



wherein R^{28} is $-C(=Z^1)-R^{28a}$.

17. The compound of claim 16, or a pharmaceutically acceptable salt or tautomer thereof, wherein Z^1 is O.

18. The compound of claim 16, or a pharmaceutically acceptable salt or tautomer thereof, wherein Z^1 is S.

19. The compound of any one of claims 16-18, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{28a} is $-A^1-L^1-A^2-B$, wherein A^1 and A^2 are absent.

20. The compound of any one of claims 16-18, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{28a} is $-A^1-L^1-A^2-B$, wherein A^2 is absent.

21. The compound of any one of claims 16-18, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{28a} is $-A^1-L^1-A^2-B$, wherein A^1 is absent.

22. The compound of any one of claims 16-18, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{28a} is $-A^1-L^1-A^2-B$.

23. The compound of any one of claims 16-18, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{28a} is $-A^1-A^2-B$.

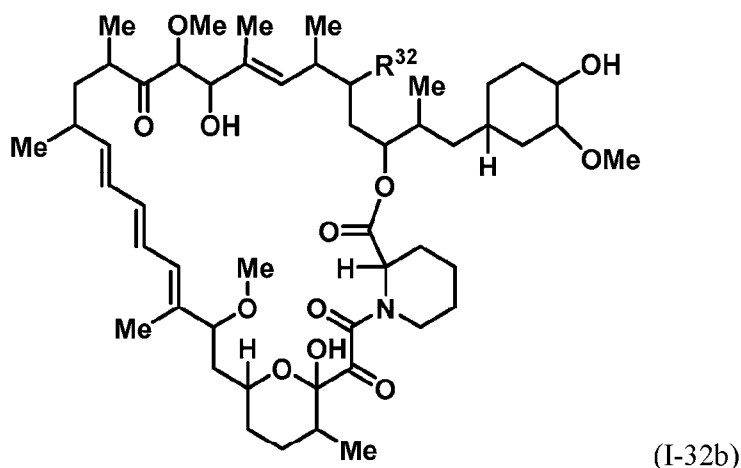
24. The compound of any one of claims 16-18, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{28a} is $-L^2-A^1-L^1-A^2-L^3-B$, wherein L^2 and A^1 are absent.

25. The compound of any one of claims 16-18, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{28a} is $-L^2-A^1-L^1-A^2-L^3-B$, wherein L^2 is absent.

26. The compound of any one of claims 16-18, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{28a} is $-L^2-A^1-L^1-A^2-L^3-B$, wherein L^3 is absent.

27. The compound of any one of claims 16-18, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{28a} is $-O-(C_1-C_6)\text{alkyl}$ or $-O-(C_6-C_{10})\text{aryl}$; wherein the aryl of $-O-(C_6-C_{10})\text{aryl}$ is unsubstituted or substituted with 1-5 substituents selected from $-\text{NO}_2$ and halogen.

28. The compound of claim 1, or a pharmaceutically acceptable salt or tautomer thereof, wherein the compound is represented by the structure of Formula (I-32b):



wherein R^{32} is $-O-C(=Z^1)-R^{32a}$.

29. The compound of claim 28, or a pharmaceutically acceptable salt or tautomer thereof, wherein Z^1 is O.

30. The compound of claim 28, or a pharmaceutically acceptable salt or tautomer thereof, wherein Z^1 is S.

31. The compound of any one of claims 28-30, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{32a} is $-A^1-L^1-A^2-B$, wherein A^1 and A^2 are absent.

32. The compound of any one of claims 28-30, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{32a} is $-A^1-L^1-A^2-B$, wherein A^2 is absent.

33. The compound of any one of claims 28-30, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{32a} is $-A^1-L^1-A^2-B$, wherein A^1 is absent.

34. The compound of any one of claims 28-30, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{32a} is $-A^1-L^1-A^2-B$.

35. The compound of any one of claims 28-30, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{32a} is $-A^1-A^2-B$.

36. The compound of any one of claims 28-30, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{32a} is $-L^2-A^1-L^1-A^2-L^3-B$, wherein L^2 and A^1 are absent.

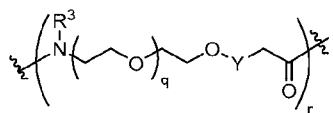
37. The compound of any one of claims 28-30, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{32a} is $-L^2-A^1-L^1-A^2-L^3-B$, wherein L^2 is absent.

38. The compound of any one of claims 28-30, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{32a} is $-L^2-A^1-L^1-A^2-L^3-B$, wherein L^3 is absent.

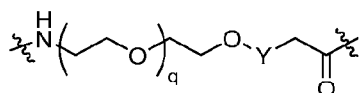
39. The compound of any one of claims 28-30, or a pharmaceutically acceptable salt or tautomer thereof, or a pharmaceutically acceptable salt or tautomer thereof, wherein

R^{32a} is -O-(C₁-C₆)alkyl or -O-(C₆-C₁₀)aryl; wherein the aryl of -O-(C₆-C₁₀)aryl is unsubstituted or substituted with 1-5 substituents selected from -NO₂ and halogen.

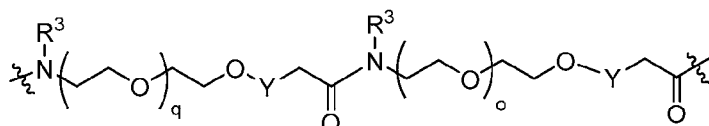
40. The compound of any one of claims 1-10, 12-22, 24-35, and 36-39, or a pharmaceutically acceptable salt or tautomer thereof, wherein L¹ is



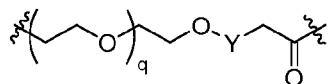
41. The compound of any one of claims 1-10, 12-22, 24-35, and 36-39, or a pharmaceutically acceptable salt or tautomer thereof, wherein L¹ is



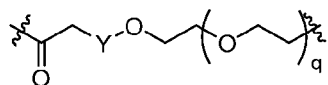
42. The compound of any one of claims 1-10, 12-22, 24-35, and 36-39, or a pharmaceutically acceptable salt or tautomer thereof, wherein L¹ is



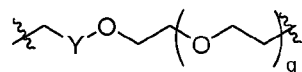
43. The compound of any one of claims 1-10, 12-22, 24-35, and 36-39, or a pharmaceutically acceptable salt or tautomer thereof, wherein L¹ is



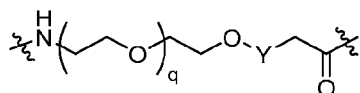
44. The compound of any one of claims 1-10, 12-22, 24-35, and 36-39, or a pharmaceutically acceptable salt or tautomer thereof, wherein L¹ is



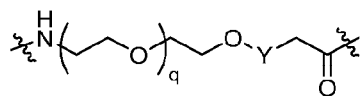
45. The compound of any one of claims 1-10, 12-22, 24-35, and 36-39, or a pharmaceutically acceptable salt or tautomer thereof, wherein L¹ is



46. The compound of any one of claims 1-6, 12-18, 24-30, and 36-45, or a pharmaceutically acceptable salt or tautomer thereof, wherein L² is

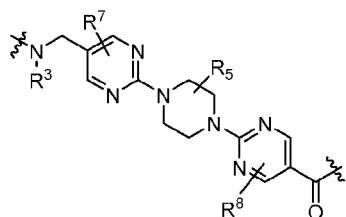


47. The compound of any one of claims 1-6, 12-18, 24-30, and 36-45, or a pharmaceutically acceptable salt or tautomer thereof, wherein L^3 is

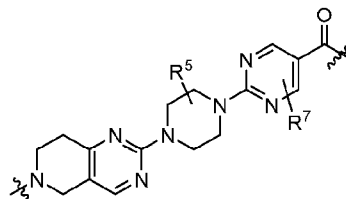


48. The compound of any one of claims 1-7, 9, 12, 16-19, 21, 24, 28-31, 33, 36, and 39-45, or a pharmaceutically acceptable salt or tautomer thereof, wherein A^1 is absent.

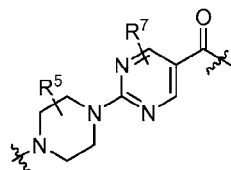
49. The compound of any one of claims 1-6, 8, 10-11, 13-18, 20, 22-23, 25-30, 32, 34-35, and 37-45, or a pharmaceutically acceptable salt or tautomer thereof, wherein A^1 is



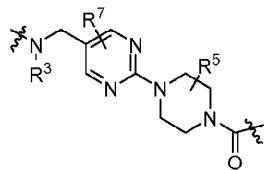
50. The compound of any one of claims 1-6, 8, 10-11, 13-18, 20, 22-23, 25-30, 32, 34-35, and 37-45, or a pharmaceutically acceptable salt or tautomer thereof, wherein A^1 is



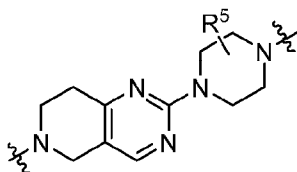
51. The compound of any one of claims 1-6, 8, 10-11, 13-18, 20, 22-23, 25-30, 32, 34-35, and 37-45, or a pharmaceutically acceptable salt or tautomer thereof, wherein A^1 is



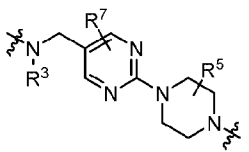
52. The compound of any one of claims 1-6, 8, 10-11, 13-18, 20, 22-23, 25-30, 32, 34-35, and 37-45, or a pharmaceutically acceptable salt or tautomer thereof, wherein A^1 is



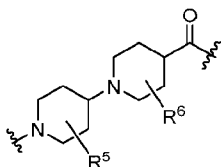
53. The compound of any one of claims 1-6, 8, 10-11, 13-18, 20, 22-23, 25-30, 32, 34-35, and 37-45, or a pharmaceutically acceptable salt or tautomer thereof, wherein A¹ is



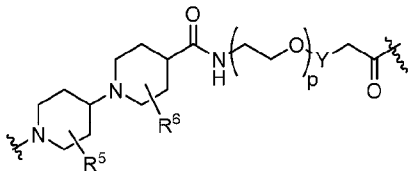
54. The compound of any one of claims 1-6, 8, 10-11, 13-18, 20, 22-23, 25-30, 32, 34-35, and 37-45, or a pharmaceutically acceptable salt or tautomer thereof, wherein A¹ is



55. The compound of any one of claims 1-6, 8, 10-11, 13-18, 20, 22-23, 25-30, 32, 34-35, and 37-45, or a pharmaceutically acceptable salt or tautomer thereof, wherein A¹ is

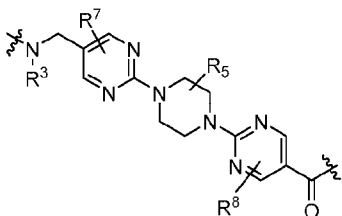


56. The compound of any one of claims 1-6, 8, 10-11, 13-18, 20, 22-23, 25-30, 32, 34-35, and 37-45, or a pharmaceutically acceptable salt or tautomer thereof, wherein A¹ is

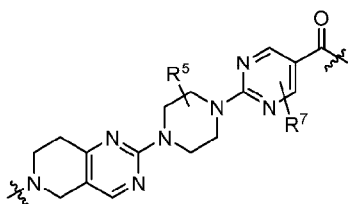


57. The compound of any one of claims 1-8, 15-20, 27-32, and 39-45, or a pharmaceutically acceptable salt or tautomer thereof, wherein A² is absent.

58. The compound of any one of claims 1-6, 9-18, 21-30, and 33-45, or a pharmaceutically acceptable salt or tautomer thereof, wherein A² is

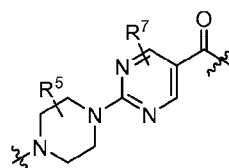


59. The compound of any one of claims 1-6, 9-18, 21-30, and 33-45, or a pharmaceutically acceptable salt or tautomer thereof, wherein A² is



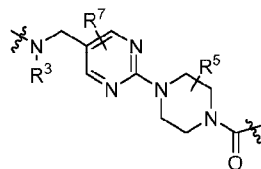
60. The compound of any one of claims 1-6, 9-18, 21-30, and 33-45, or a

pharmaceutically acceptable salt or tautomer thereof, wherein A² is



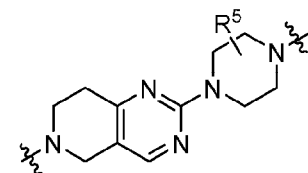
61. The compound of any one of claims 1-6, 9-18, 21-30, and 33-45, or a

pharmaceutically acceptable salt or tautomer thereof, wherein A² is



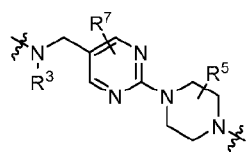
62. The compound of any one of claims 1-6, 9-18, 21-30, and 33-45, or a

pharmaceutically acceptable salt or tautomer thereof, wherein A² is



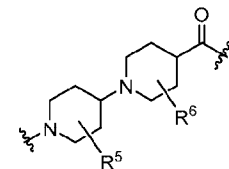
63. The compound of any one of claims 1-6, 9-18, 21-30, and 33-45, or a

pharmaceutically acceptable salt or tautomer thereof, wherein A² is

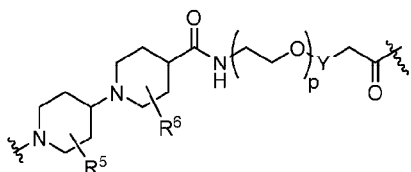


64. The compound of any one of claims 1-6, 9-18, 21-30, and 33-45, or a

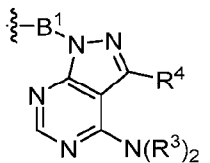
pharmaceutically acceptable salt or tautomer thereof, wherein A² is



65. The compound of any one of claims 1-6, 9-18, 21-30, and 33-45, or a pharmaceutically acceptable salt or tautomer thereof, wherein A² is

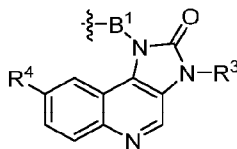


66. The compound of any one of claims 1-65, or a pharmaceutically acceptable



salt or tautomer thereof, wherein B is

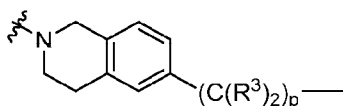
67. The compound of any one of claims 1-65, or a pharmaceutically acceptable



salt or tautomer thereof, wherein B is

68. The compound of any one of claims 1-65, or a pharmaceutically acceptable salt or tautomer thereof, wherein B¹ is $^{-}\text{S}^{-}\text{NR}^3\text{-(C(R}^3\text{)}_2)_n\text{-}$.

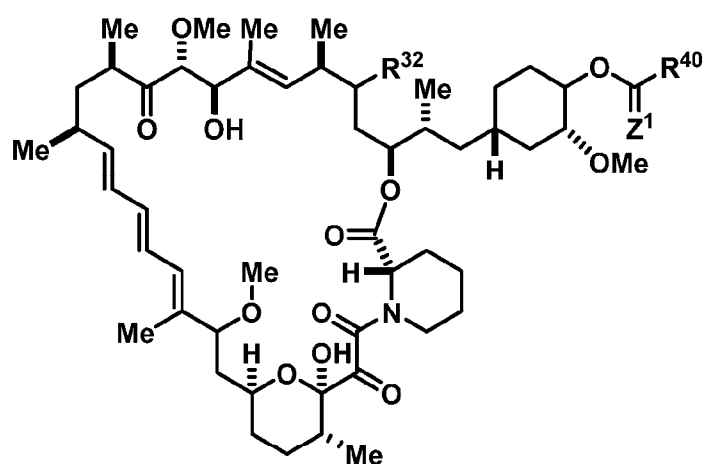
69. The compound of any one of claims 1-65, or a pharmaceutically acceptable



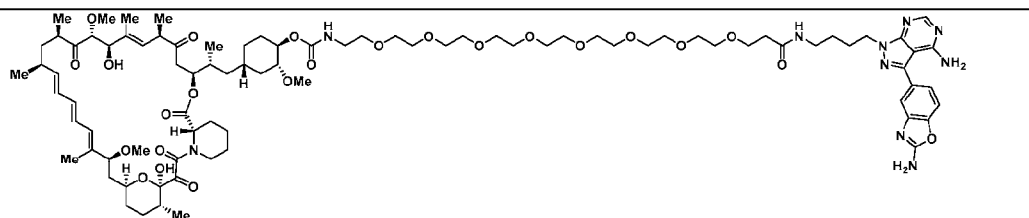
salt or tautomer thereof, wherein B¹ is

70. The compound of any one of claims 1-69, or a pharmaceutically acceptable salt or tautomer thereof, wherein R⁴ is 5-12 membered heteroaryl, optionally substituted with -N(R³)₂, -OR³, halogen, (C₁-C₆)alkyl, -(C₁-C₆)alkylene-heteroaryl, -(C₁-C₆)alkylene-CN, or -C(O)NR³-heteroaryl.

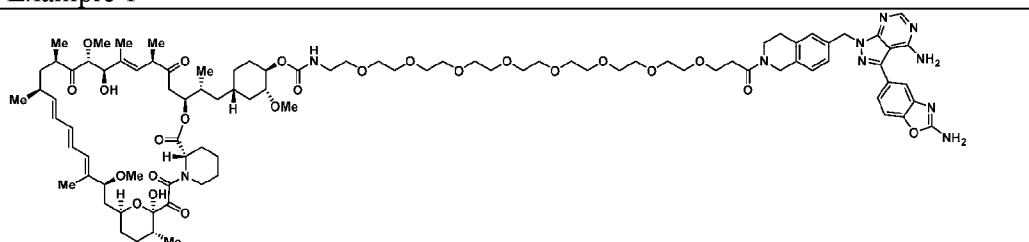
71. The compound of any one of claims 1-70, or a pharmaceutically acceptable salt or tautomer thereof, or a pharmaceutically acceptable salt or tautomer thereof, wherein compound has the following formula:



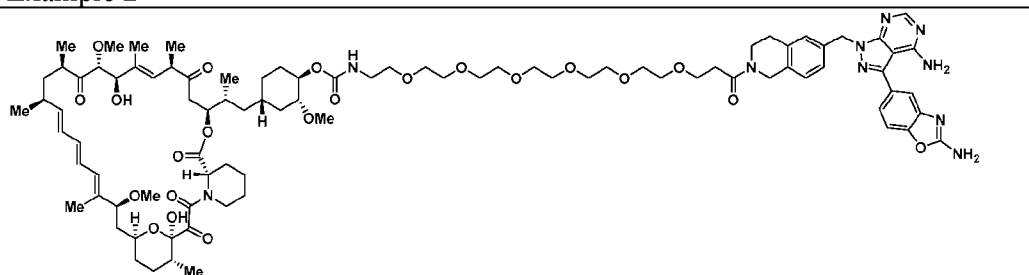
72. A compound selected from the group consisting of:



