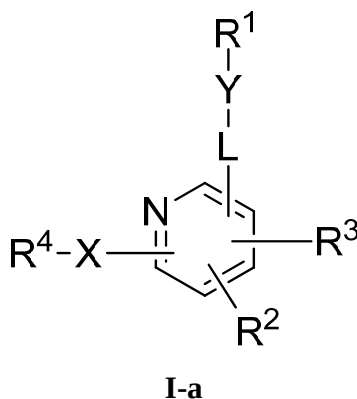


CLAIMS

We claim:

1. A compound of formula **I-a**,



or a pharmaceutically acceptable salt thereof, wherein:

R^2 is $-CN$, or $-NRC(O)R$;

R^3 is H;

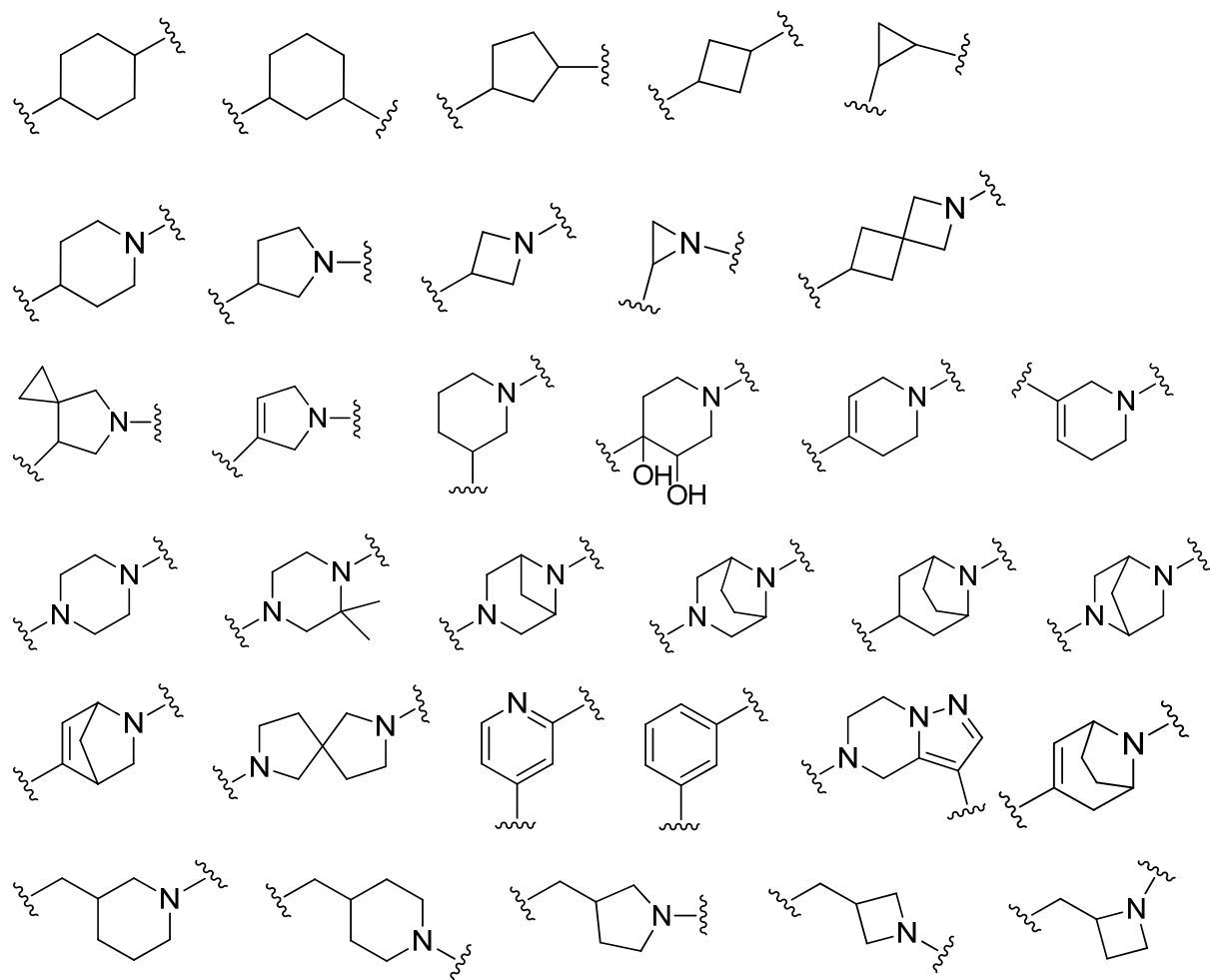
each R is independently hydrogen, C_{1-6} aliphatic, C_{3-10} aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted; or

