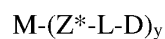


CLAIMS

1. A conjugate having the formula



wherein M is a macromolecular carrier;

y is a number describing the number of linker-drugs L-D attached to M;

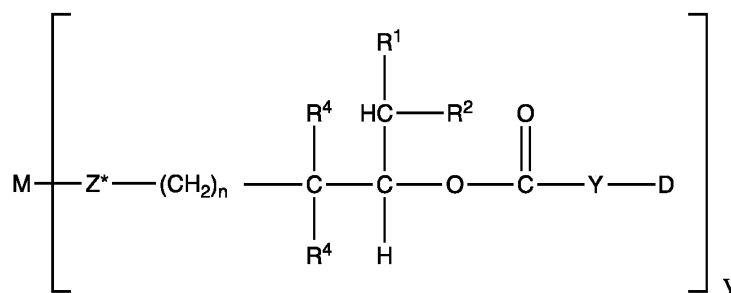
Z* is a connecting group;

L is a releasable linker; and

D is an inhibitor of the DNA damage response.

2. The conjugate of Claim 1 wherein D is a PARP inhibitor, ATM inhibitor, or ATR inhibitor.

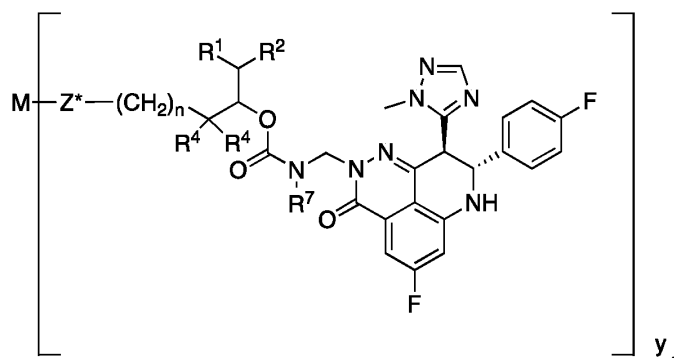
3. The conjugate of Claim 1 or 2 having the formula



wherein Z* is a connecting group; n = 0-6; R¹ and R² are each independently H, CN, or SO₂R⁵, wherein R⁵ is optionally substituted C₁-C₆ alkyl, optionally substituted aryl, optionally substituted heteroaryl, or N(R⁶)₂, wherein each R⁶ is independently optionally substituted C₁-C₆ alkyl, optionally substituted aryl, optionally substituted heteroaryl, or wherein N(R⁶)₂ forms a ring of 4-8 atoms; each R⁴ is independently H or C₁-C₃ alkyl or taken together form a 3-6 member ring; and Y is either absent or has the formula N(R⁷)CH₂, wherein R⁷ is optionally substituted C₁-C₄ alkyl or optionally substituted aryl; and wherein at least one of R¹ and R² is other than H.

4. The conjugate of Claim 3 wherein Y is absent and D is connected to linker L through a carbamate linkage to a primary or secondary amine nitrogen atom of D.

5. The conjugate of any one of Claims 1-4 wherein D is rucaparib, veliparib, niraparib, or berzosertib.
6. The conjugate of Claims 1-3 wherein Y has the formula $N(R^7)CH_2$ and D is connected to linker L through an alkyl linkage to a non-basic nitrogen atom of D.
7. The conjugate of Claim 6 wherein D is talazoparib, olaparib, tamiparib, E7016, or CEP-9722.
8. The conjugate of any one of Claims 1-7 wherein M is a PEG of molecular weight between 1,000 and 100,000 Daltons, and $y = 1-8$.
9. The conjugate of any one of Claims 1-8 wherein M has a hydrodynamic radius between 5 and 50 nm.
10. The conjugate of any one of Claims 1-7 wherein M is an insoluble macromolecular carrier.
11. The conjugate of any one of Claims 1-10 wherein Z^* is a carboxamide, carbamate, urea, oxime, thioether, or 1,2,3-triazole.
12. The conjugate of any one of Claims 3-10 wherein R^1 and R^2 are selected to provide a half-life for D release between 100-1000 hours at a pH of 7.4 and a temperature of 37 °C.
13. The conjugate of Claim 1 having the formula