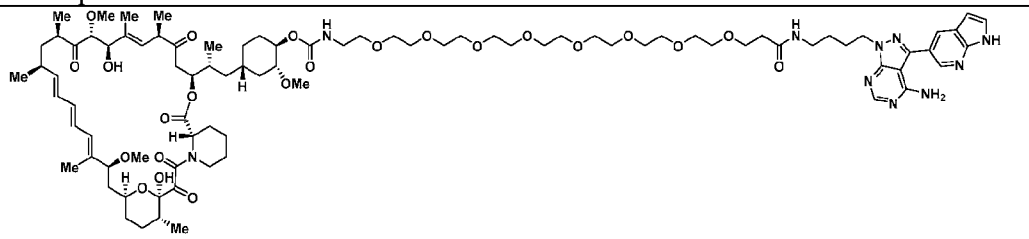
Example 1



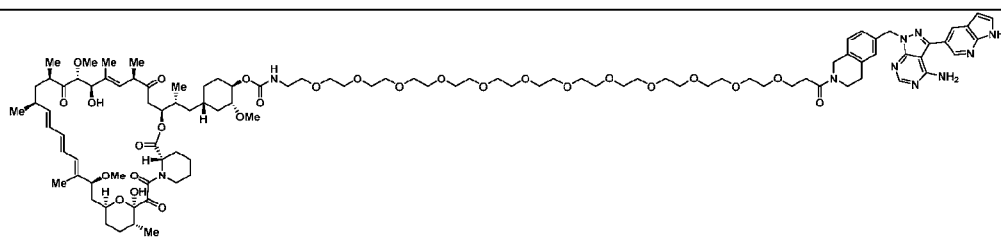
Example 2



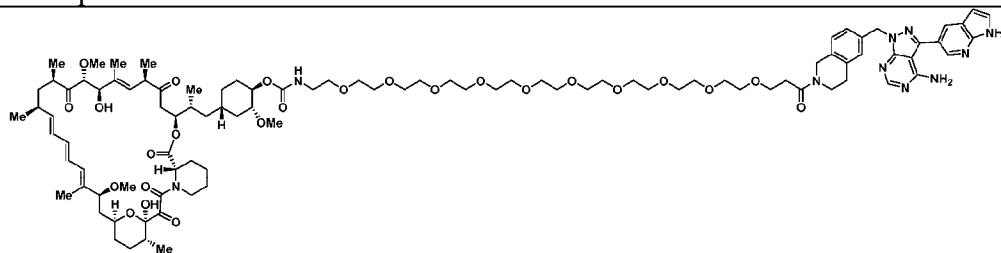
Example 3



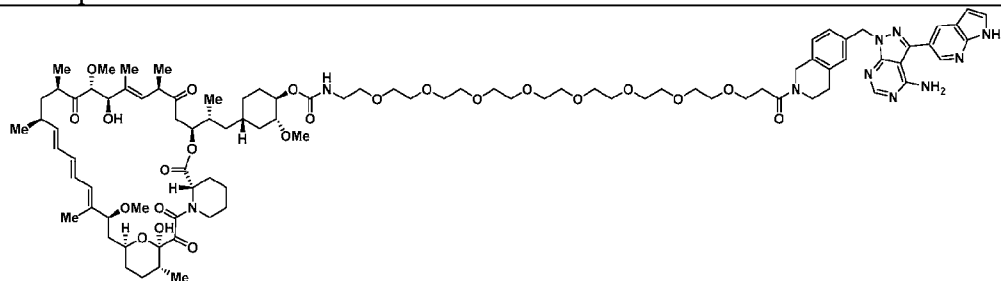
Example 4



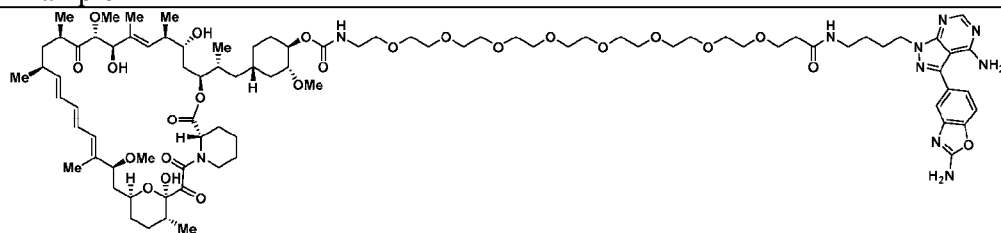
Example 5



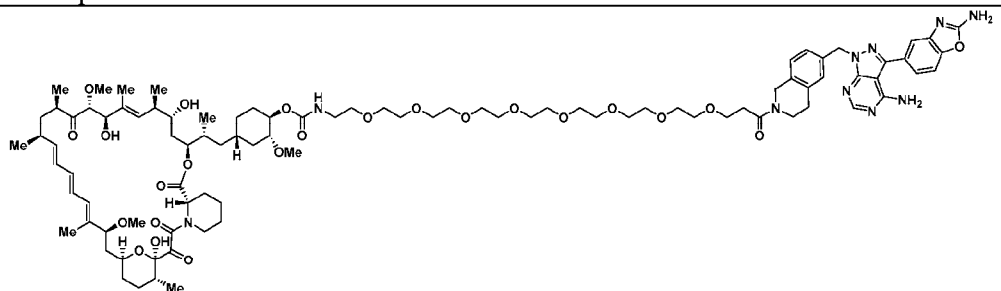
Example 6



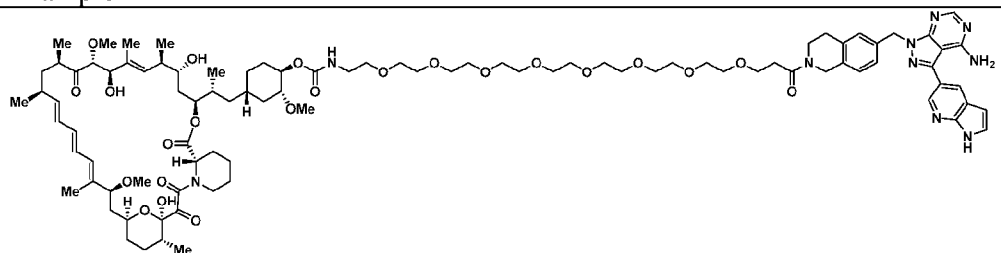
Example 7



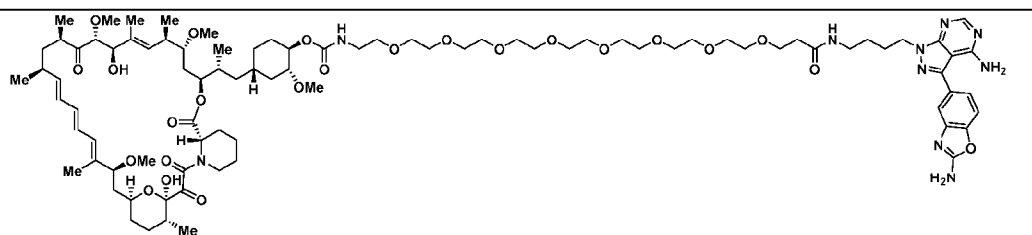
Example 8



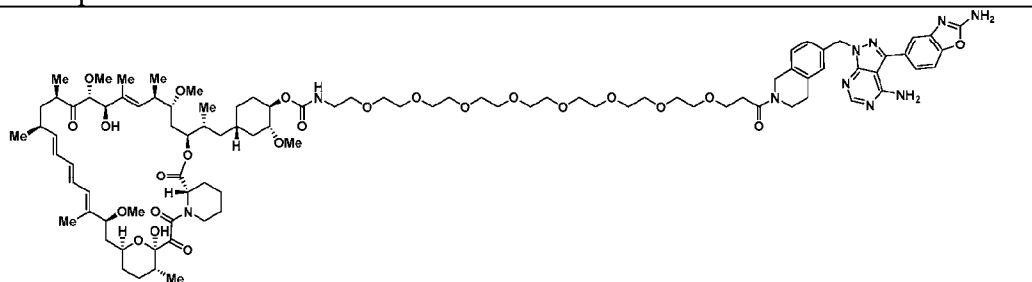
Example 9



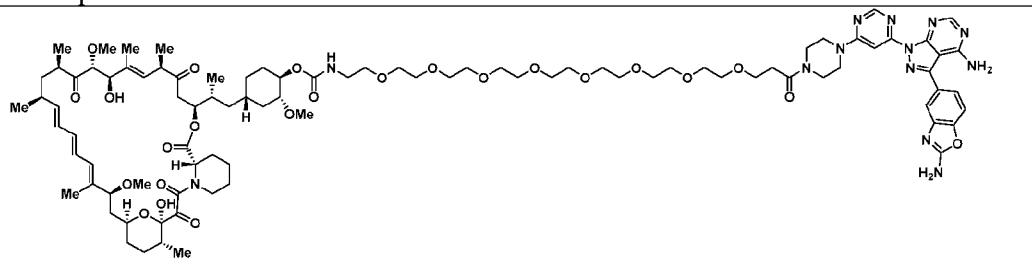
Example 10



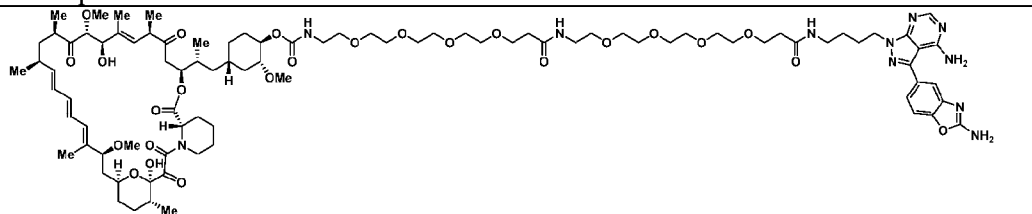
Example 11



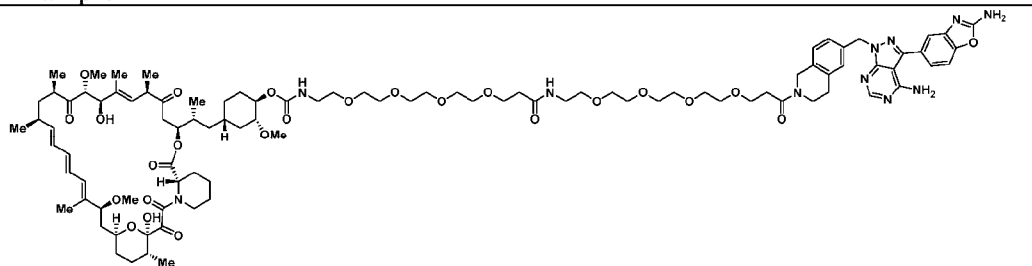
Example 12



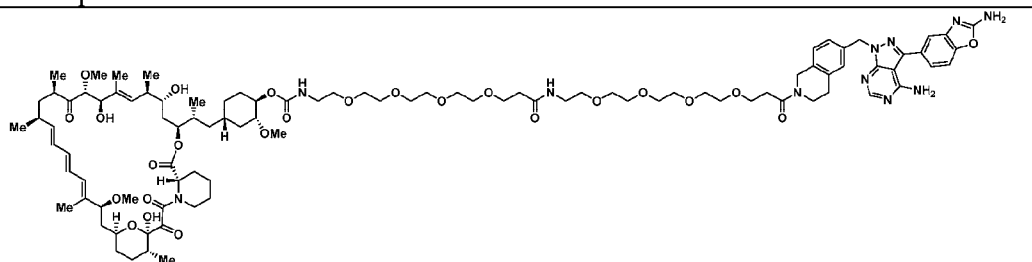
Example 13



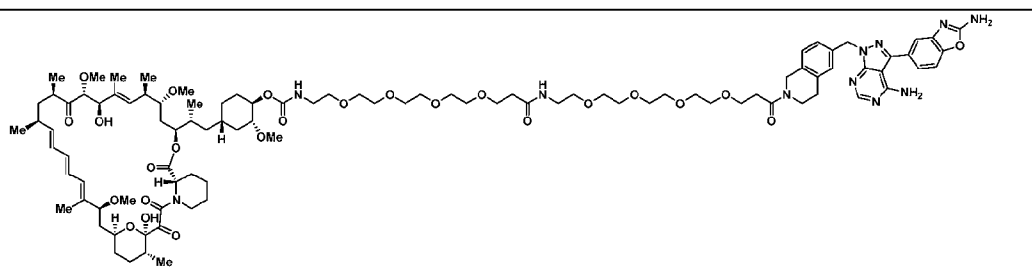
Example 14



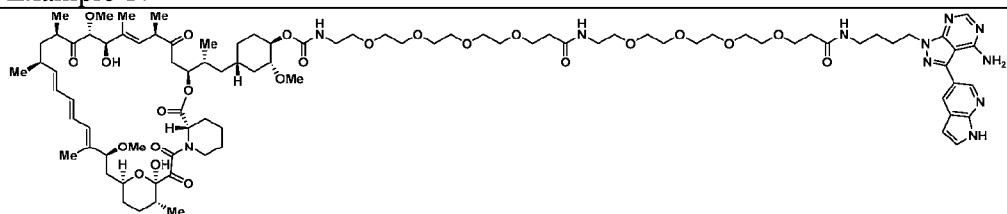
Example 15



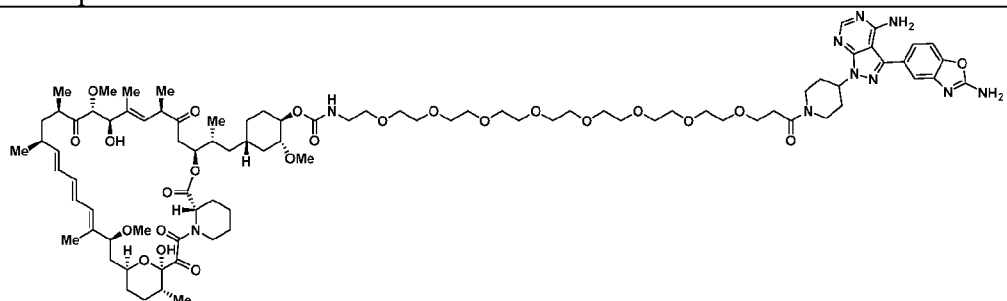
Example 16



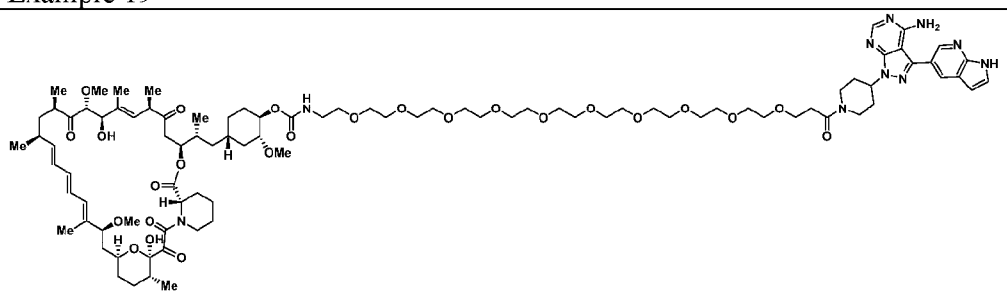
Example 17



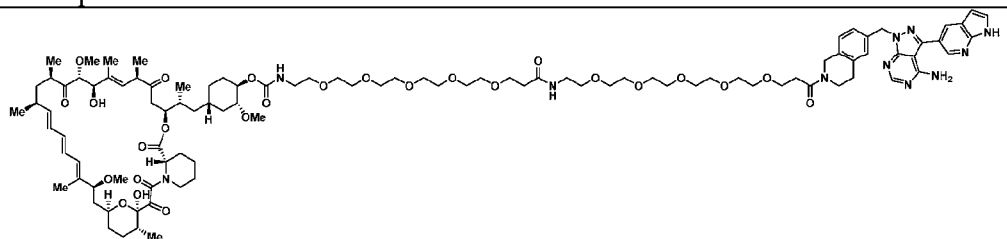
Example 18



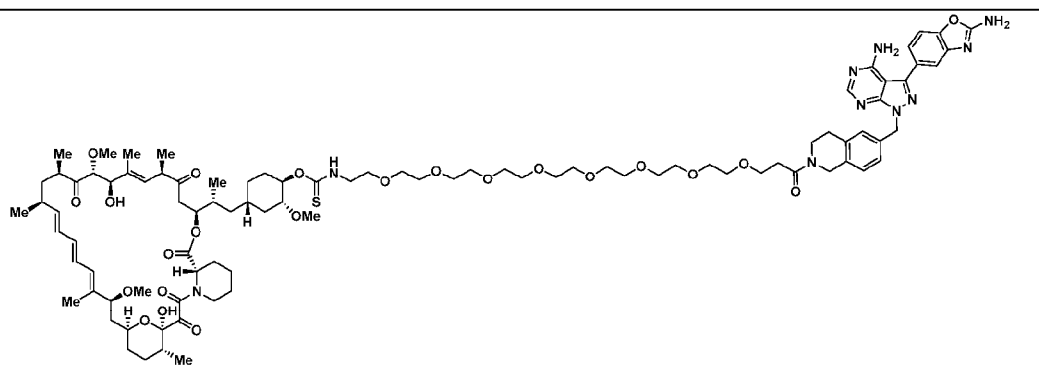
Example 19



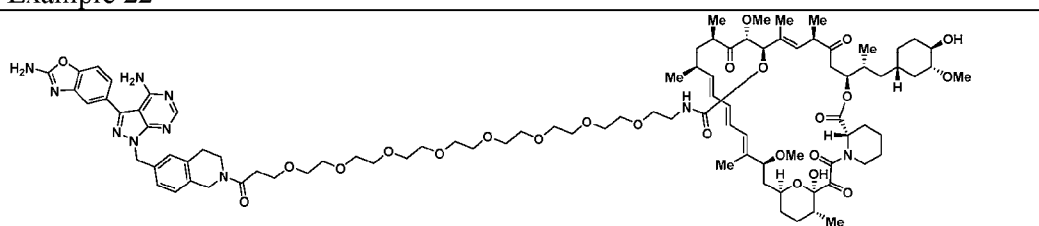
Example 20



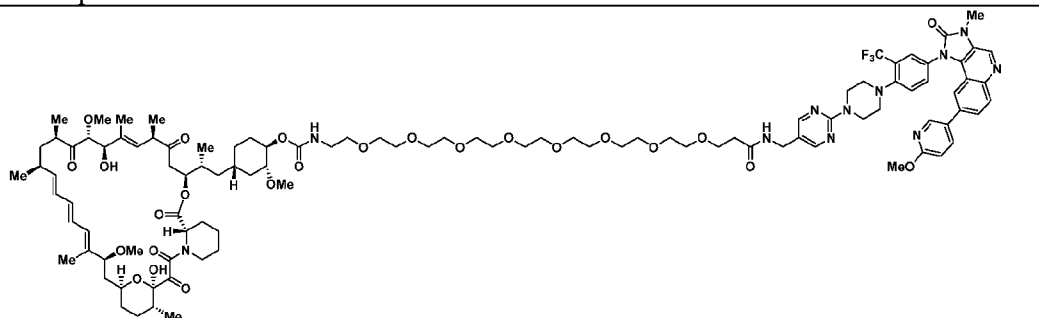
Example 21



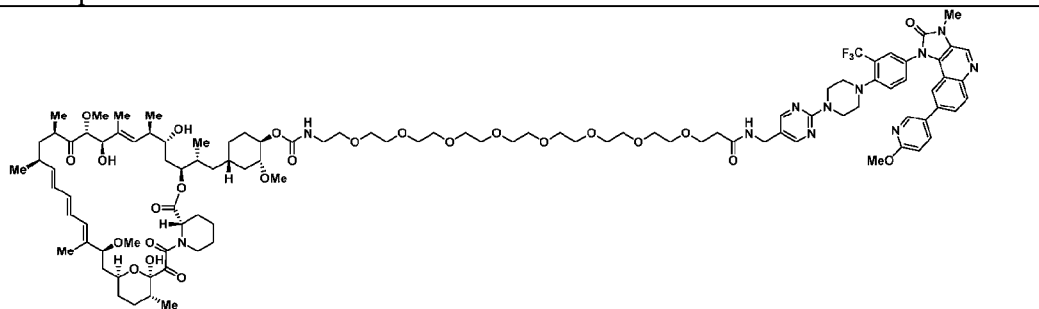
Example 22



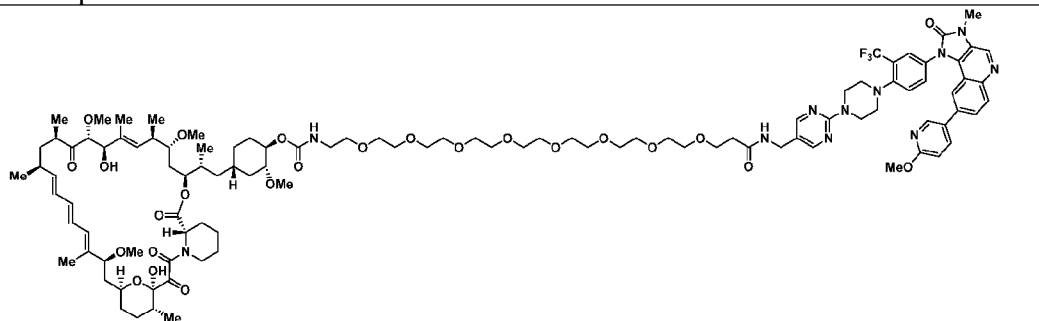
Example 23



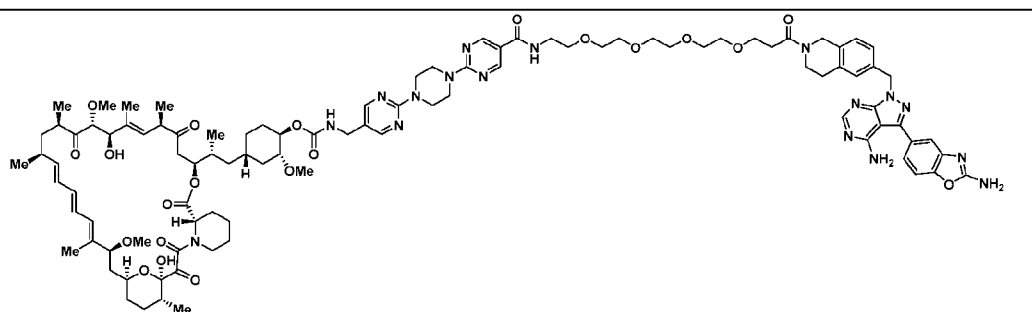
Example 24



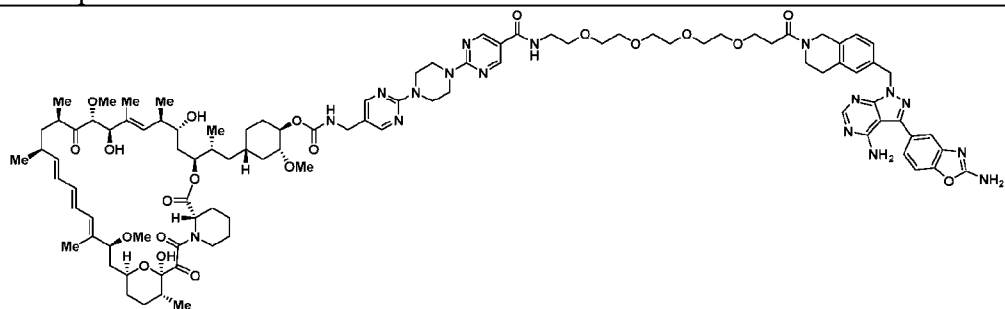