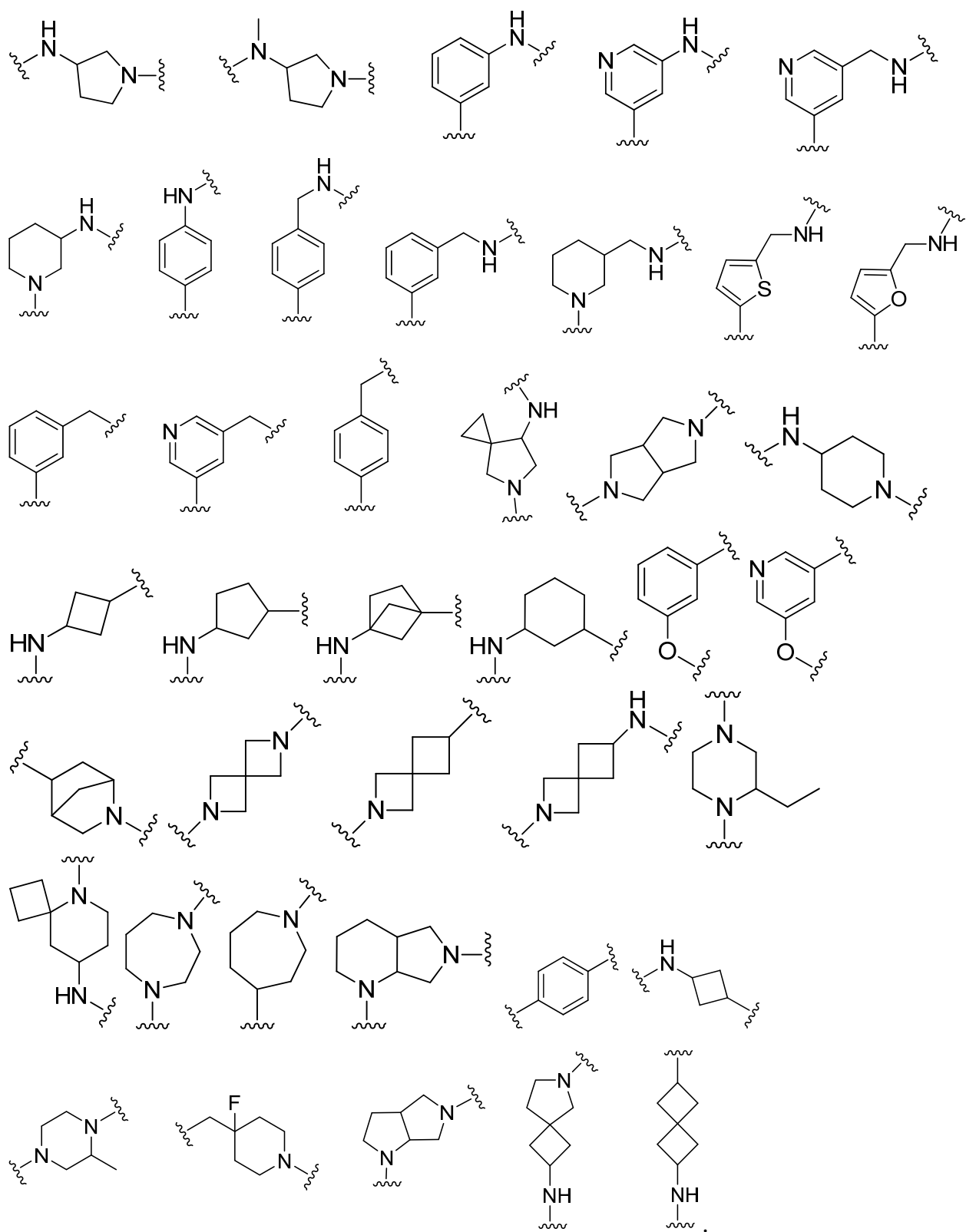
L is a divalent group selected from C_{1-6} aliphatic, C_{3-10} aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or L is a divalent group selected from C_{1-6} aliphatic- C_{3-10} aryl, C_{1-6} aliphatic-3-8 membered saturated or partially unsaturated carbocyclic ring, C_{1-6} aliphatic-3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and a C_{1-6} aliphatic-5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Y is O, S, SO_2 , SO, C(O), CO_2 , C(O)N(R), $-NRC(O)$, $-NRC(O)N(R)$, $-NRSO_2$, or N(R); or Y is absent;