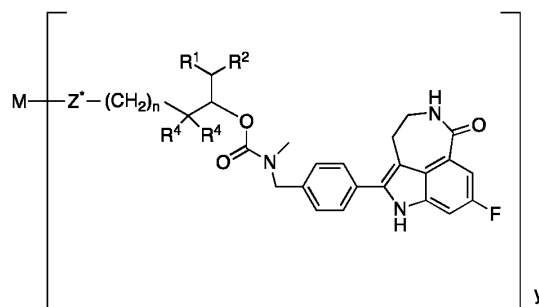


wherein M is a macromolecular carrier; $n = 0-6$; Z^* is a connecting group; R^1 and R^2 are each independently H, CN, or SO_2R^5 , wherein R^5 is optionally substituted C_1-C_6 alkyl, optionally substituted aryl, optionally substituted heteroaryl, or $N(R^6)_2$, wherein each R^6 is independently optionally substituted C_1-C_6 alkyl, optionally substituted aryl, optionally substituted heteroaryl, or wherein $N(R^6)_2$ forms a ring of 4-8 atoms; each R^4 is independently H or C_1-C_3 alkyl or taken together form a 3-6 member ring; R^7 is optionally substituted C_1-C_3 alkyl or optionally substituted aryl; and $y = 1$ to 8; and wherein at least one of R^1 and R^2 is other than H.

14. The conjugate of Claim 13 wherein M is a 40-kDa 4-armed PEG and $y = 4$.

15. The conjugate of Claim 13 or 14 wherein Z^* is carboxamide, carbamate, oxime, thioether, or triazole.

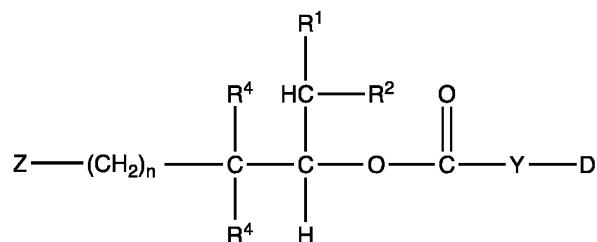
16. The conjugate of Claim 1 having the formula



wherein M is a macromolecular carrier; $n = 0-6$; Z^* is a connecting group; R^1 and R^2 are each independently H, CN, or SO_2R^5 , wherein R^5 is optionally substituted C_1-C_6 alkyl, optionally substituted aryl, optionally substituted heteroaryl, or $N(R^6)_2$, wherein each R^6 is independently optionally substituted C_1-C_6 alkyl, optionally substituted aryl, optionally substituted heteroaryl, or wherein $N(R^6)_2$ forms a ring of 4-8 atoms; each R^4 is independently H or C_1-C_3 alkyl or taken together form a 3-6 member ring; and $y = 1$ to 8; and wherein at least one of R^1 and R^2 is other than H.

17. The conjugate of Claim 16 wherein M is a 40-kDa 4-armed PEG and $y = 4$.

18. A linker-drug of the formula



wherein Z is a connecting group; n = 0-6; R¹ and R² are each independently H, CN, or SO₂R⁵, wherein R⁵ is optionally substituted C₁-C₆ alkyl, optionally substituted aryl, optionally substituted heteroaryl, or N(R⁶)₂, wherein each R⁶ is independently optionally substituted C₁-C₆ alkyl, optionally substituted aryl, optionally substituted heteroaryl, or wherein N(R⁶)₂ forms a ring of 4-8 atoms; each R⁴ is independently H or C₁-C₃ alkyl or taken together form a 3-6 member ring; Y is either absent or has the formula N(R⁷)CH₂, wherein R⁷ is optionally substituted C₁-C₄ alkyl or optionally substituted aryl; and D is an inhibitor of DNA damage response; and wherein at least one of R¹ and R² is other than H.

19. Use of a conjugate of any one of Claims 1-17 in the treatment of cancer.
20. A method of preparing a conjugated inhibitor of DNA damage response, said method comprising the step of contacting a linker-drug of Claim 18 with an activated macromolecular carrier comprising a cognate functional group Z' capable of reacting with functional group Z under conditions such that connecting group Z* is formed, and optionally isolating the conjugate.