Example 25



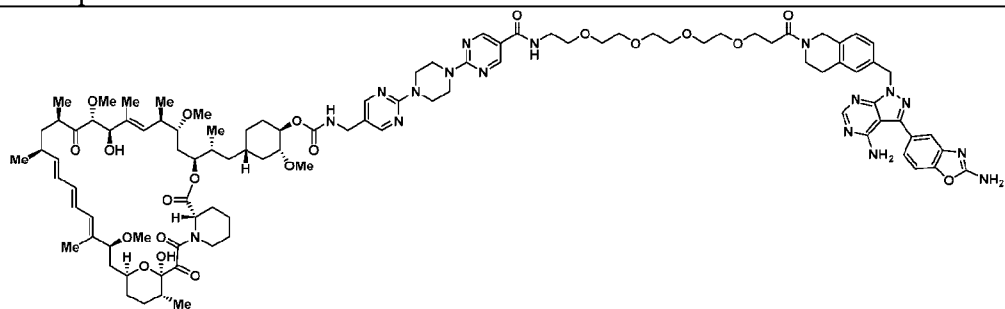
Example 26



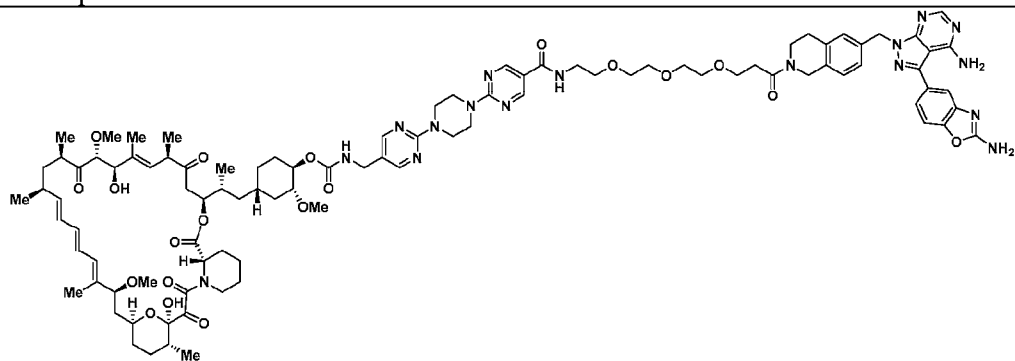
Example 27



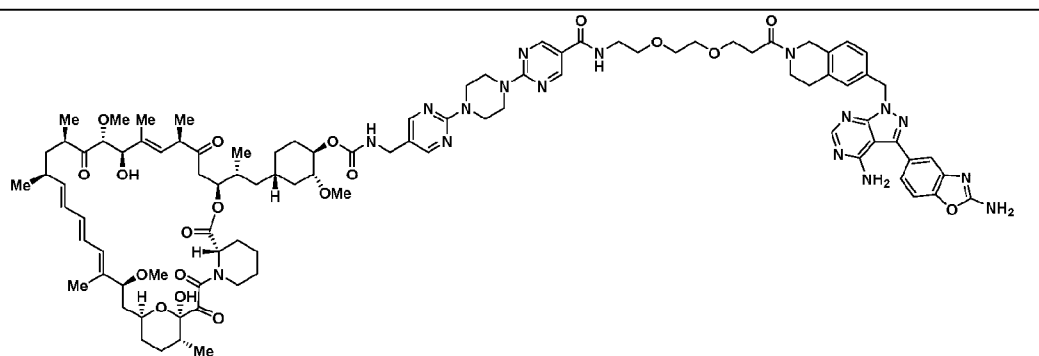
Example 28



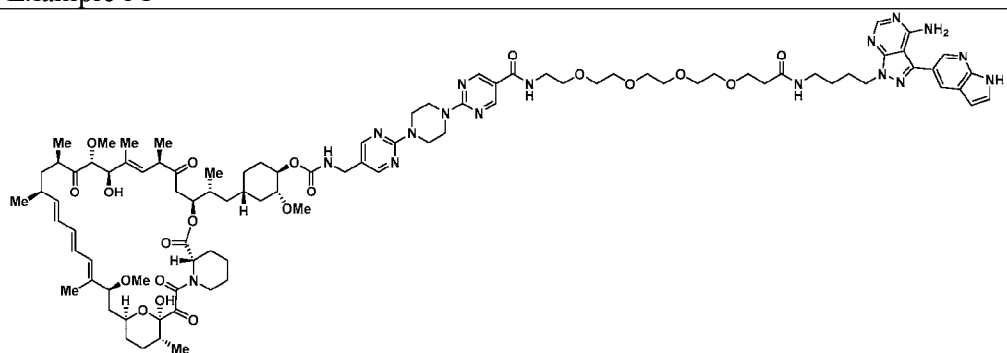
Example 29



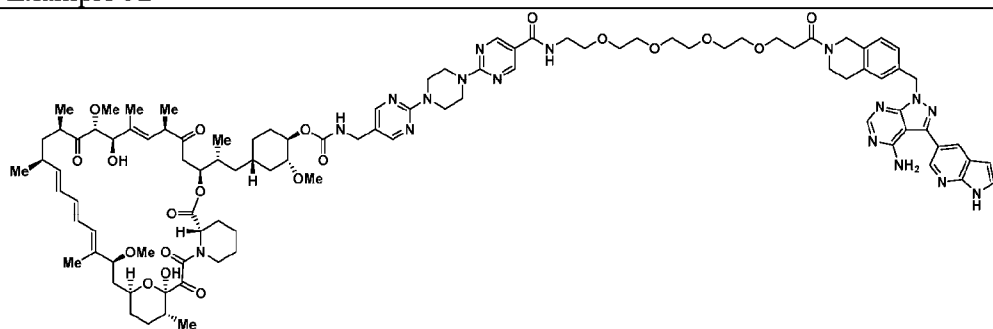
Example 30



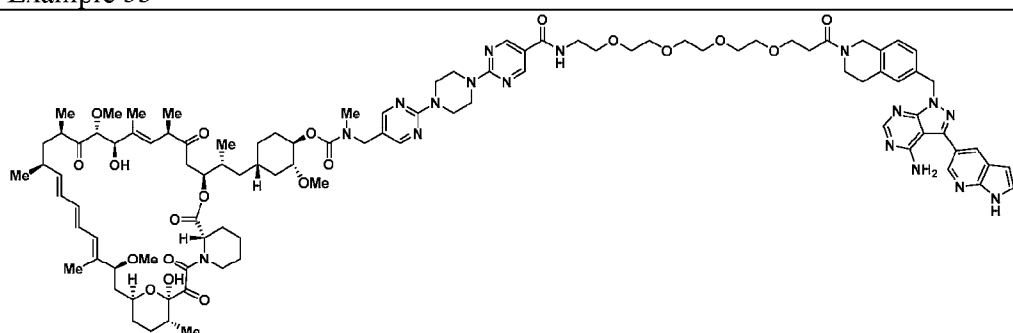
Example 31



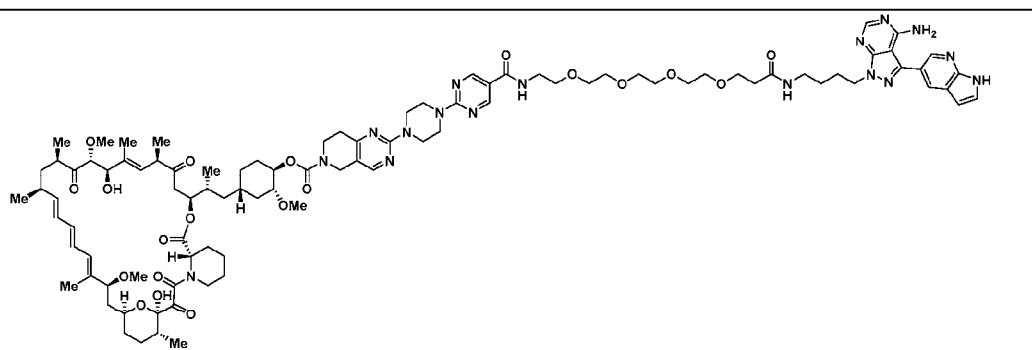
Example 32



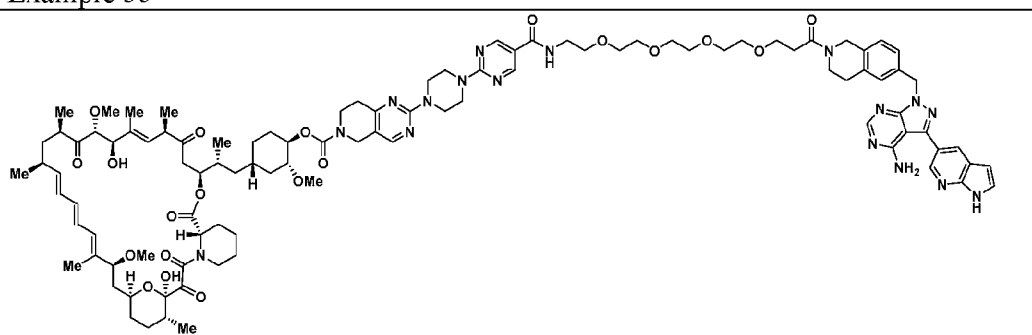
Example 33



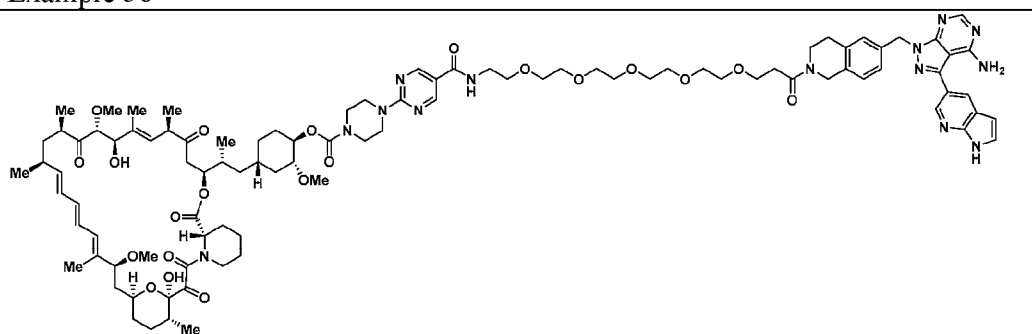
Example 34



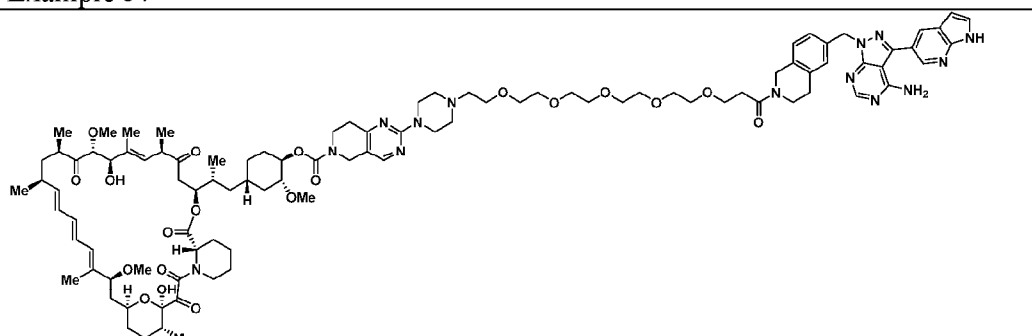
Example 35



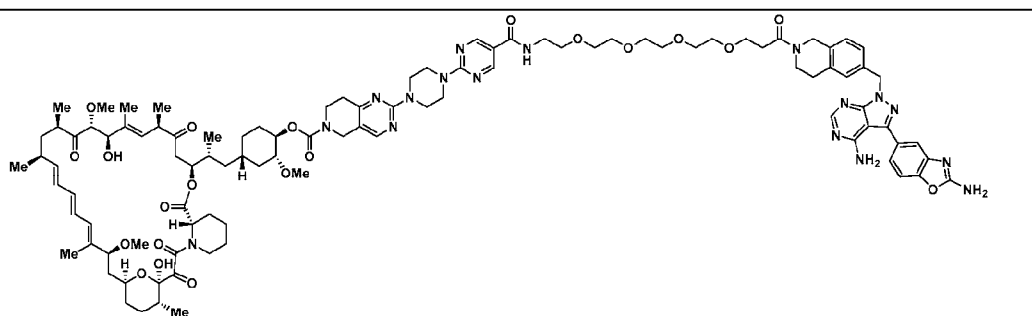
Example 36



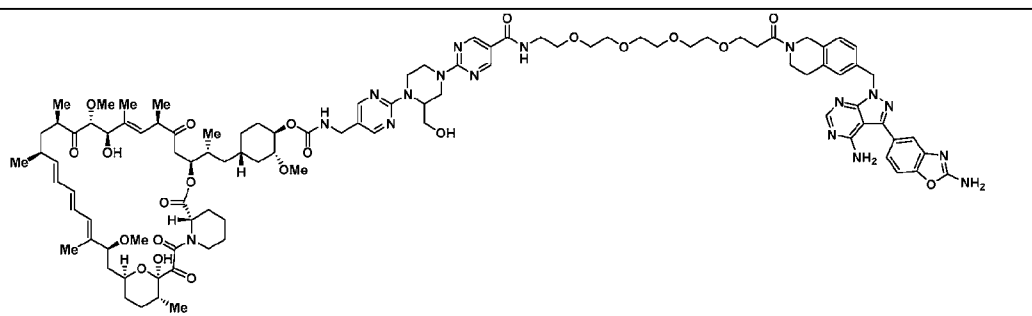
Example 37



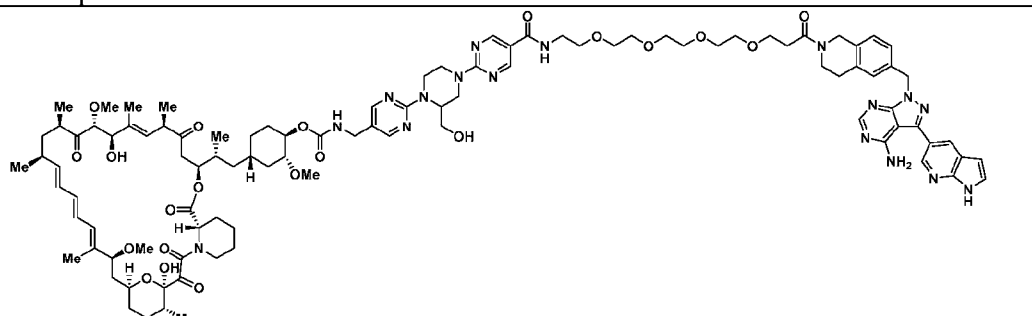
Example 38



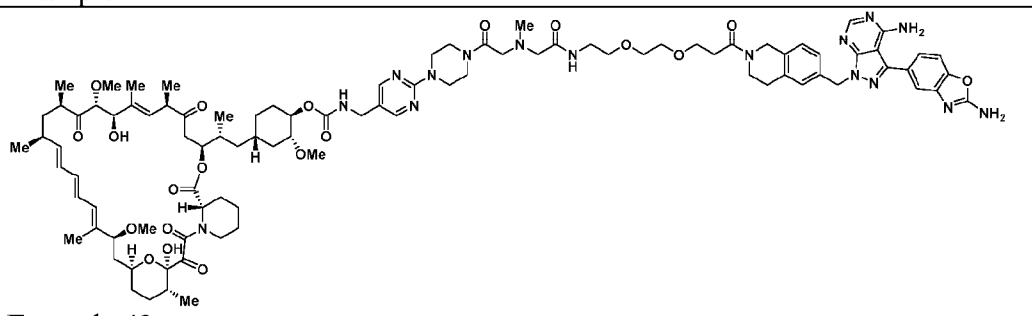
Example 39



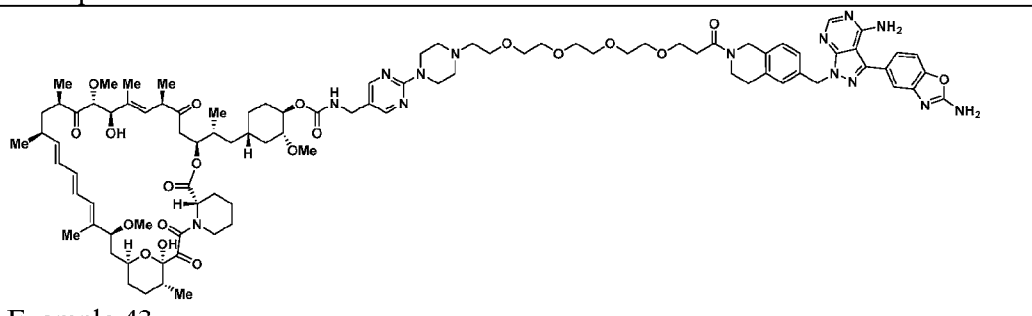
Example 40



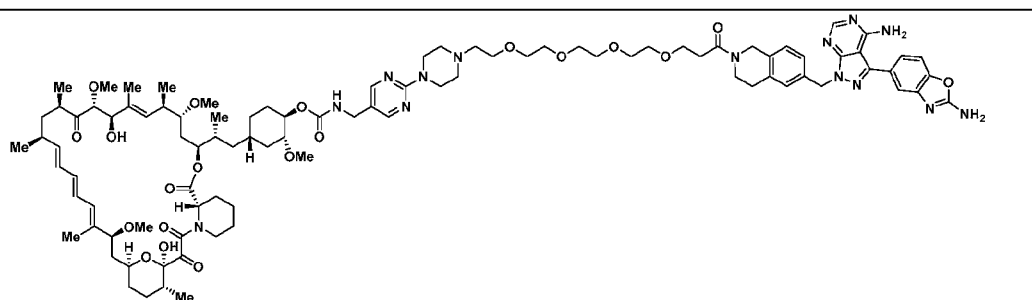
Example 41



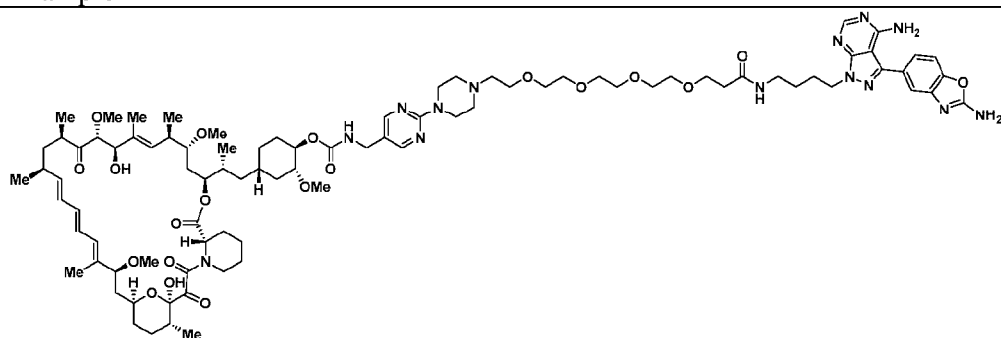
Example 42



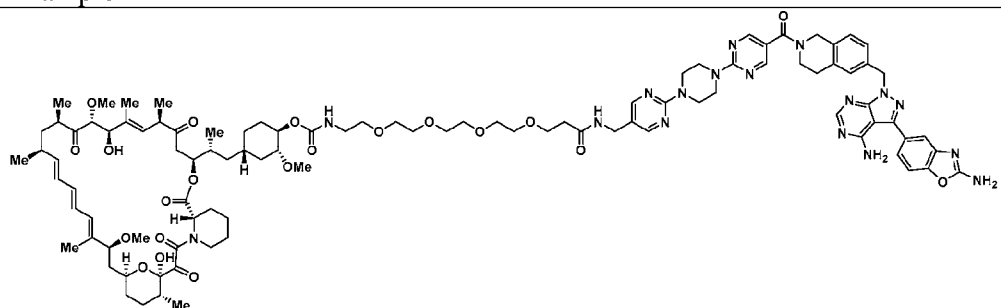
Example 43



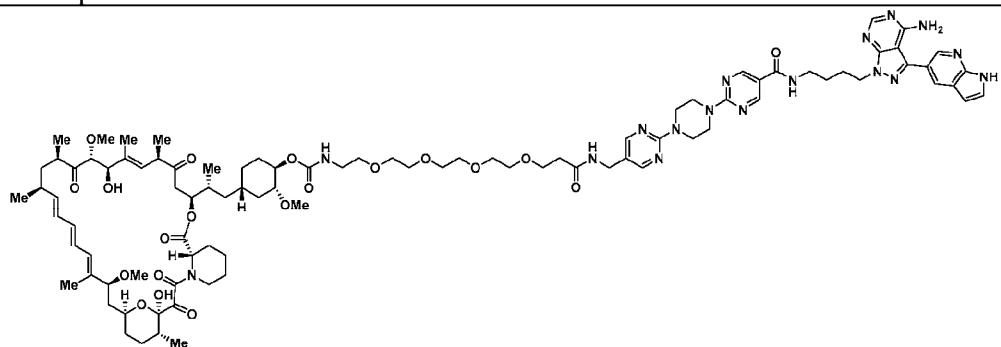
Example 44



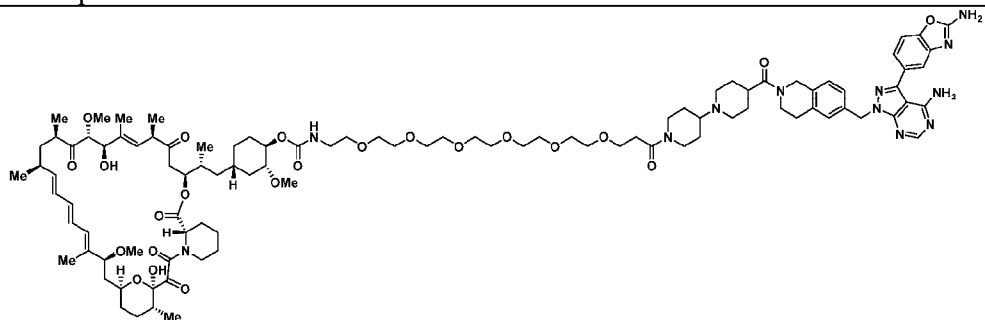
Example 45



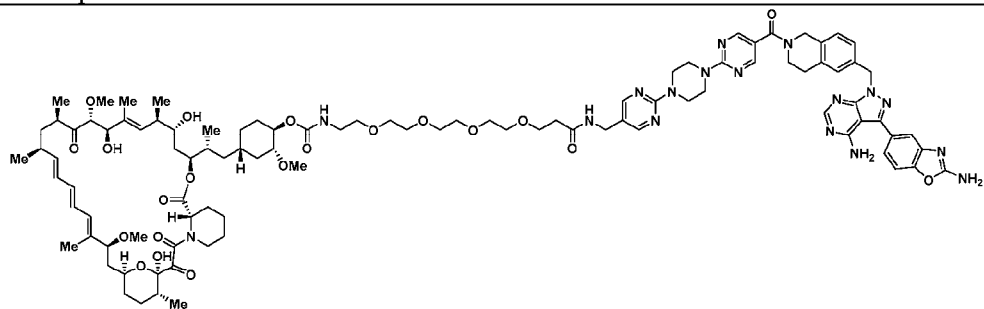
Example 46



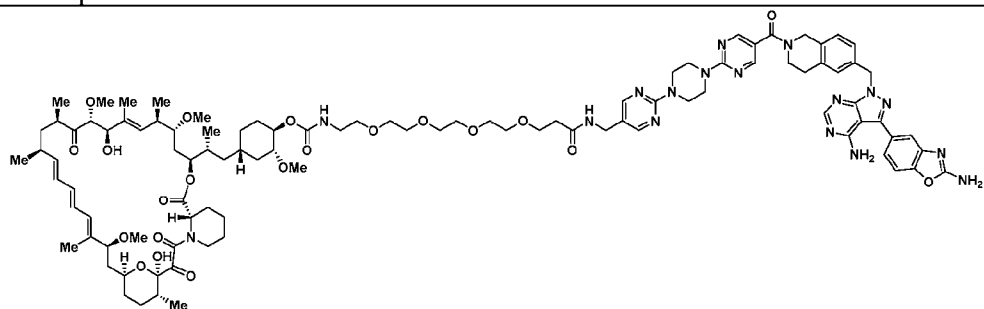
Example 47



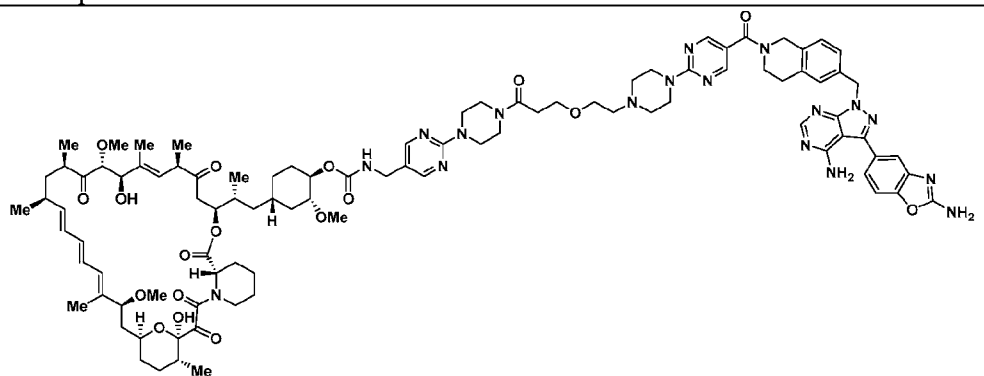
Example 48



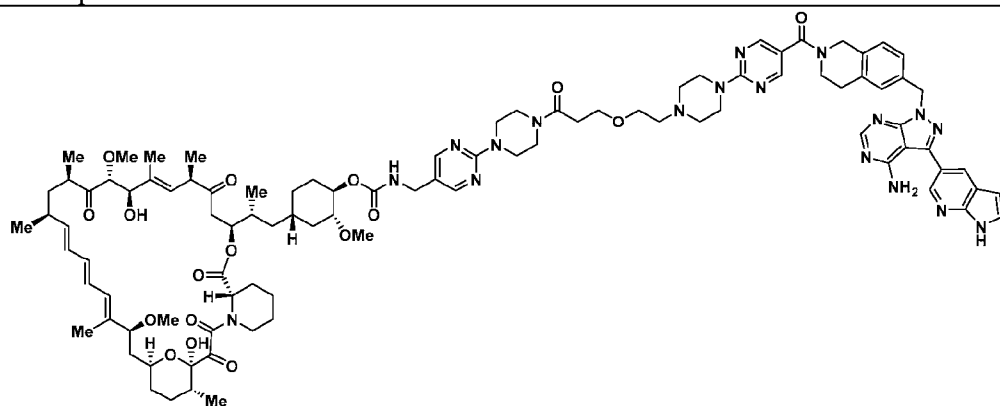