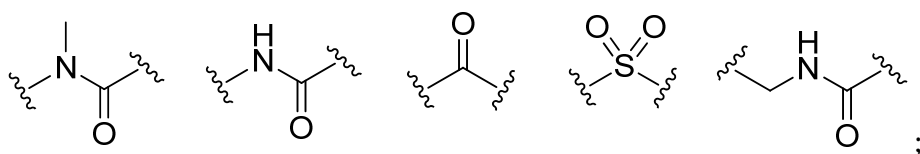
X is O, S, SO₂, SO, C(O), CO₂, C(O)N(R), -NRC(O), -NRC(O)N(R), -NRSO₂, or N(R); or X is absent; and

2. The compound of claim 1, wherein L is

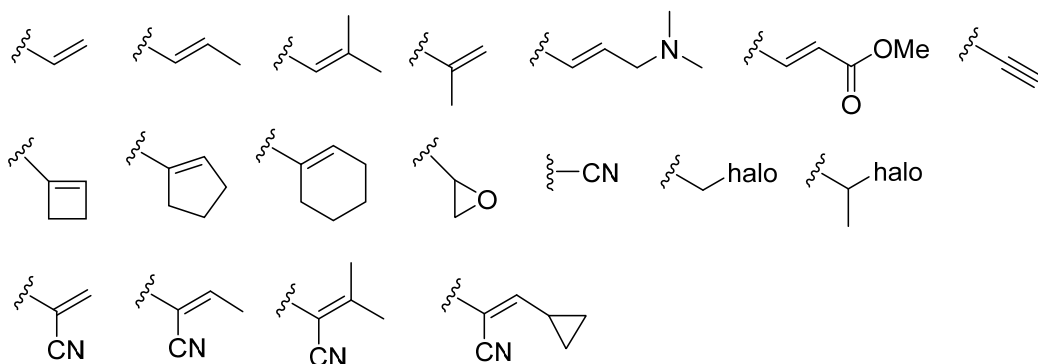




3. The compound of claim 1, wherein Y is

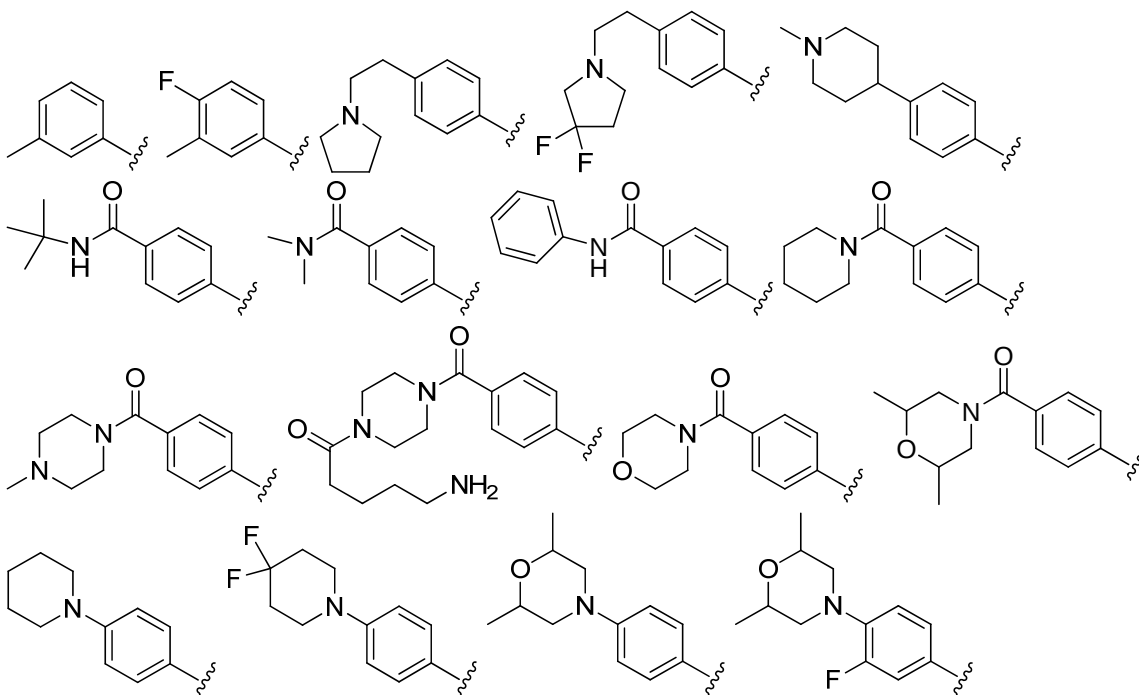


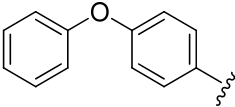
and R¹ is

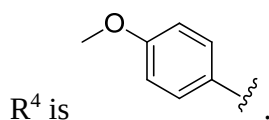


4. The compound of claim 1, wherein X is O, C(O)NH, -NHC(O), NH, or N(Me); or X is absent.

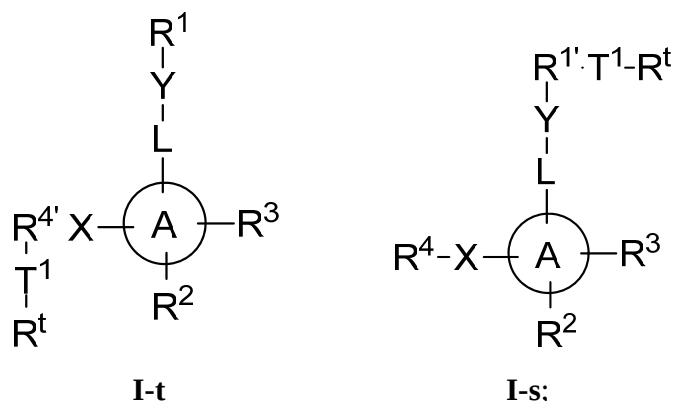
5. The compound of claim 1, wherein R⁴ is



6. The compound of claim 1, wherein X is O and R⁴ is ; or X is NH and



7. The compound of claim 1, selected from Compounds 1-134, 156-161, 163-171, 177, 179-181, 184-191, 196-202, 205, 212-217, 219-224, 226-238, 240,241, and 243-253.
8. A pharmaceutical composition comprising a compound of claim 1, and a pharmaceutically acceptable adjuvant, carrier, or vehicle.
9. Use of a compound or physiologically acceptable salt thereof as set forth in claim 1, in the manufacture of a medicament for inhibiting BTK, or a mutant thereof, activity in a patient or in a biological sample.
10. Use of a compound or physiologically acceptable salt thereof as set forth in claim 1, in the manufacture of a medicament for the treatment of a BTK-mediated disorder by administering to a patient or a biological sample with said medicament.