Example 49



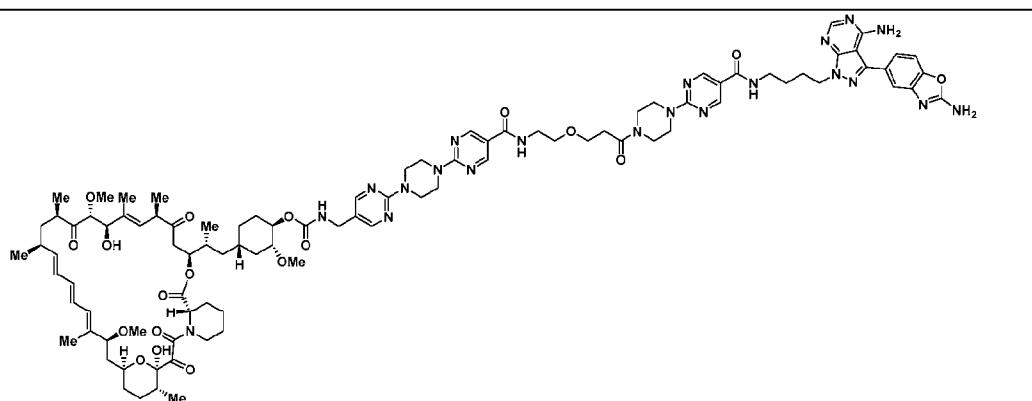
Example 50



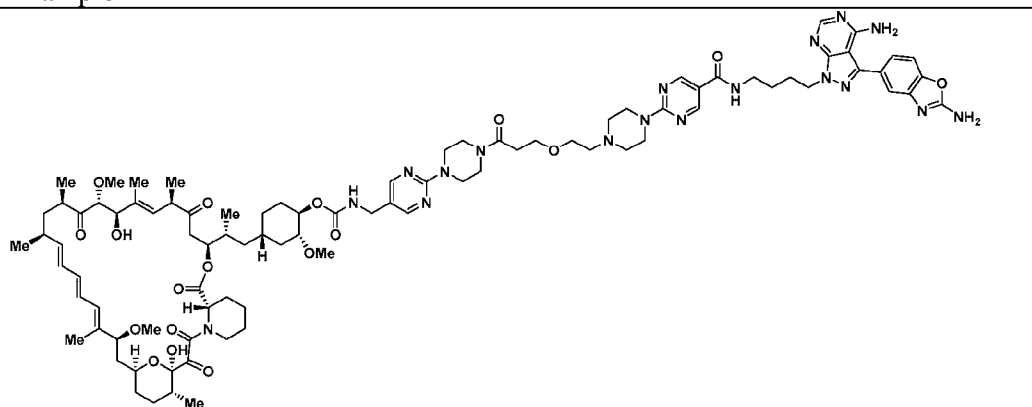
Example 51



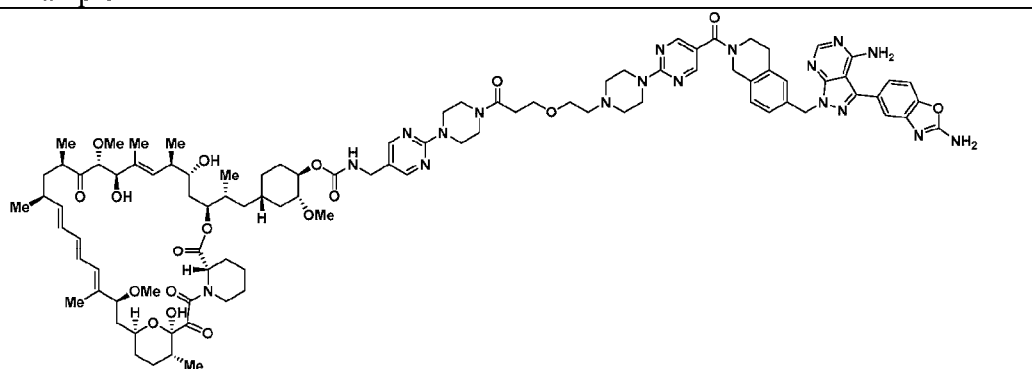
Example 52



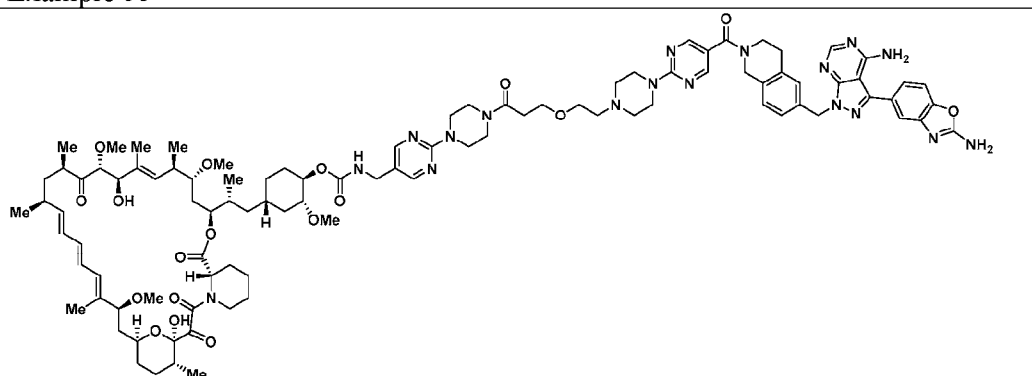
Example 53



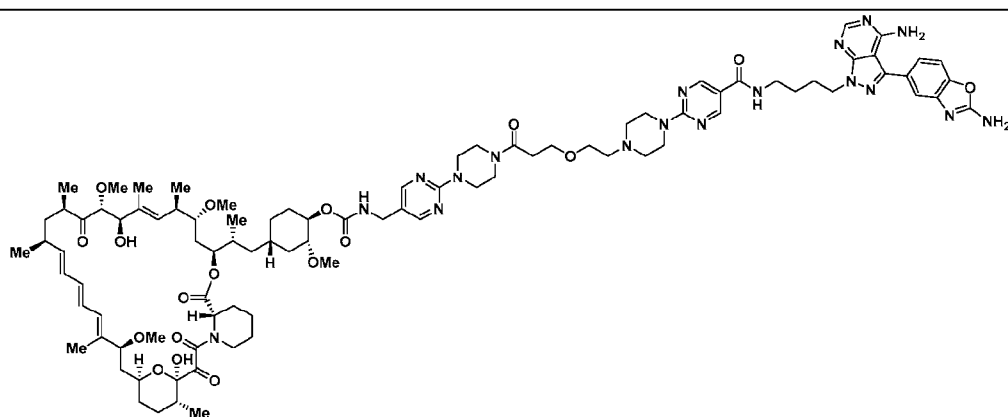
Example 54



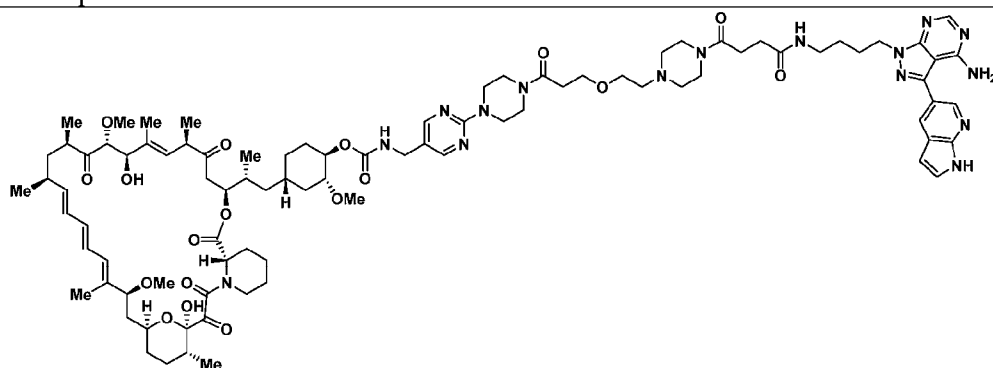
Example 55



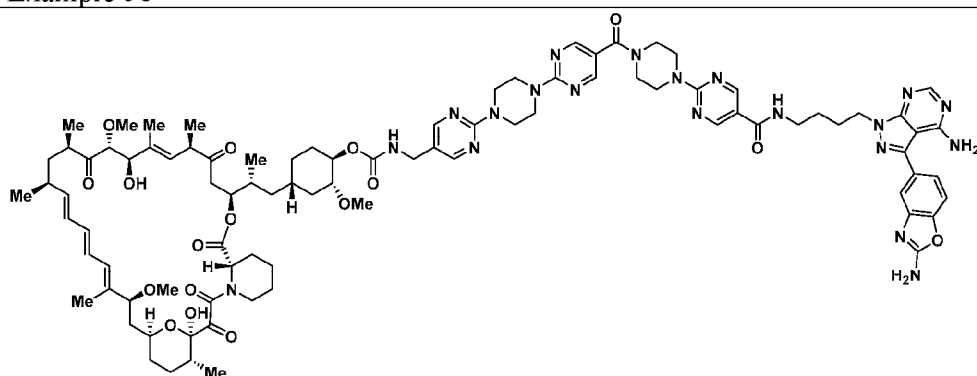
Example 56



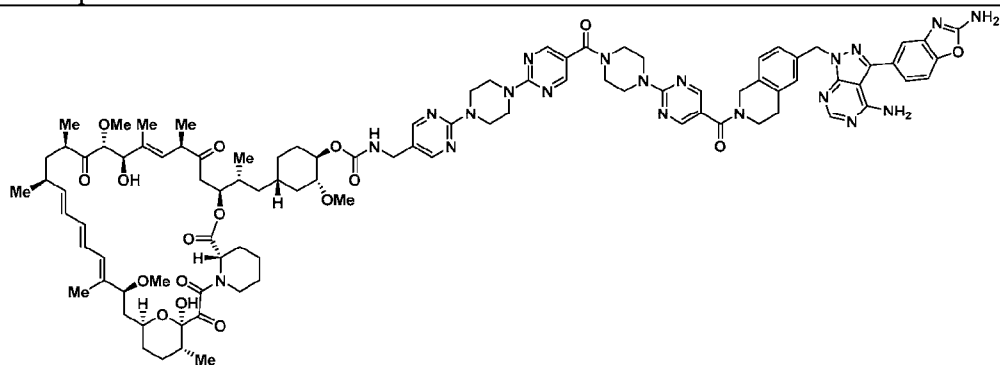
Example 57



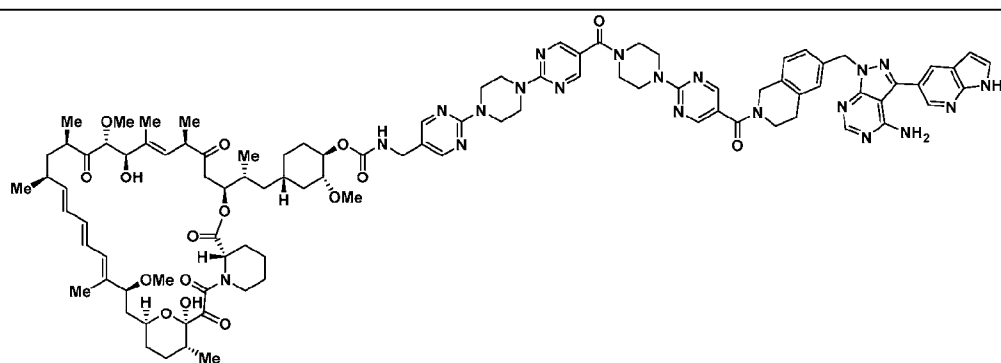
Example 58



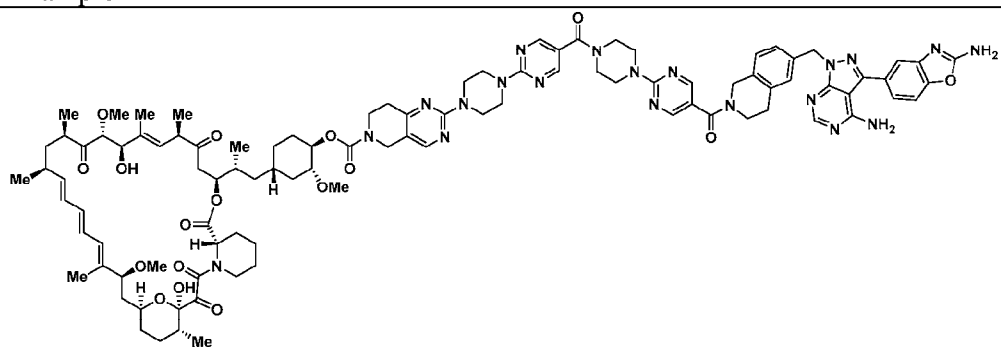
Example 59



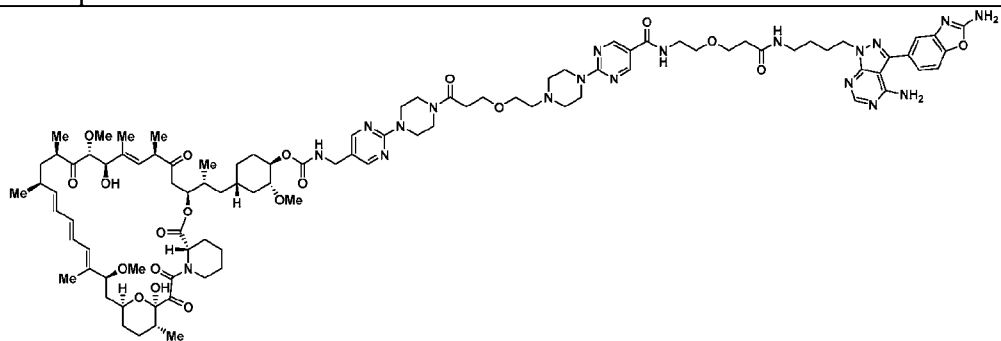
Example 60



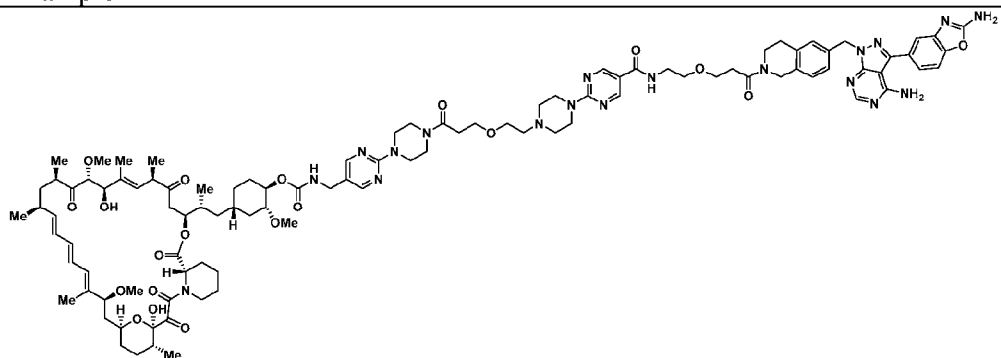
Example 61



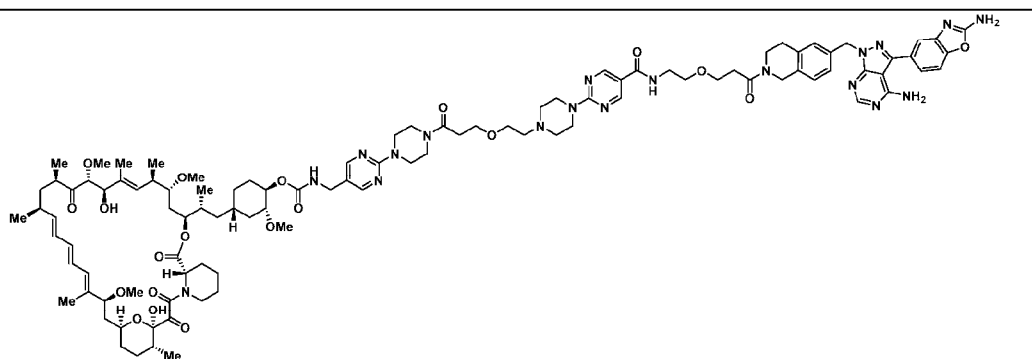
Example 62



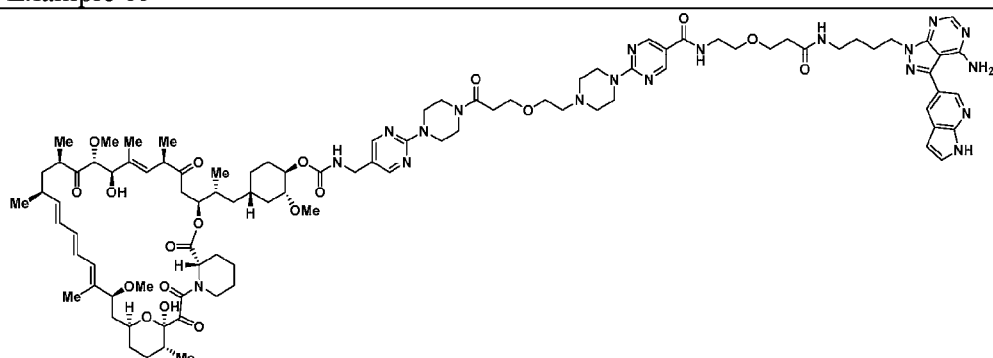
Example 63



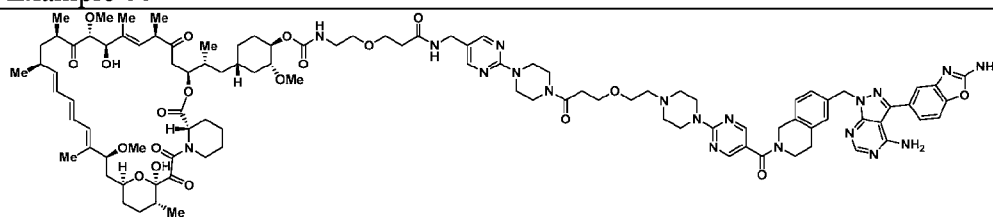
Example 64



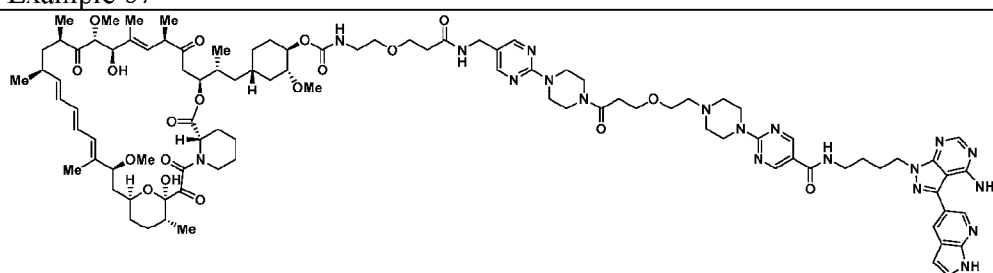
Example 65



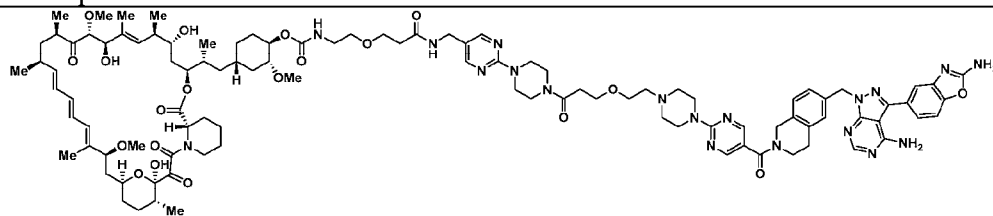
Example 66



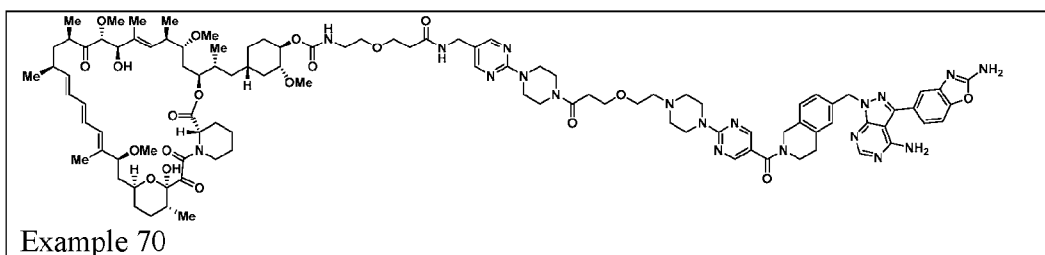
Example 67



Example 68

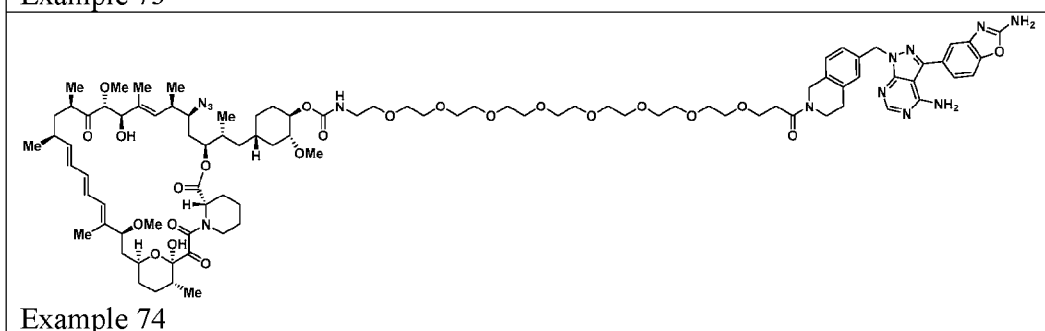
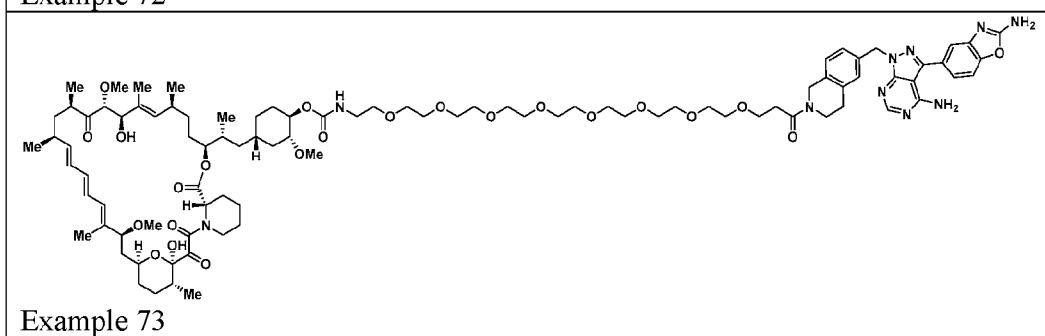
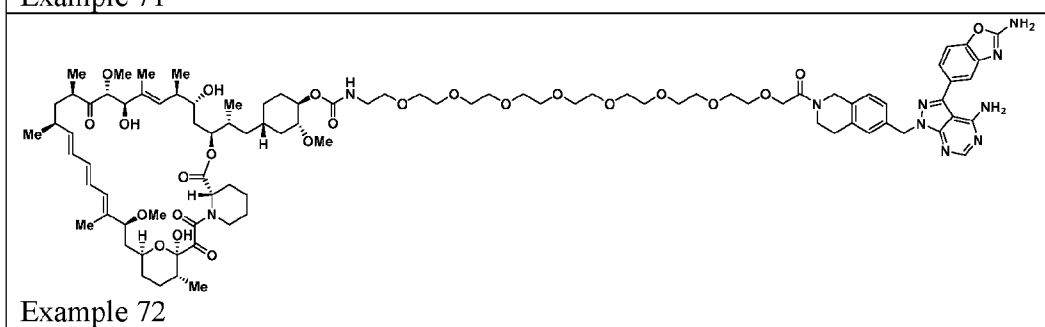
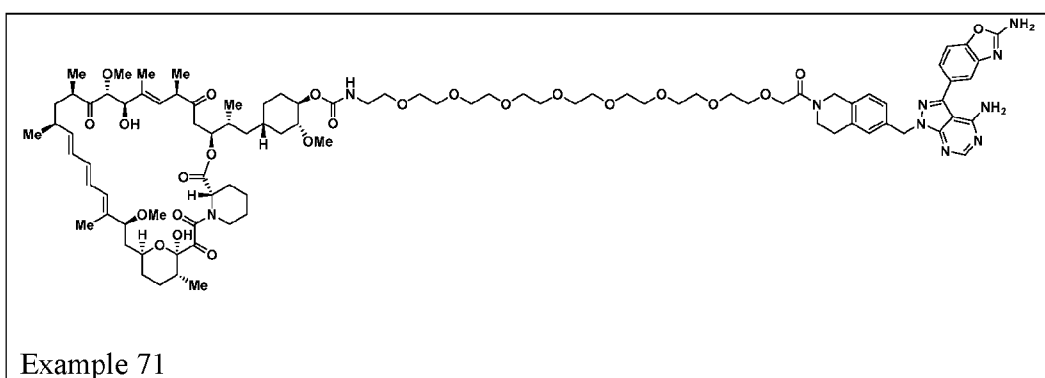


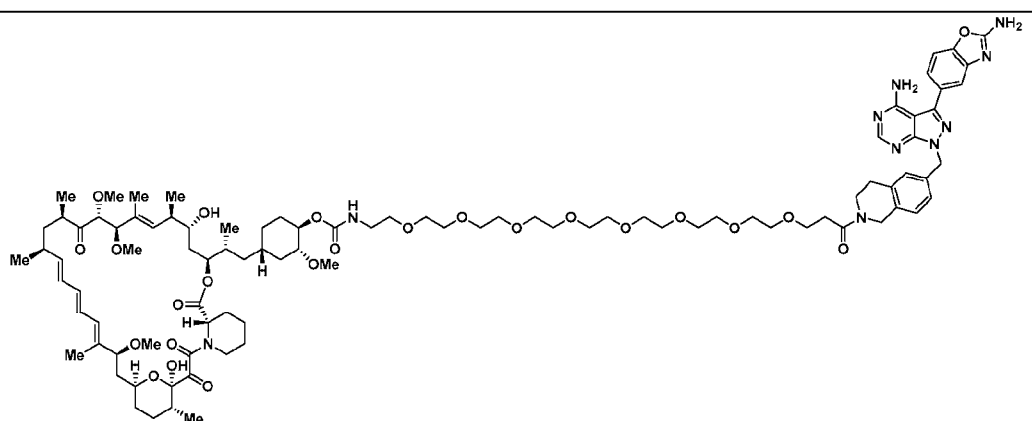
Example 69



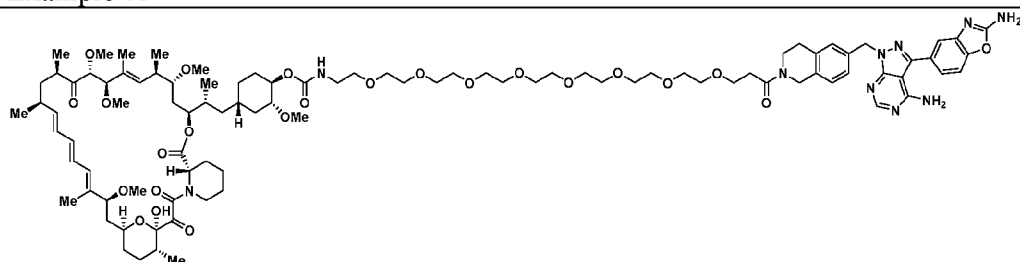
or a pharmaceutically acceptable salt or tautomer thereof.

73. A compound selected from the group consisting of:

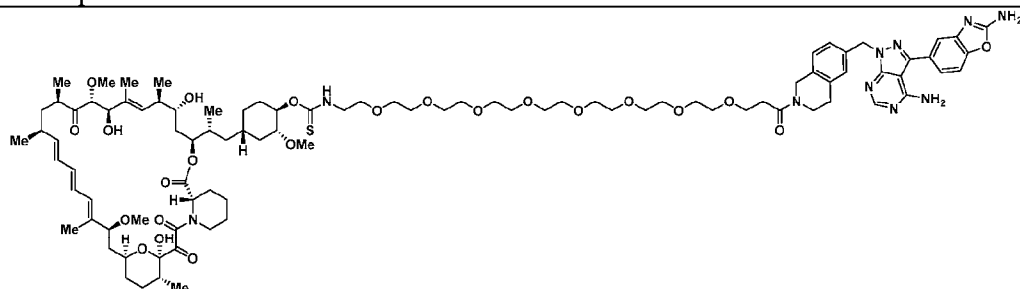




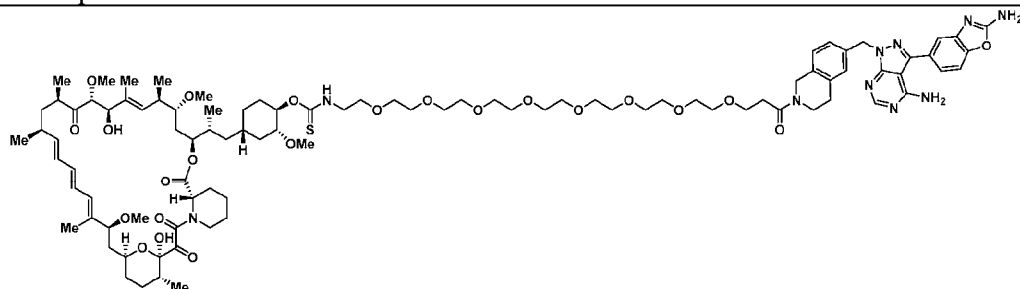
Example 75



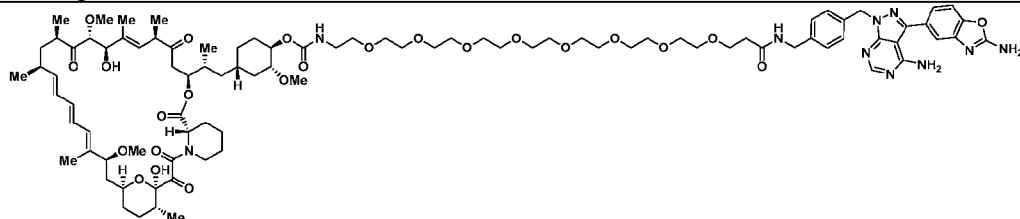
Example 76



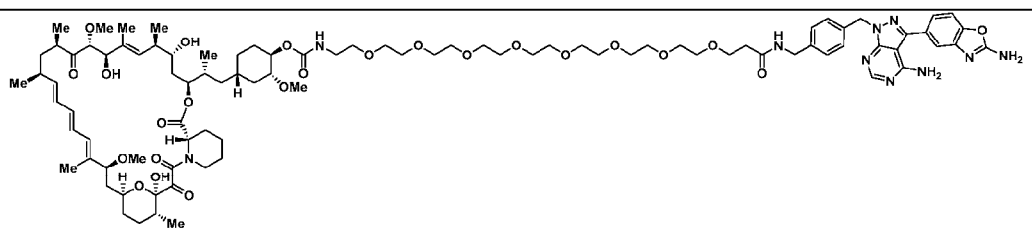
Example 77



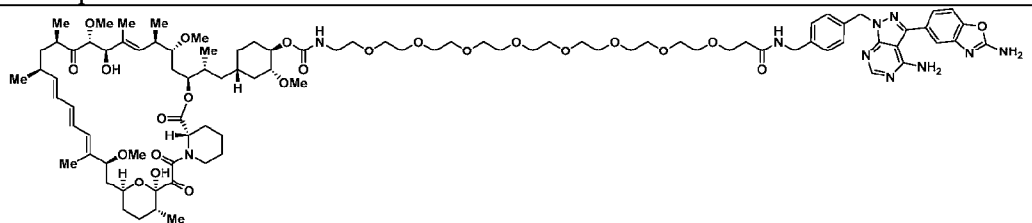
Example 78



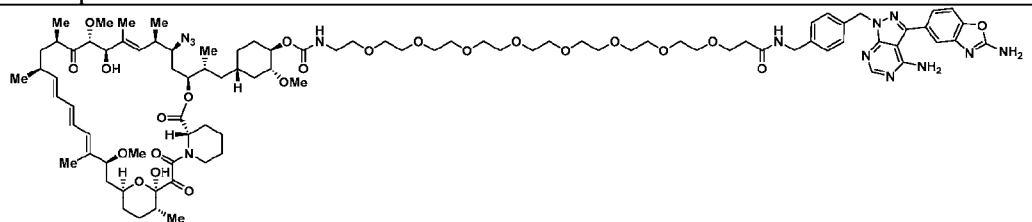
Example 79



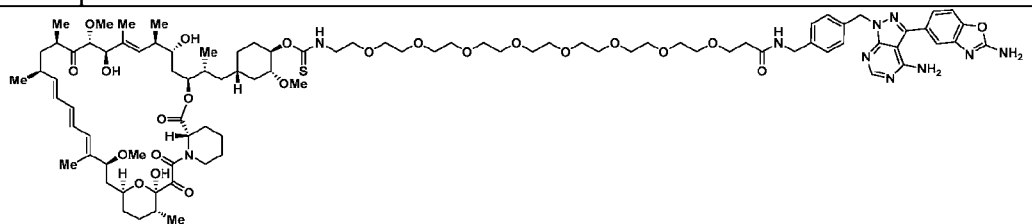
Example 80



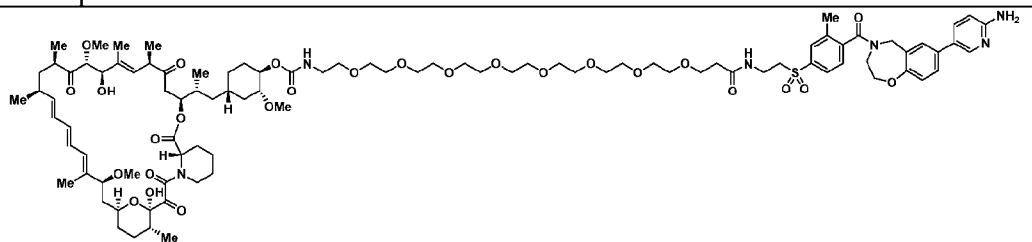
Example 81



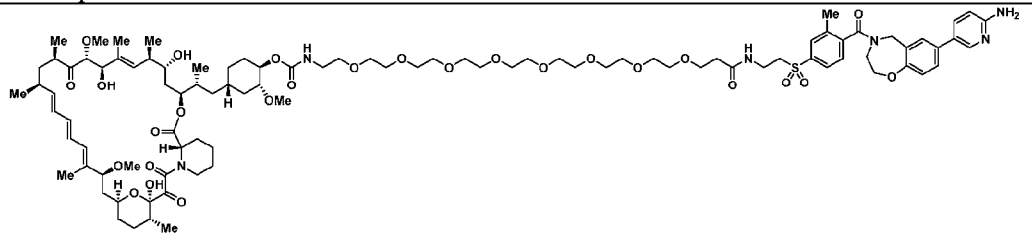
Example 82



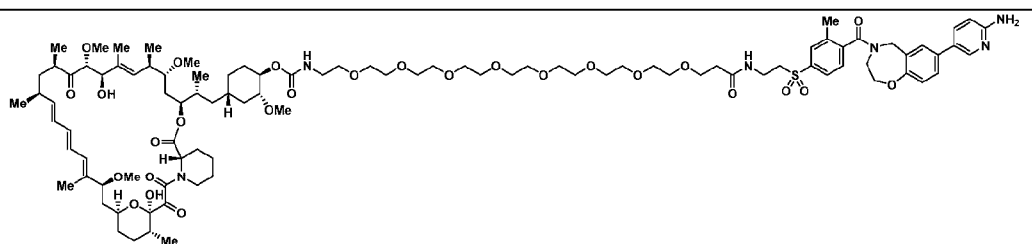
Example 83



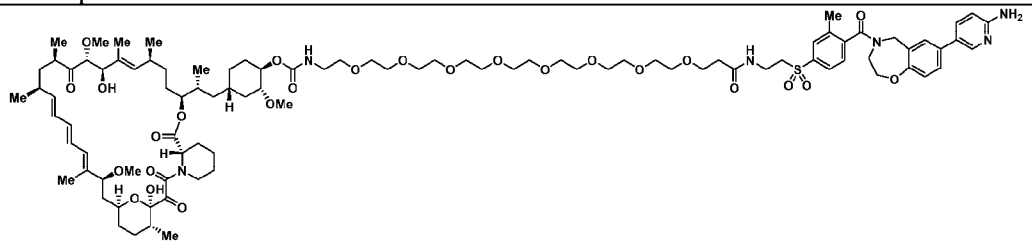
Example 84



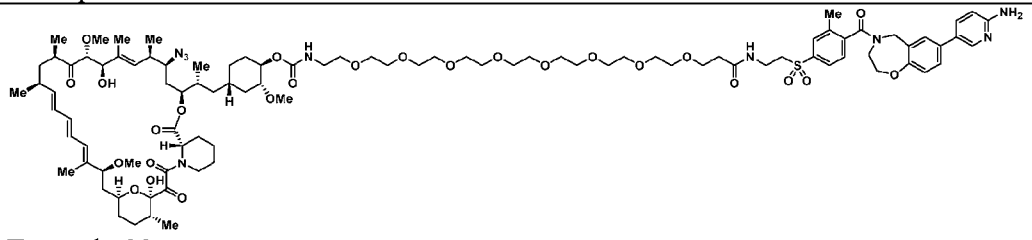
Example 85



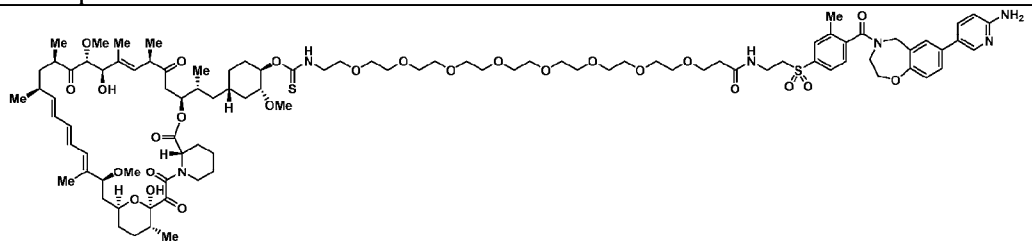
Example 86



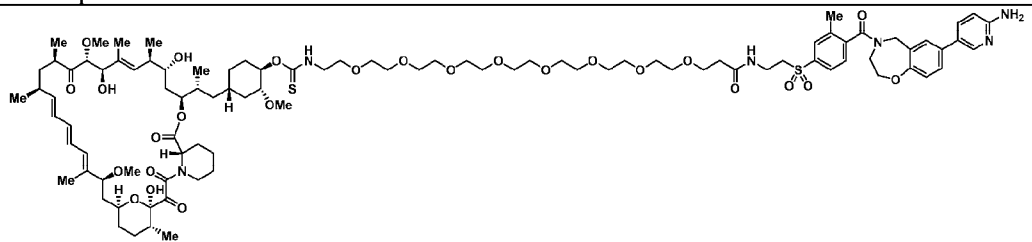
Example 87



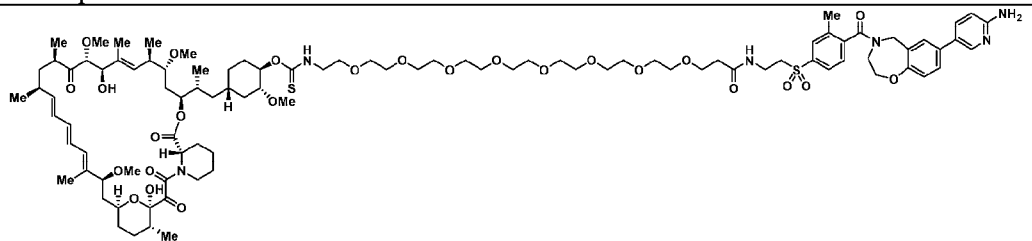
Example 88



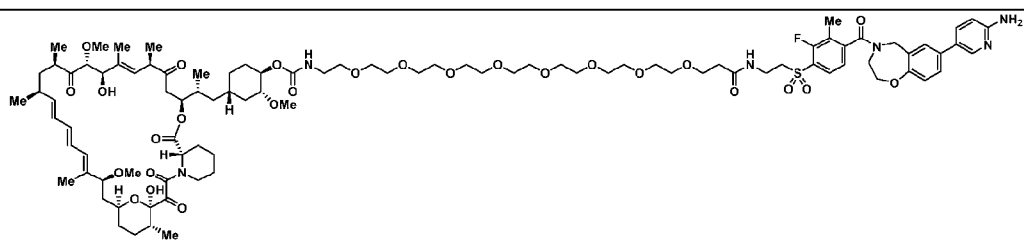
Example 89



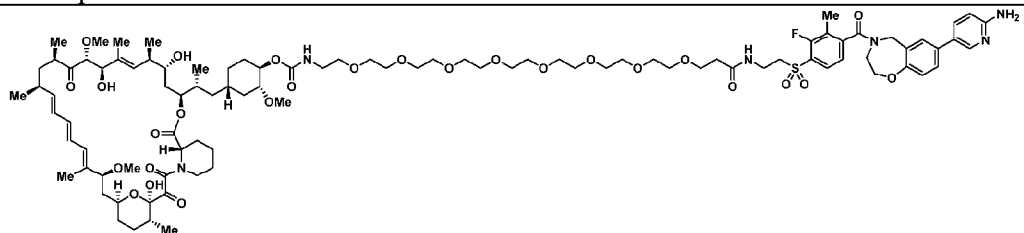
Example 90



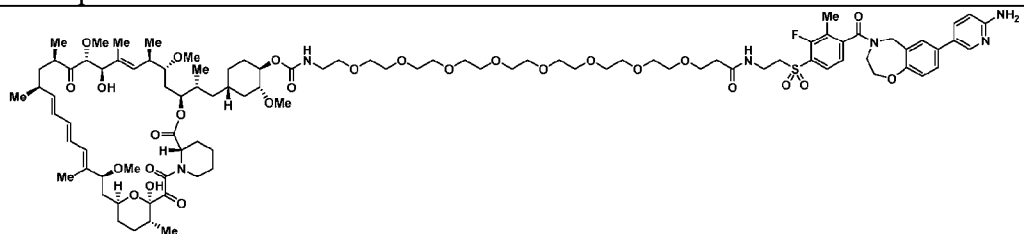
Example 91



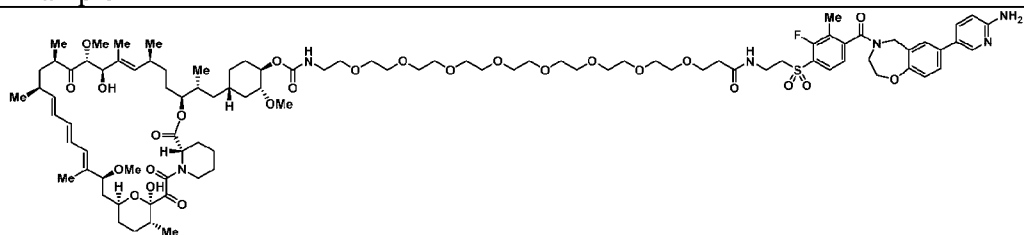
Example 92



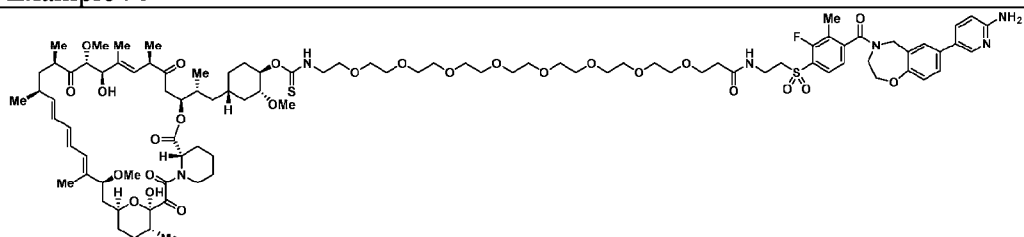
Example 93



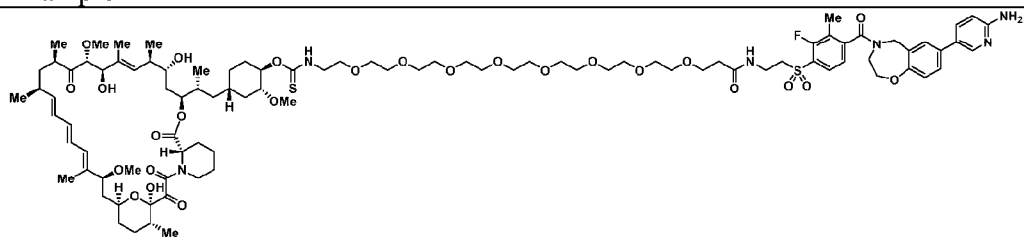