11. Use of a compound or physiologically acceptable salt thereof as set forth in claim 1, in the manufacture of a medicament for the treatment of lupus by administering to a patient or a biological sample with said medicament.
12. Use of a compound or physiologically acceptable salt thereof as set forth in claim 1 in the manufacture of a medicament for prophylactic or therapeutic treatment of lupus, rheumatoid arthritis, or multiple sclerosis.
13. A compound of formula **I-t or I-s**



or a pharmaceutically acceptable salt thereof, wherein:

Ring A is pyridine;

R² is -CN, or -NRC(O)R;

R³ is -H;

each R is independently hydrogen, C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

L is a divalent group selected from C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or L is a divalent group selected from C₁₋₆ aliphatic-C₃₋₁₀ aryl, C₁₋₆ aliphatic-3-8 membered saturated or partially unsaturated carbocyclic ring, C₁₋₆ aliphatic-3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and a C₁₋₆ aliphatic-5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Y is O, S, SO₂, SO, C(O), CO₂, C(O)N(R), -NRC(O), -NRC(O)N(R), -NRSO₂, or N(R); or Y is absent;

R¹ is C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from

nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

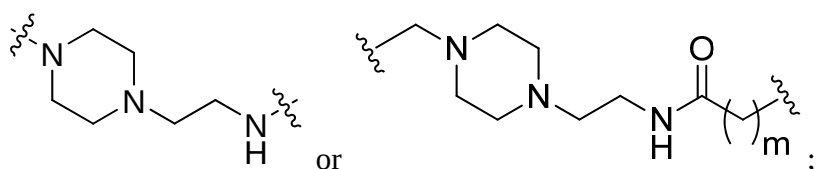
R^{1'} is a bivalent group selected from C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