Example 94



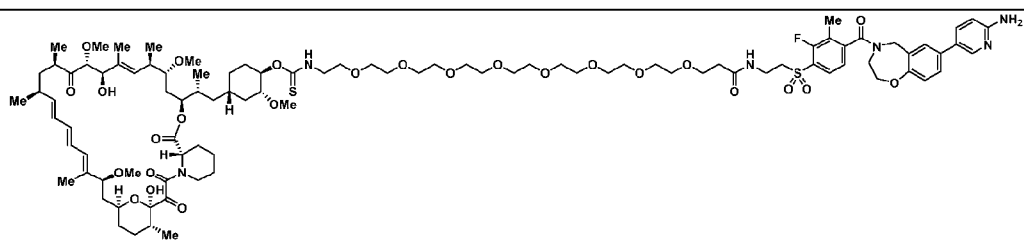
Example 95



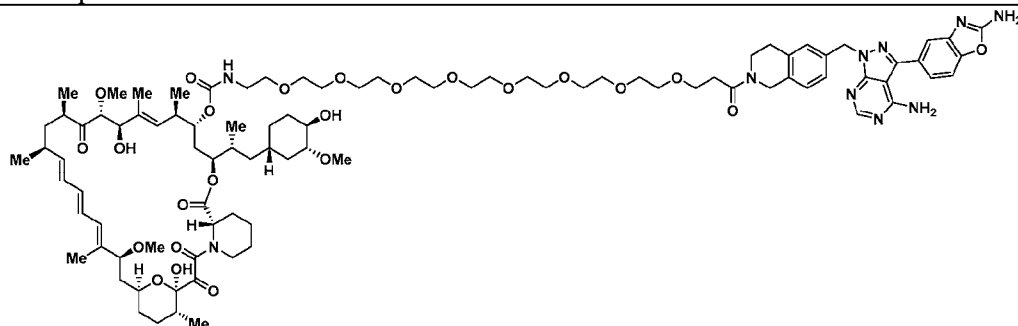
Example 96



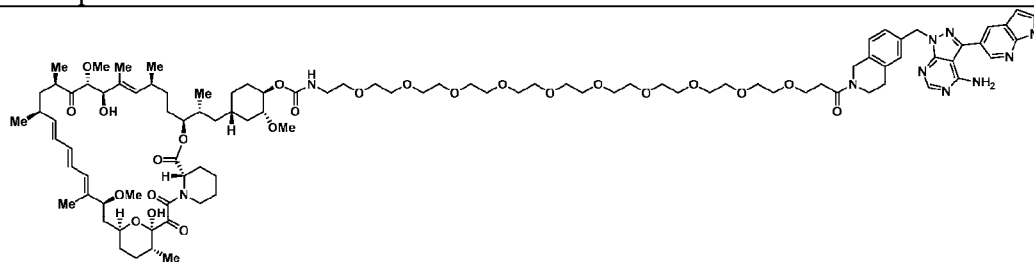
Example 97



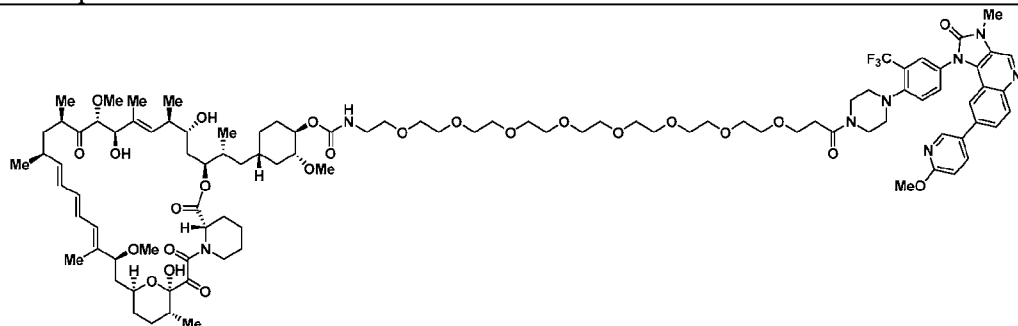
Example 98



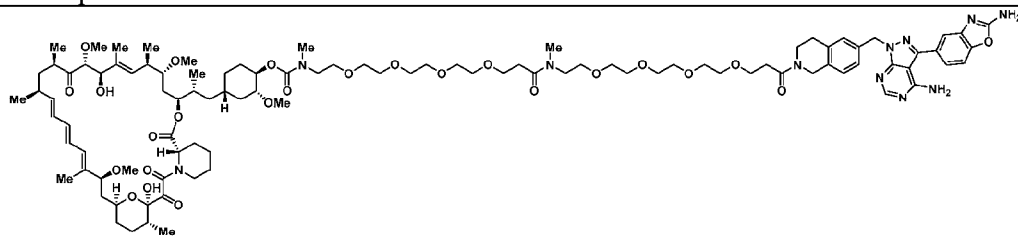
Example 99



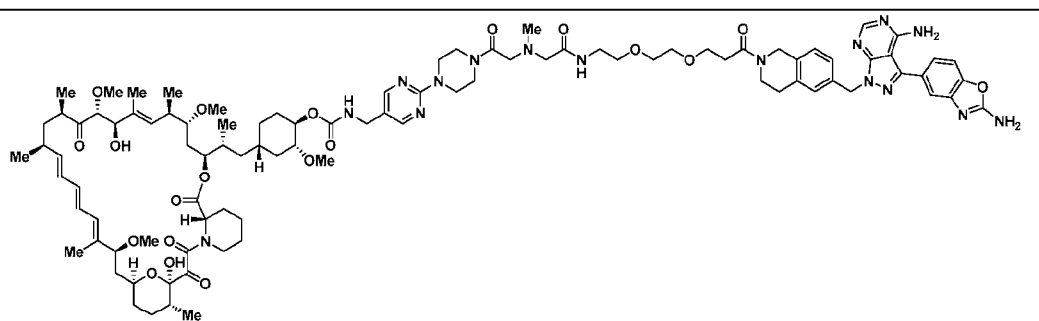
Example 100



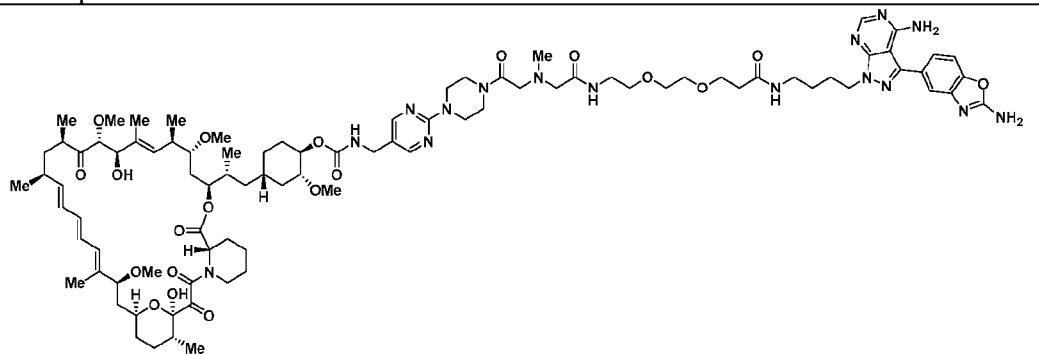
Example 101



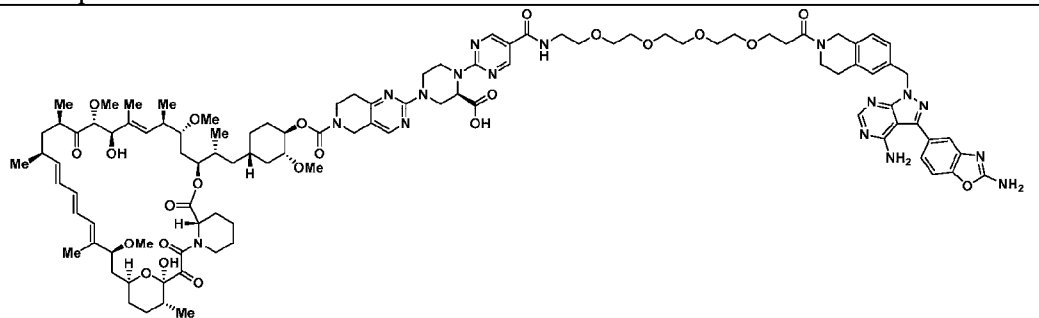
Example 102



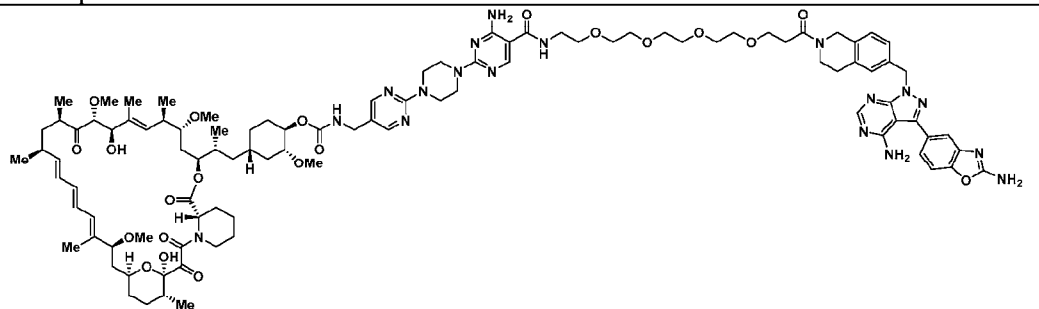
Example 103



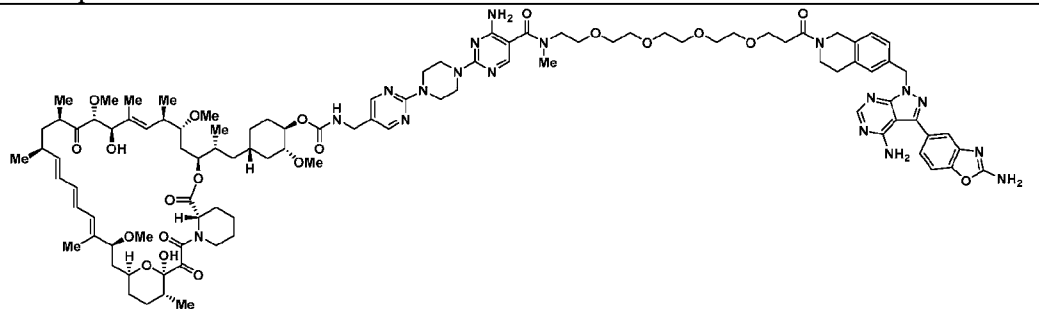
Example 104



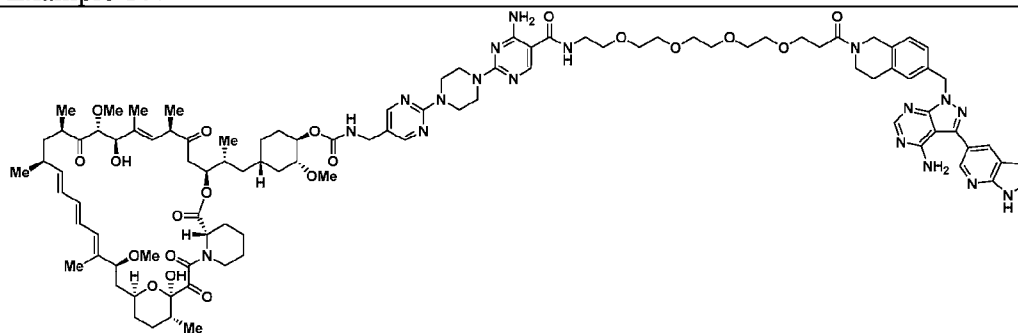
Example 105



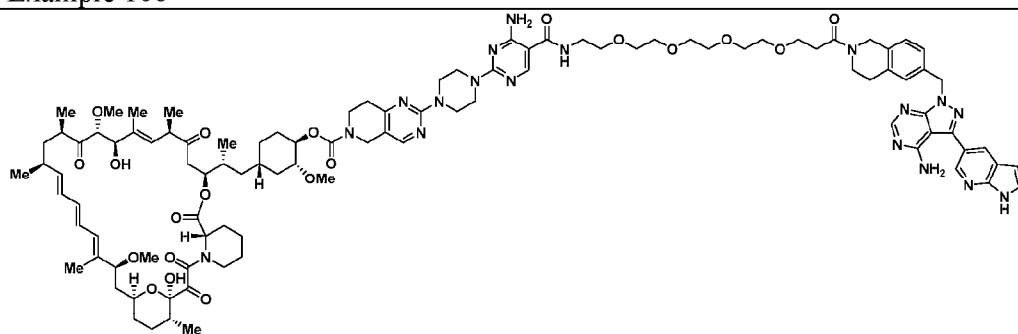
Example 106



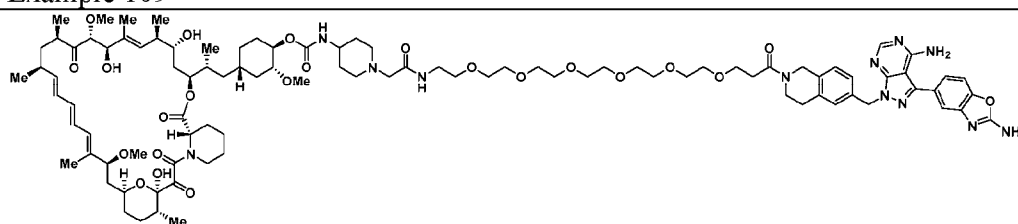
Example 107



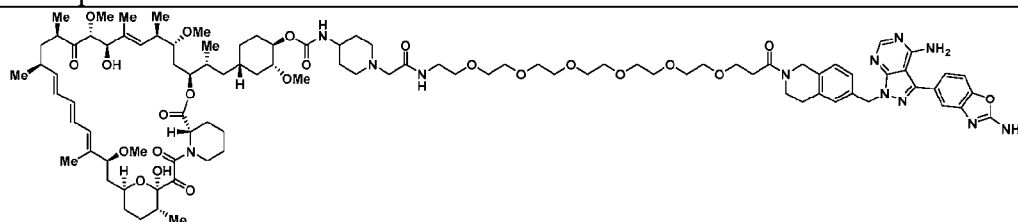
Example 108



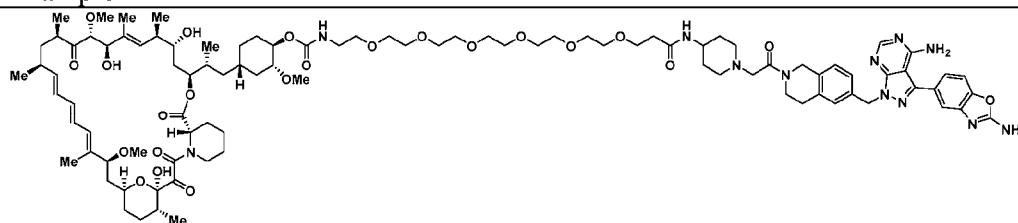
Example 109



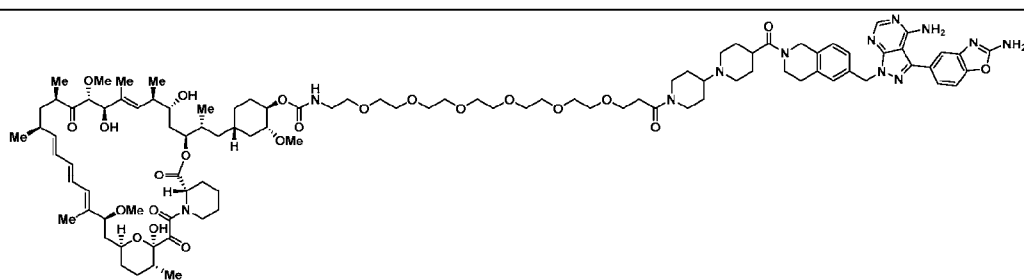
Example 110



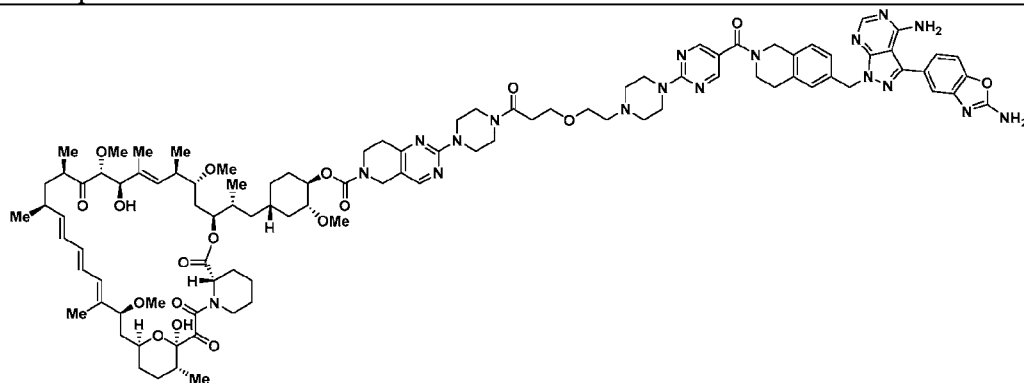
Example 111



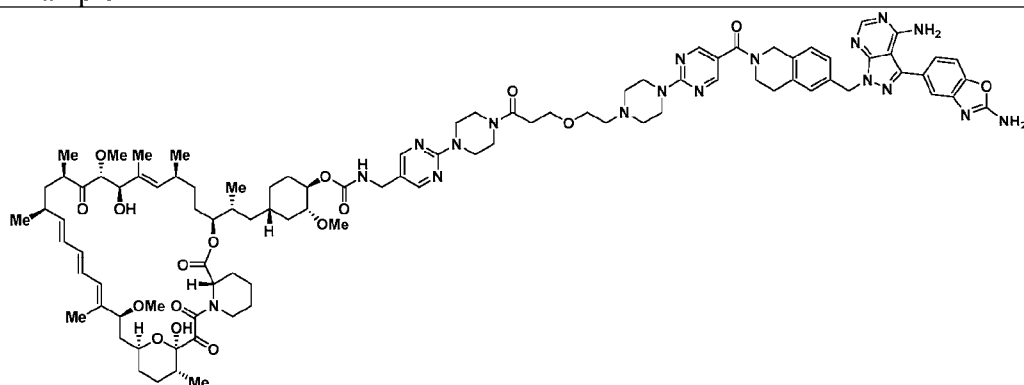
Example 112



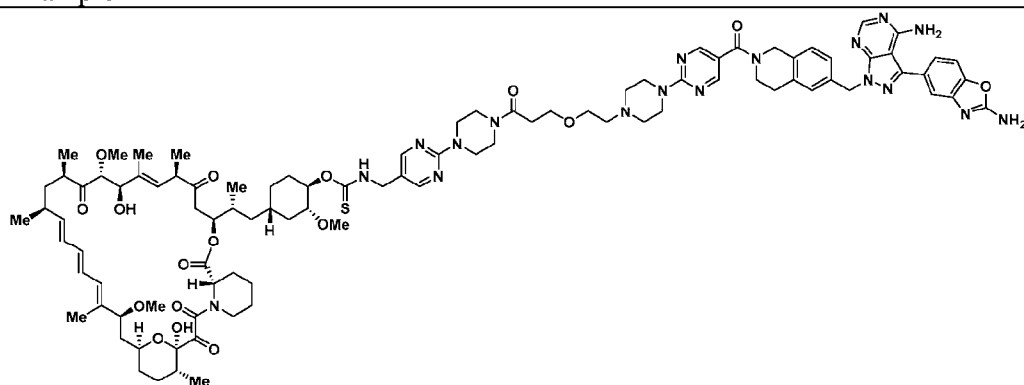
Example 113



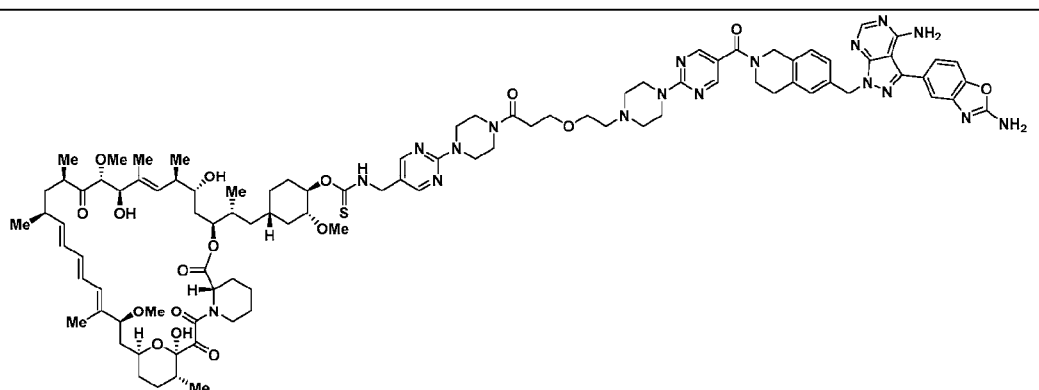
Example 114



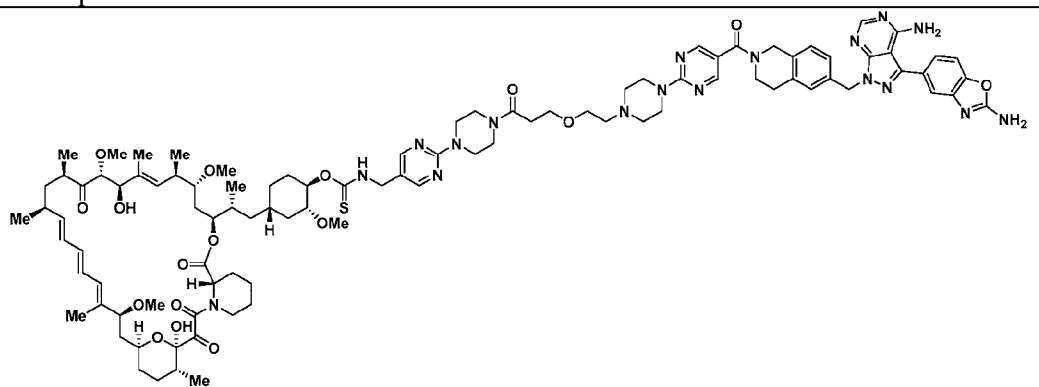
Example 115



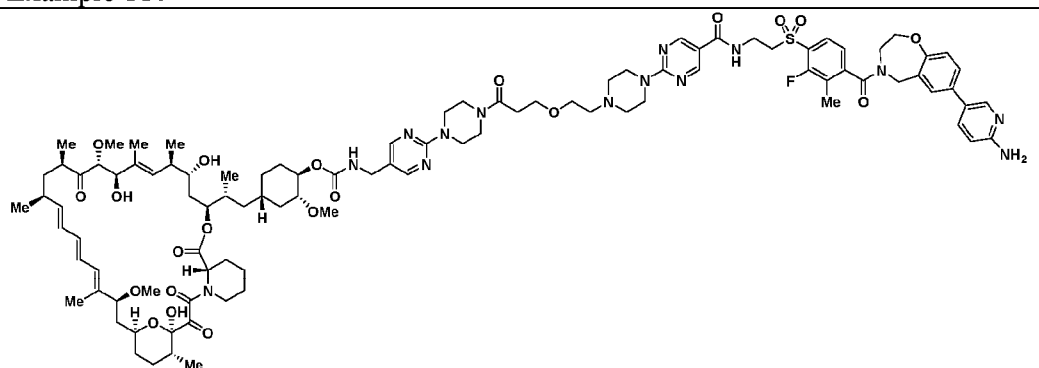
Example 116



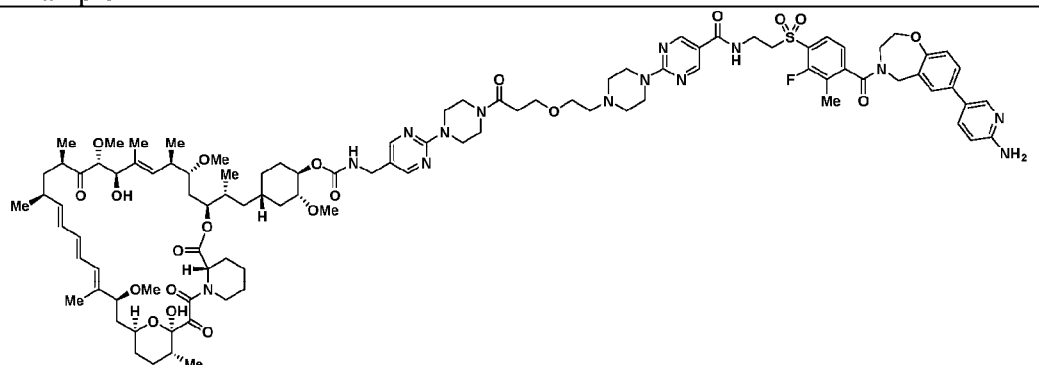
Example 117



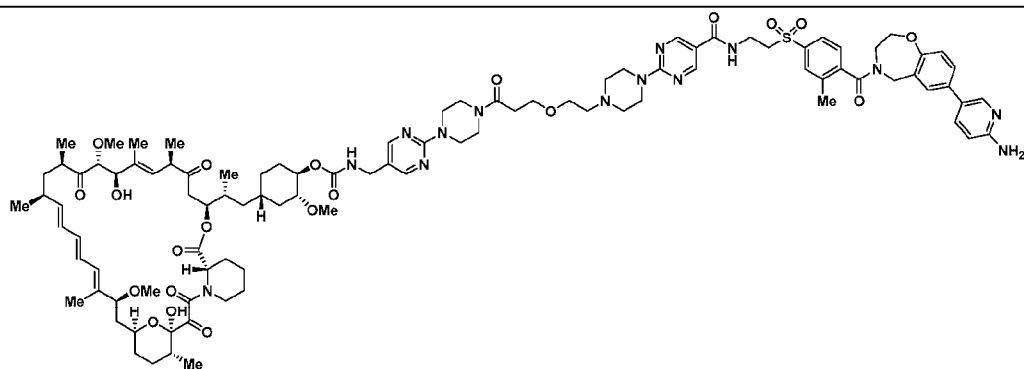
Example 118



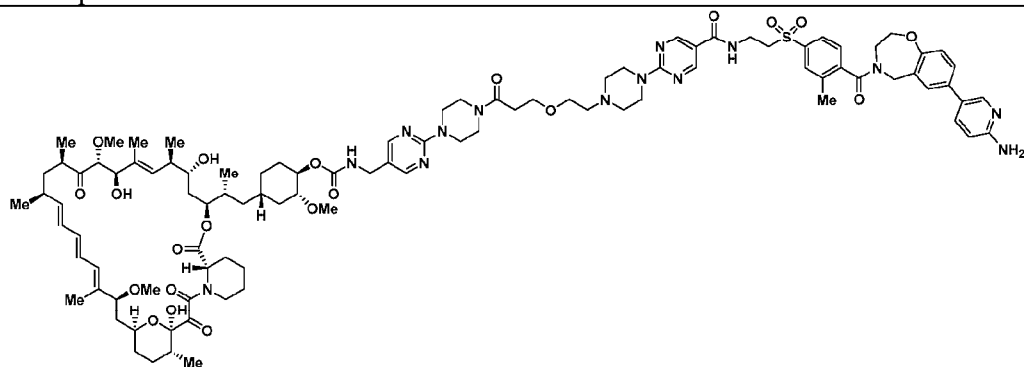
Example 119



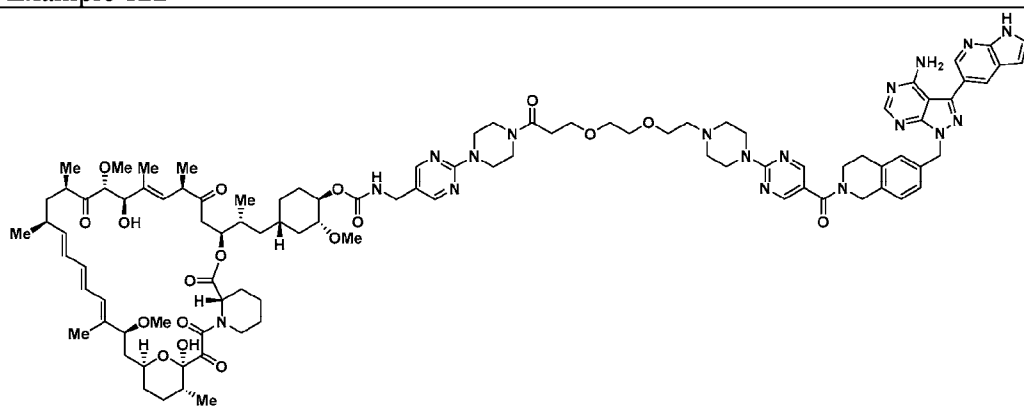
Example 120



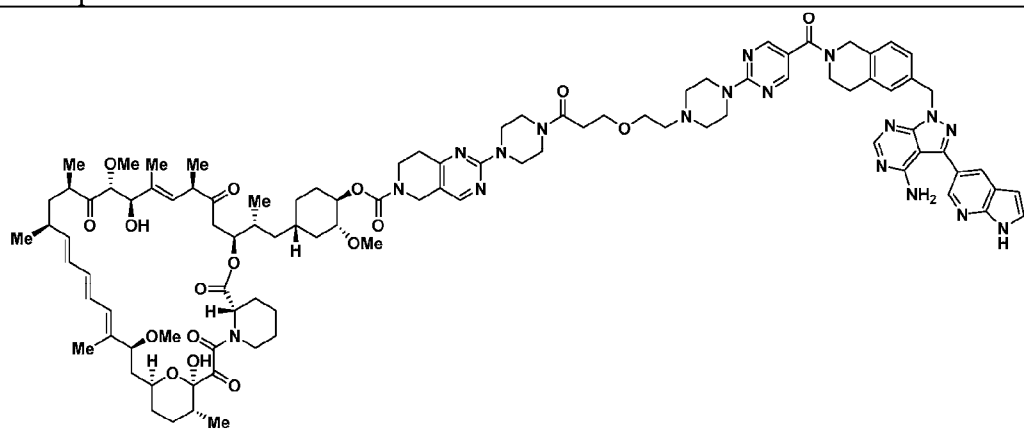
Example 121



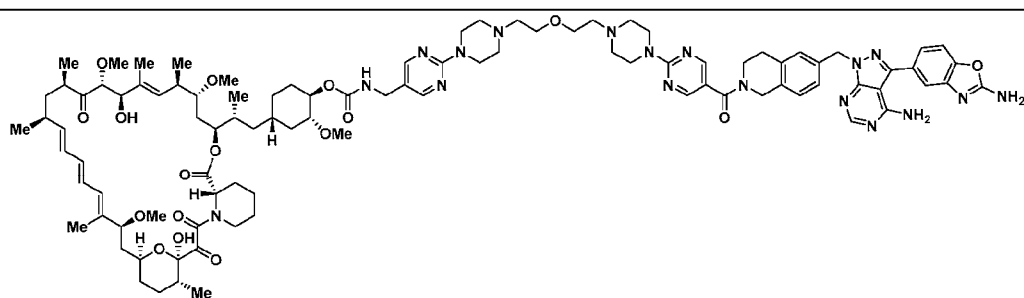
Example 122



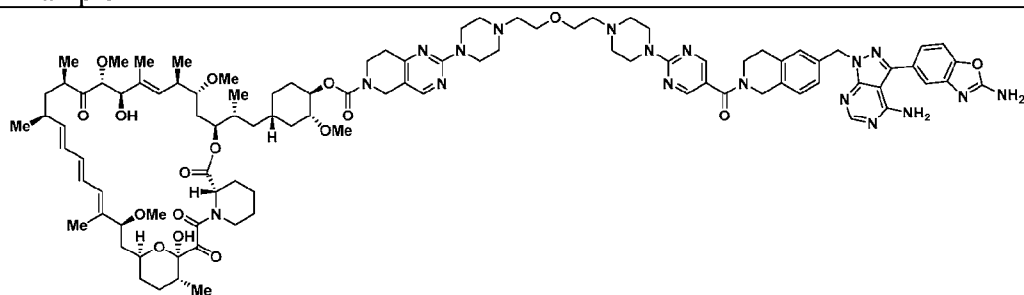
Example 123



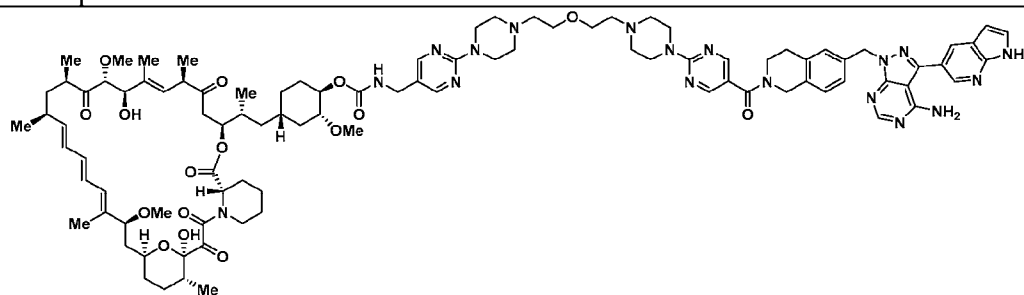
Example 124



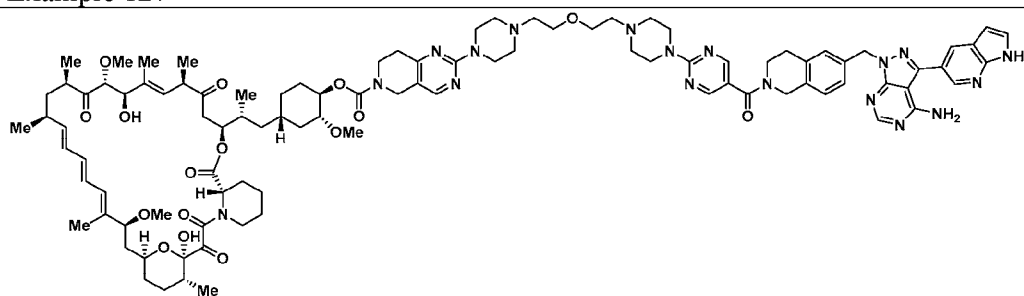
Example 125



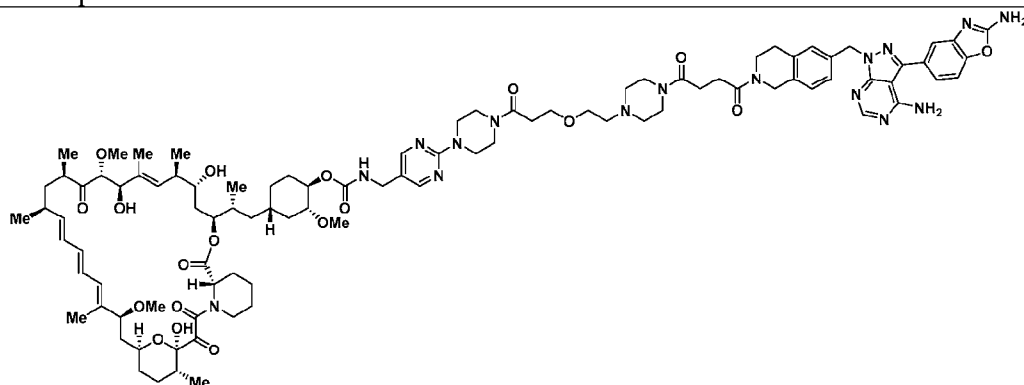
Example 126



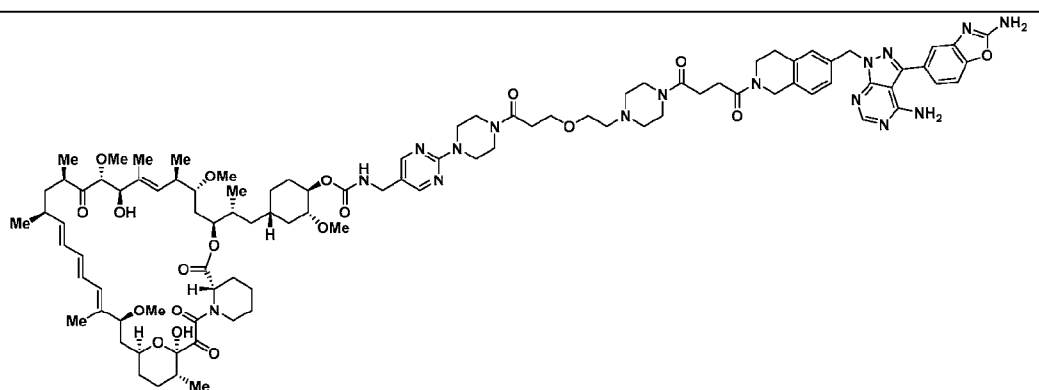
Example 127



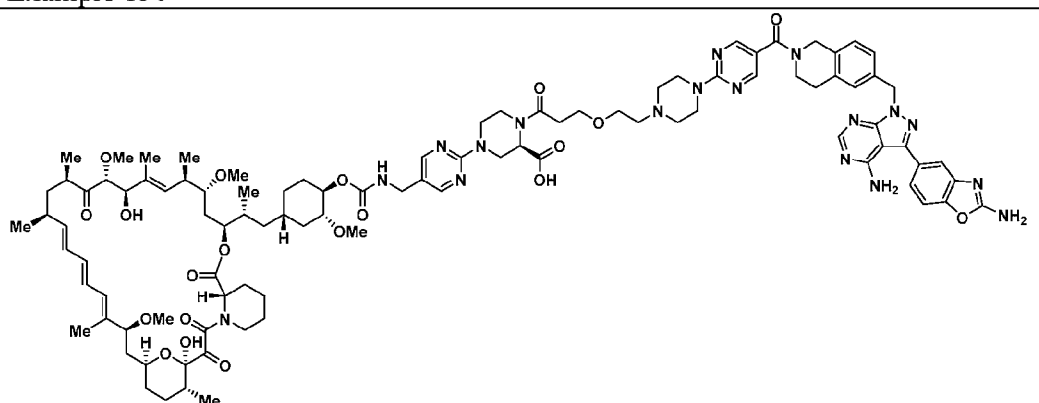
Example 128



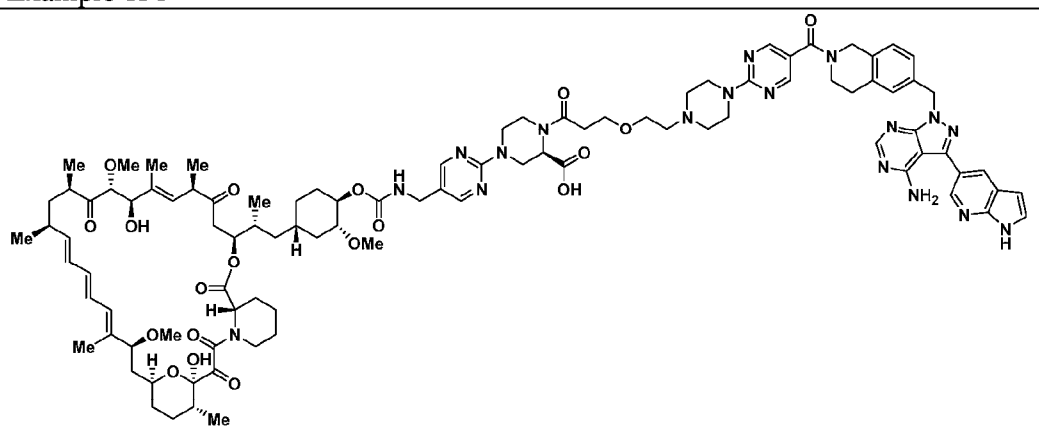
Example 129



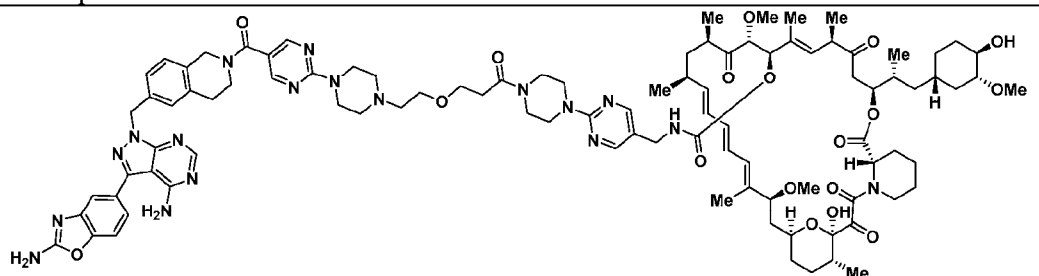
Example 130



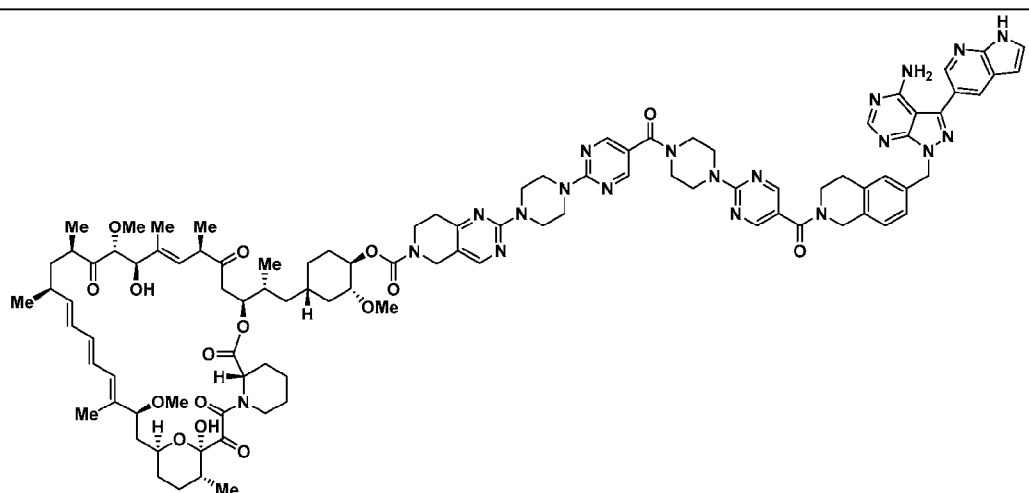
Example 131



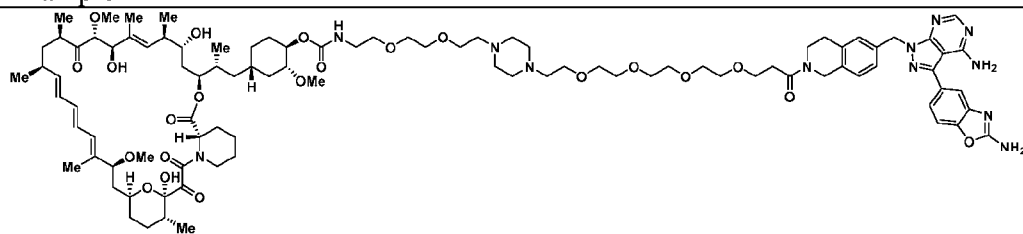
Example 132



Example 133



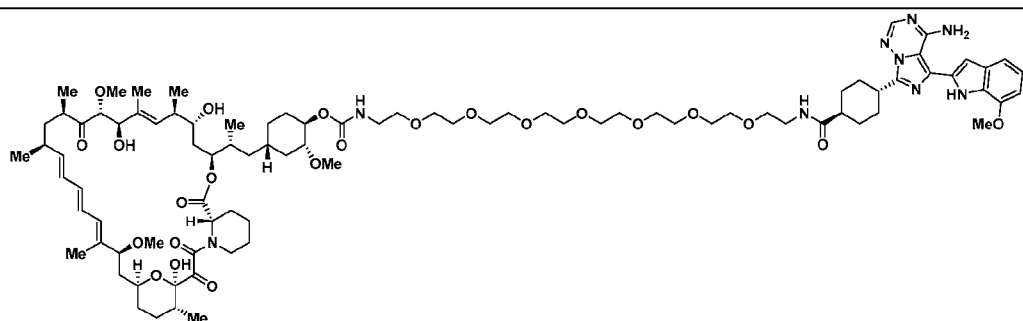
Example 134



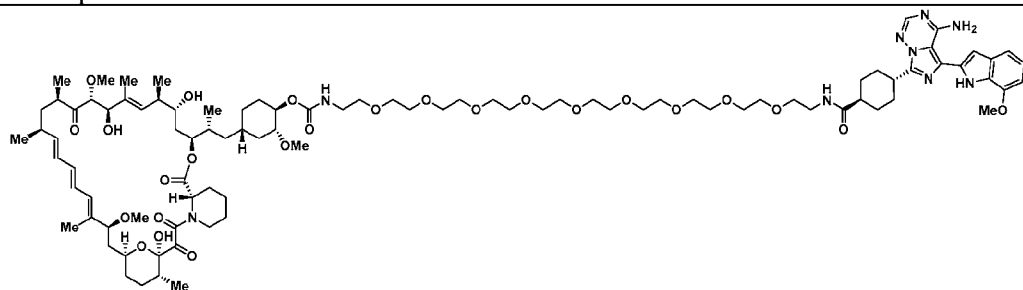
Example 135

or a pharmaceutically acceptable salt or tautomer thereof.