X is O, S, SO₂, SO, C(O), CO₂, C(O)N(R), -NRC(O), -NRC(O)N(R), -NRSO₂, or N(R); or X is absent;

R⁴ is hydrogen, C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

R^{4'} is a bivalent group selected from C₁₋₆ aliphatic, C₃₋₁₀ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocyclic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, and a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

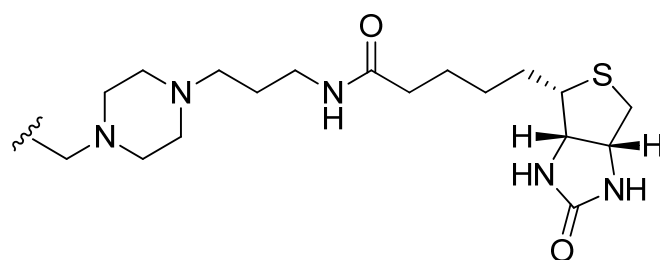
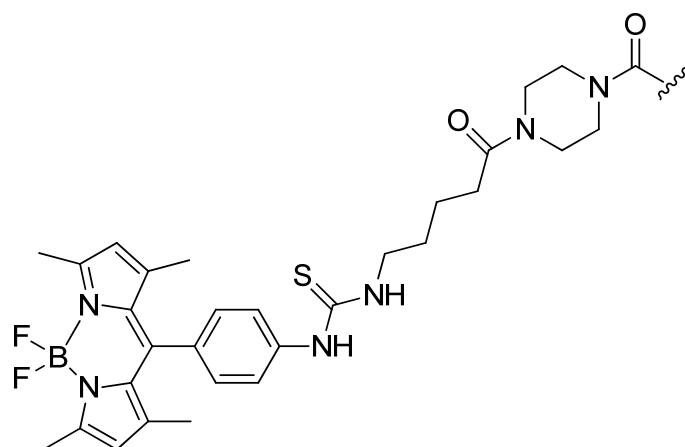
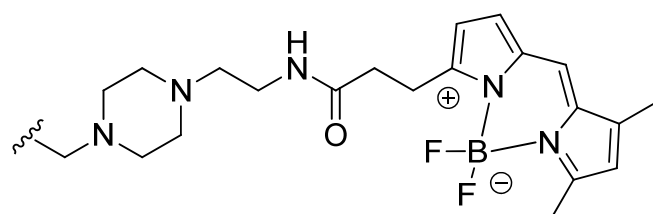
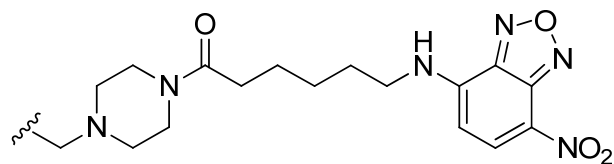
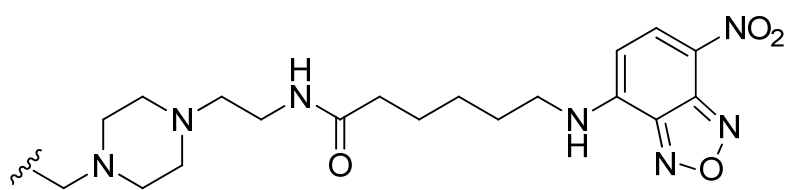
T¹ is