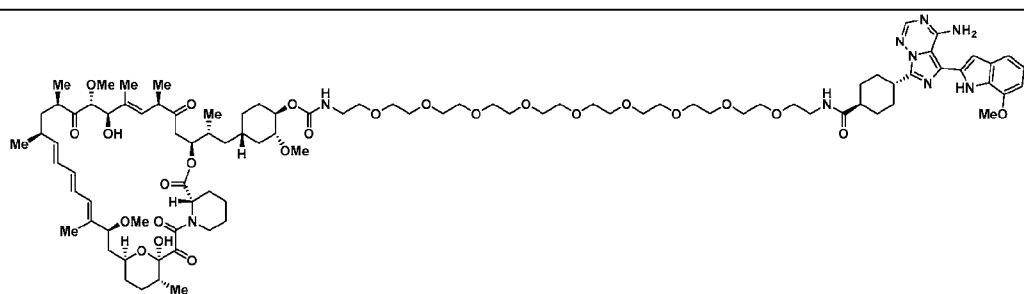
74. A compound selected from the group consisting of:



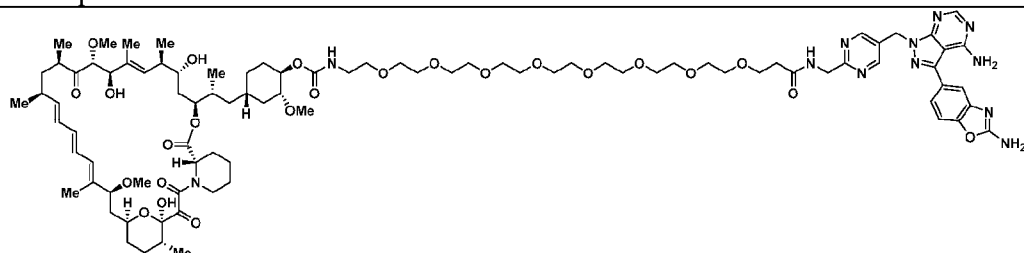
Example 136



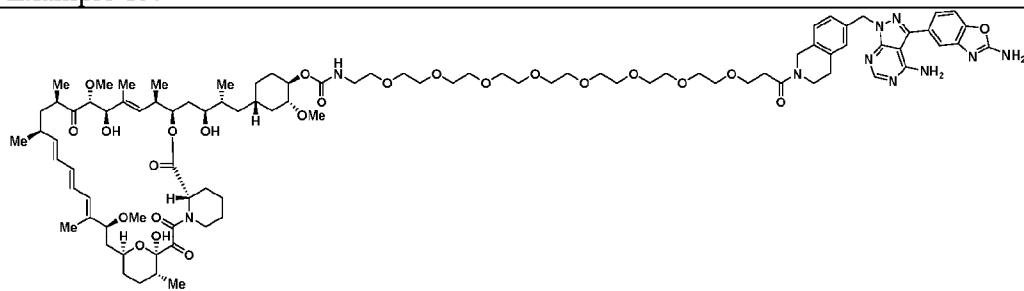
Example 137



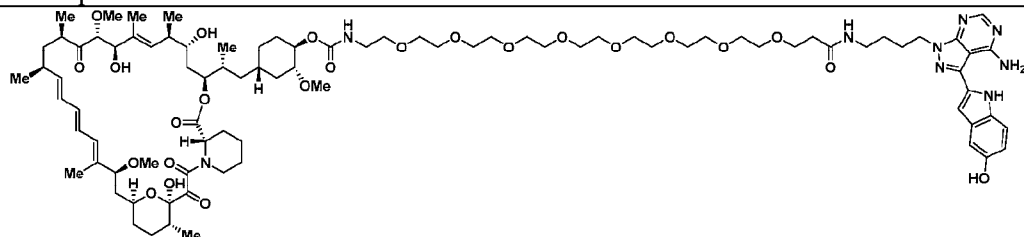
Example 138



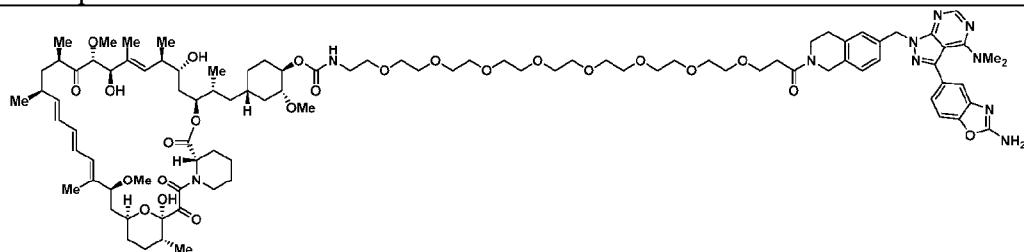
Example 139



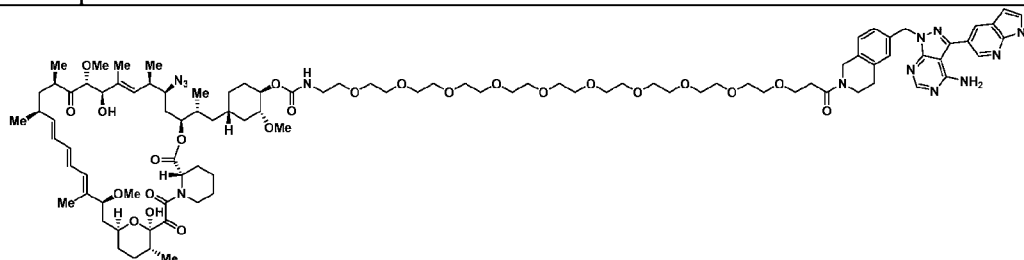
Example 140



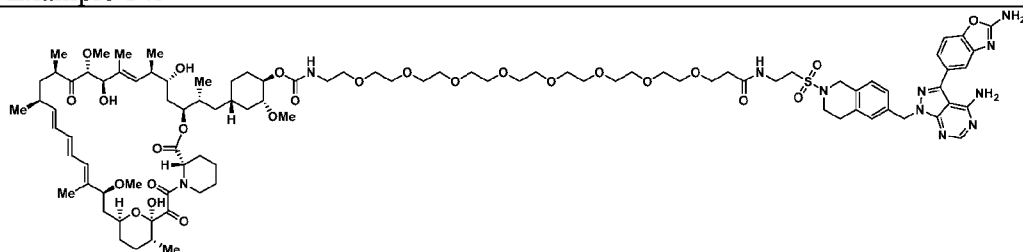
Example 141



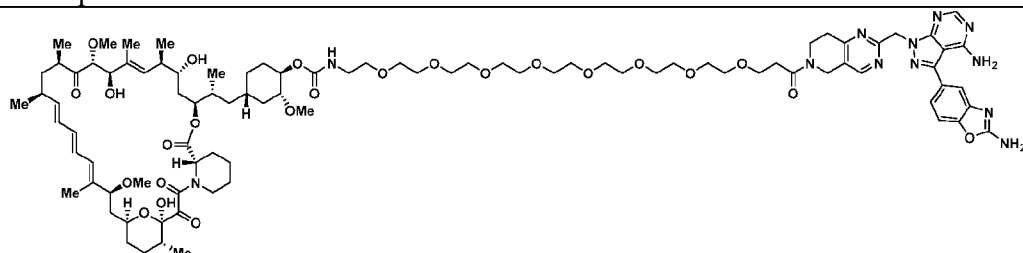
Example 142



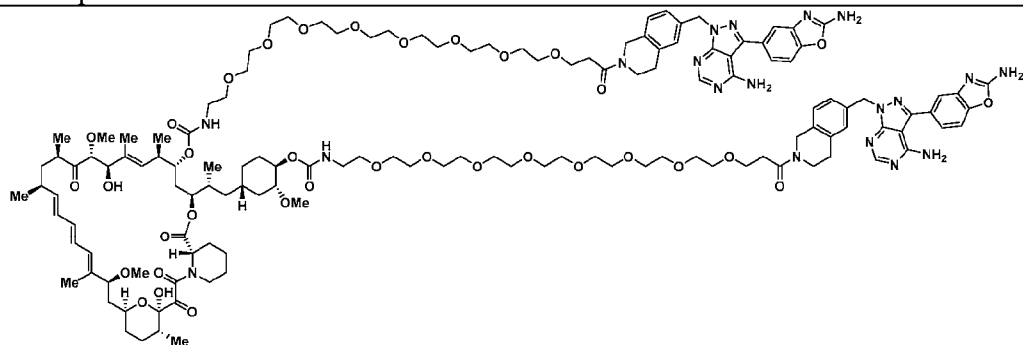
Example 143



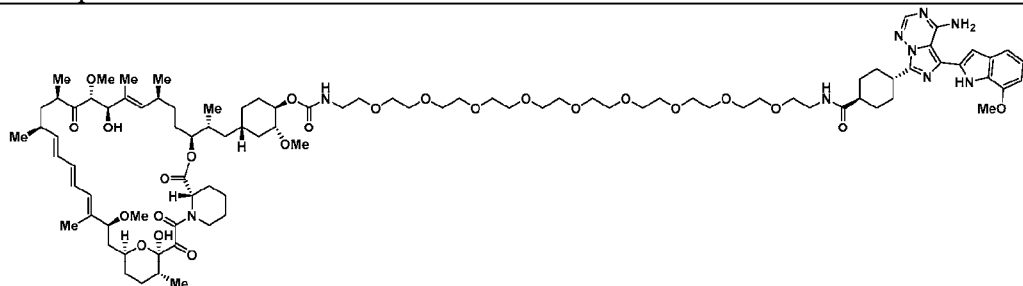
Example 144



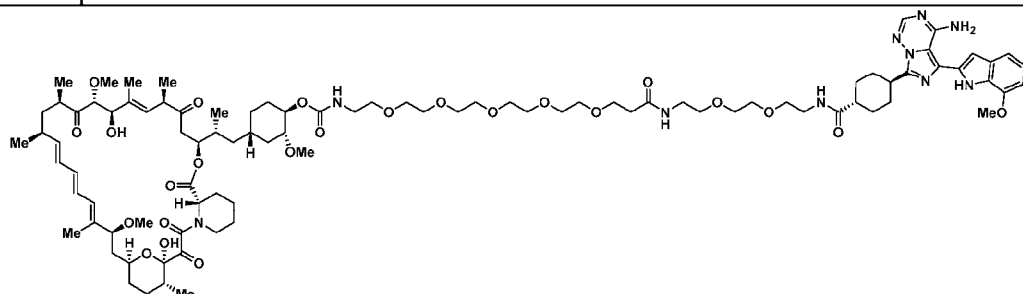
Example 145



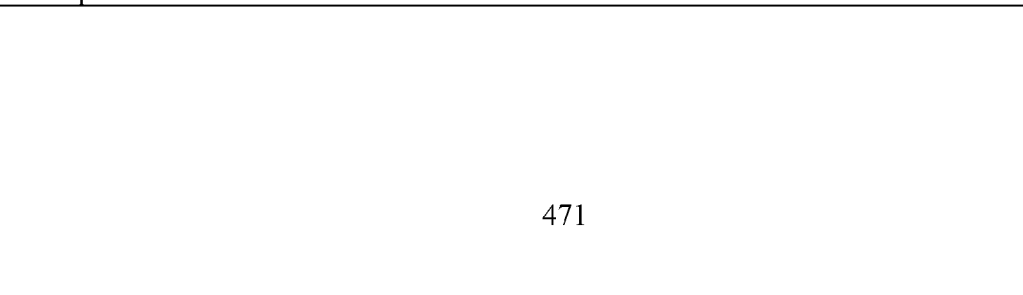
Example 146

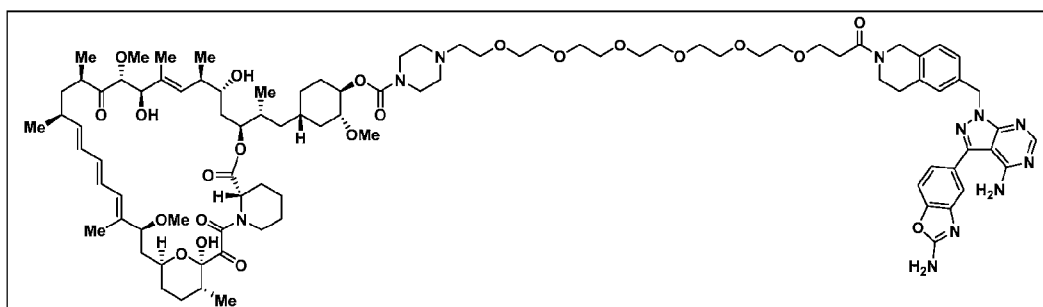


Example 147

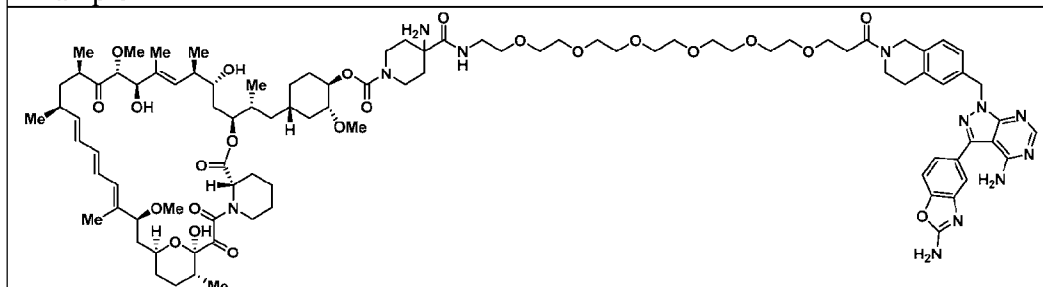


Example 148

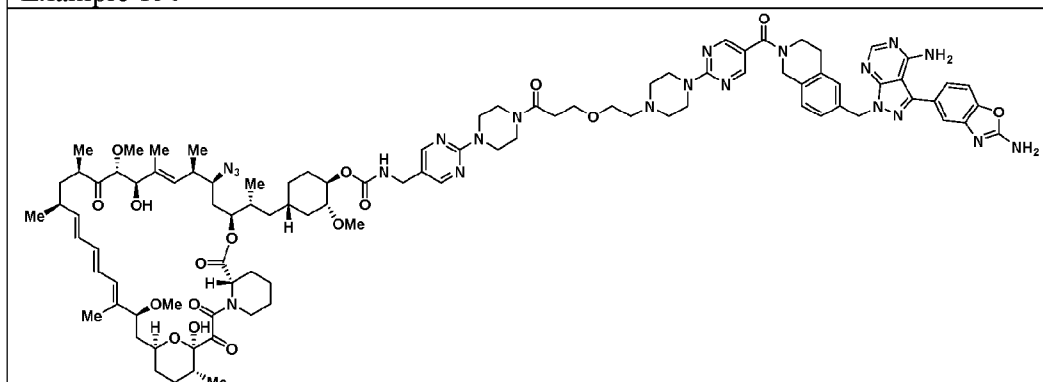




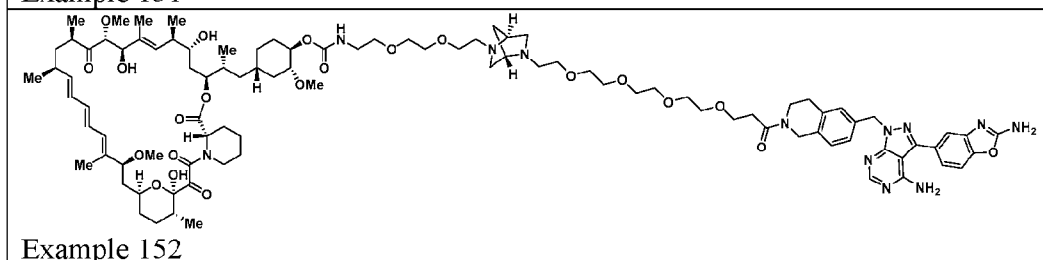
Example 149



Example 150



Example 151



Example 152

or a pharmaceutically acceptable salt or tautomer thereof.

75. A pharmaceutical composition comprising a compound of any one of claims 1-74, or a pharmaceutically acceptable salt thereof, and at least one of a pharmaceutically acceptable carrier, diluent, or excipient.

76. A method of treating a disease or disorder mediated by mTOR comprising administering to the subject suffering from or susceptible to developing a disease or disorder

mediated by mTOR a therapeutically effective amount of one or more compounds of any one of claims 1-74, or a pharmaceutically acceptable salt thereof.

77. A method of preventing a disease or disorder mediated by mTOR comprising administering to the subject suffering from or susceptible to developing a disease or disorder mediated by mTOR a therapeutically effective amount of one or more compounds of any one of claims 1-74, or a pharmaceutically acceptable salt thereof.

78. A method of reducing the risk of a disease or disorder mediated by mTOR comprising administering to the subject suffering from or susceptible to developing a disease or disorder mediated by mTOR a therapeutically effective amount of one or more compounds of any one of claims 1-74, or a pharmaceutically acceptable salt thereof.

79. The method of any one of claims 76-78, wherein the disease is cancer or an immune-mediated disease.

80. The method of claim 79, wherein the cancer is selected from brain and neurovascular tumors, head and neck cancers, breast cancer, lung cancer, mesothelioma, lymphoid cancer, stomach cancer, kidney cancer, renal carcinoma, liver cancer, ovarian cancer, ovary endometriosis, testicular cancer, gastrointestinal cancer, prostate cancer, glioblastoma, skin cancer, melanoma, neuro cancers, spleen cancers, pancreatic cancers, blood proliferative disorders, lymphoma, leukemia, endometrial cancer, cervical cancer, vulva cancer, prostate cancer, penile cancer, bone cancers, muscle cancers, soft tissue cancers, intestinal or rectal cancer, anal cancer, bladder cancer, bile duct cancer, ocular cancer, gastrointestinal stromal tumors, and neuro-endocrine tumors.

81. The method of claim 79, wherein the immune-mediated disease is selected from resistance by transplantation of heart, kidney, liver, medulla ossium, skin, cornea, lung, pancreas, intestinum tenue, limb, muscle, nerves, duodenum, small-bowel, or pancreatic-islet-cell; graft-versus-host diseases brought about by medulla ossium transplantation; rheumatoid arthritis, systemic lupus erythematosus, Hashimoto's thyroiditis, multiple sclerosis, myasthenia gravis, type I diabetes, uveitis, allergic encephalomyelitis, and glomerulonephritis.

82. A method of treating cancer comprising administering to the subject a therapeutically effective amount of one or more compounds of any one of claims 1-74, or a pharmaceutically acceptable salt thereof.

83. The method of claim 82, wherein the cancer is selected from brain and neurovascular tumors, head and neck cancers, breast cancer, lung cancer, mesothelioma, lymphoid cancer, stomach cancer, kidney cancer, renal carcinoma, liver cancer, ovarian

cancer, ovary endometriosis, testicular cancer, gastrointestinal cancer, prostate cancer, glioblastoma, skin cancer, melanoma, neuro cancers, spleen cancers, pancreatic cancers, blood proliferative disorders, lymphoma, leukemia, endometrial cancer, cervical cancer, vulva cancer, prostate cancer, penile cancer, bone cancers, muscle cancers, soft tissue cancers, intestinal or rectal cancer, anal cancer, bladder cancer, bile duct cancer, ocular cancer, gastrointestinal stromal tumors, and neuro-endocrine tumors.

84. A method of treating an immune-mediated disease comprising administering to the subject a therapeutically effective amount of one or more compounds of any one of claims 1-74, or a pharmaceutically acceptable salt thereof.

85. The method of claim 84, wherein the immune-mediated disease is selected from resistance by transplantation of heart, kidney, liver, medulla ossium, skin, cornea, lung, pancreas, intestinum tenue, limb, muscle, nerves, duodenum, small-bowel, or pancreatic-islet-cell; graft-versus-host diseases brought about by medulla ossium transplantation; rheumatoid arthritis, systemic lupus erythematosus, Hashimoto's thyroiditis, multiple sclerosis, myasthenia gravis, type I diabetes, uveitis, allergic encephalomyelitis, and glomerulonephritis.

86. A method of treating an age related condition comprising administering to the subject a therapeutically effective amount of one or more compounds of any one of claims 1-74, or a pharmaceutically acceptable salt thereof.

87. The method of claim 86, wherein the age related condition is selected from sarcopenia, skin atrophy, muscle wasting, brain atrophy, atherosclerosis, arteriosclerosis, pulmonary emphysema, osteoporosis, osteoarthritis, high blood pressure, erectile dysfunction, dementia, Huntington's disease, Alzheimer's disease, cataracts, age-related macular degeneration, prostate cancer, stroke, diminished life expectancy, impaired kidney function, and age-related hearing loss, aging-related mobility disability (e.g., frailty), cognitive decline, age-related dementia, memory impairment, tendon stiffness, heart dysfunction such as cardiac hypertrophy and systolic and diastolic dysfunction, immunosenescence, cancer, obesity, and diabetes.

88. A compound of any one of claims 1-74, or a pharmaceutically acceptable salt thereof, for use in treating, preventing, or reducing the risk of a disease or condition mediated by mTOR.

89. Use of a compound of any of claims 1-74, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating, preventing, or reducing the risk of a disease or disorder mediated by mTOR.

90. A compound of any one of claims 1-74, or a pharmaceutically acceptable salt thereof, for use in treating cancer.

91. Use of a compound of any one of claims 1-74, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer.

92. A compound of any one of claims 1-74, or a pharmaceutically acceptable salt thereof, for use in treating an immune-mediated disease.

93. Use of a compound of any one of claims 1-74, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating an immune-mediated disease.

94. A compound of any one of claims 1-74, or a pharmaceutically acceptable salt thereof, for use in treating an age related condition.

95. Use of a compound of any one of claims 1-74, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating an age related condition.