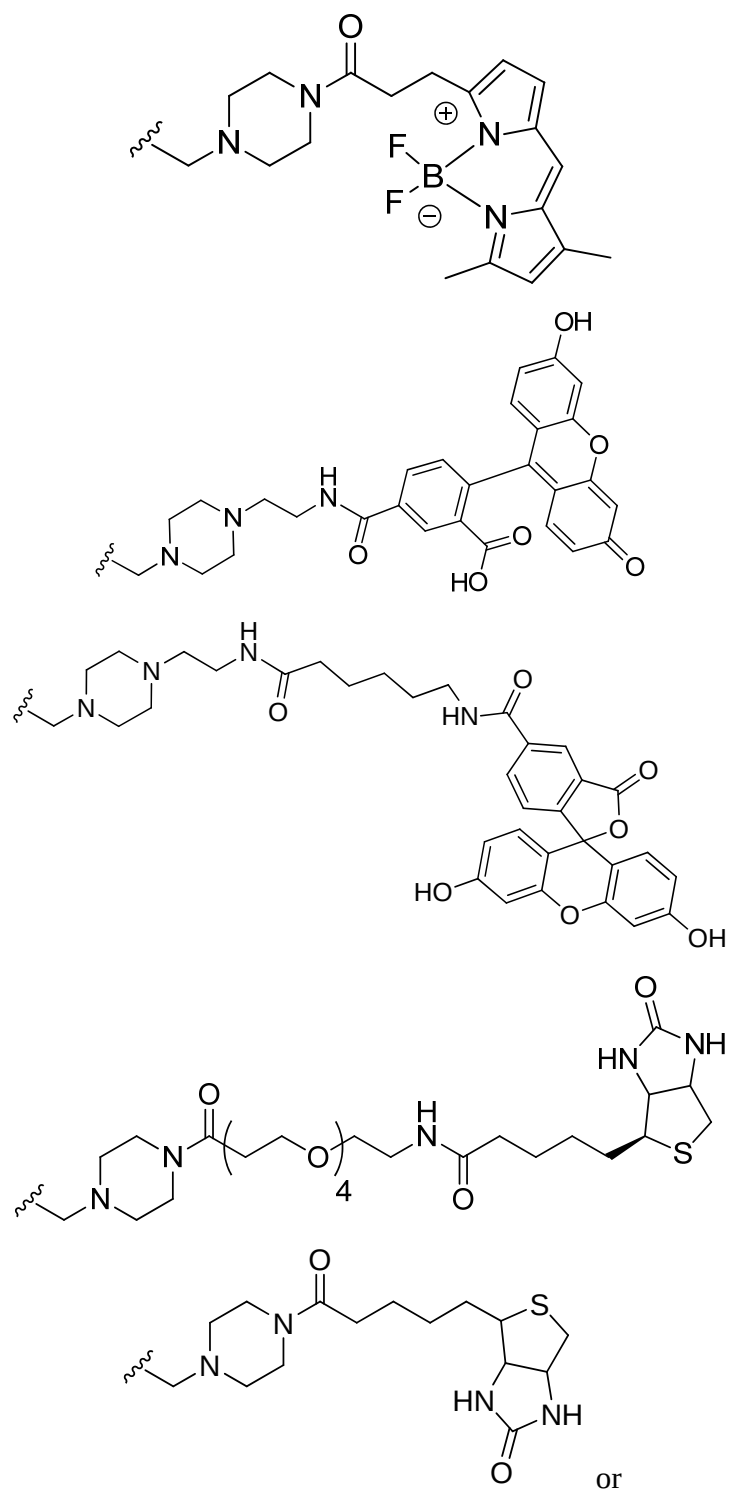


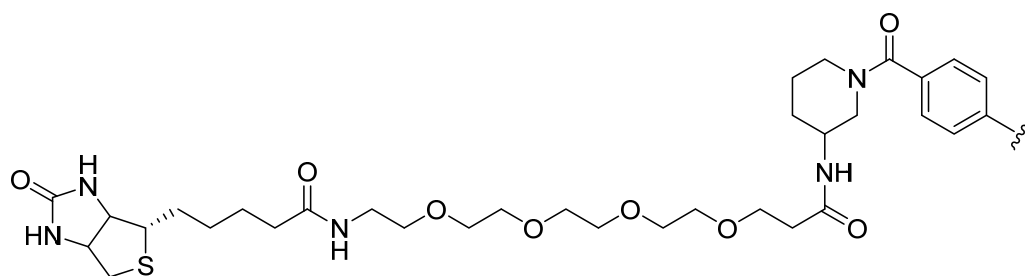
wherein m is 0, 1, 2, 3, 4, 5, 6, or 7

R^t is a detectable moiety selected from quinine, phenylalanine, tyrosine, trptophan, NADH, FMN, EDANS, Lucifer Yellow, pyrene, 4-MU, AMC, DAPI, Hoechst33342, NBD, bimane, Cascade yellow, fluorescein, RH110, TMR, SRh101, naphthofluorescein, SNARF-1, propidium, BODIPY-FL, BODIPY-TR, Cy3, Cy5, Cy7, IRDye 700DX, or resorufin.

14. The compound of claim 13, wherein - T¹-R^t is:







15. The compound of claim 14, selected from **63**, **86**, **102**, **177**, and **191**.