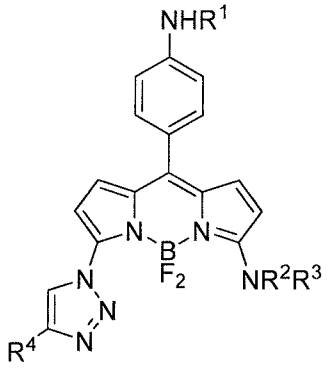
CLAIMS

What is claimed is:

1. A compound having the structure of Formula (I) or a pharmaceutically acceptable salt thereof:



(I)

wherein:

R^1 is H or $CO(C_1\text{-}C_6)$alkyl, wherein $CO(C_1\text{-}C_6)$alkyl is optionally substituted at any position with 1-3 substituents selected from halogen, hydroxyl, O-acetyl, NH-acetyl, or $-NH_2$;

R^2 and R^3 are each, independently, H, $(C_1\text{-}C_{10})$alkyl, $(C_6\text{-}C_{10})$aryl$(C_0\text{-}C_6)$alkyl, $(C_3\text{-}C_{10})$heteroaryl, $(C_3\text{-}C_8)$cycloalkyl, $(C_2\text{-}C_{10})$alkynyl or $(C_2\text{-}C_{10})$alkenyl;

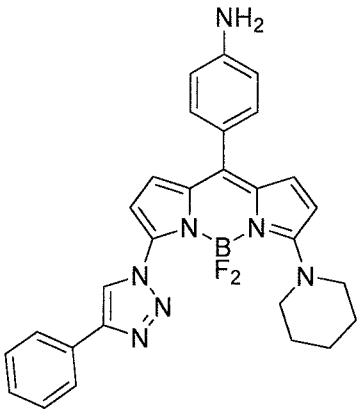
wherein $(C_1\text{-}C_{10})$alkyl, $(C_6\text{-}C_{10})$aryl$(C_0\text{-}C_6)$alkyl, $(C_3\text{-}C_{10})$heteroaryl, $(C_3\text{-}C_8)$cycloalkyl, $(C_2\text{-}C_{10})$alkynyl and $(C_2\text{-}C_{10})$alkenyl are optionally substituted at any position with 1-5 substituents selected from $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, NH_2, $-NH(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_1\text{-}C_6$ haloalkyl), $-NH(CO)(C_1\text{-}C_6$ alkoxy), $-NH(CO)(C_1\text{-}C_6$ haloalkoxy), $-NH(CO)(C_2\text{-}C_6$ alkenyl), $-Si(C_1\text{-}C_6$ alkyl), $-SO_2(C_1\text{-}C_6$ alkyl), $-SH$, $-B(OH)_2$, $-OTosyl$, $-CO(C_1\text{-}C_6$ alkoxyl), $-COH$, $-COOH$, $-CO(C_1\text{-}C_6$ alkyl) or halogen;

or R^2 and R^3 are taken together to form a ring, wherein the ring is optionally substituted with 1-5 additional substituents selected from halogen or $(C_1\text{-}C_6)$alkyl; and

R^4 is $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_8)$cycloalkyl, $(C_6\text{-}C_{10})$aryl, $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, or $(C_3\text{-}C_{10})$heteroaryl, further wherein R^4 is optionally substituted at any position with 1-5 substituents selected from $(C_1\text{-}C_{10})$alkyl, $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, $(C_3\text{-}C_8)$cycloalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_6\text{-}C_{10})$aryloxy, $(C_6\text{-}C_{10})$aryl, amino, $-NH(CO)(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_2\text{-}C_6$ alkenyl), $-NH(CO)(C_2\text{-}C_6$ alkynyl), $-NH(CO)(C_1\text{-}C_6$ haloalkyl), halo, OCF_3, CF_3, hydroxyl, or a halogen radioisotope.

2. The compound of claim 1, wherein R^1 is H, $COCH_3$, $COCH_2Cl$, $COCH_2OH$, $COCH_2NH_2$, or $COCH_2O(CO)CH_3$.

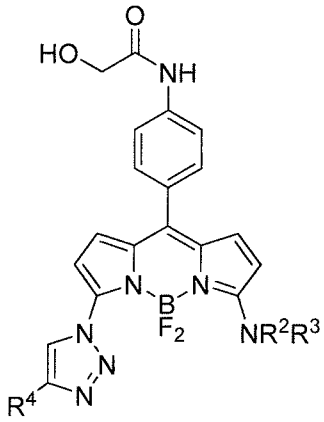
3. The compound of claim 2, having the structure of Formula (II):



(II),

or a pharmaceutically acceptable salt thereof.

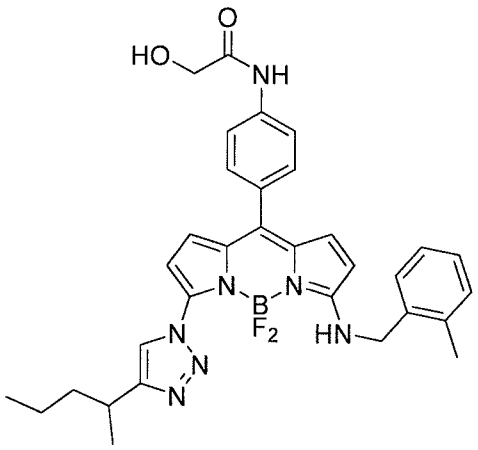
4. The compound of claim 2, having the structure of Formula (III):



(III),

or a pharmaceutically acceptable salt thereof.

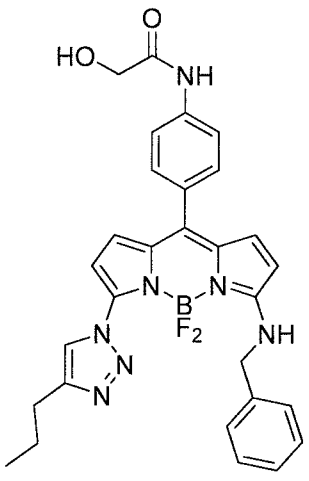
5. The compound of claim 2, having the structure of Formula (IV)



(IV),

or a pharmaceutically acceptable salt thereof.

6. The compound of claim 2, having the structure of Formula (V):

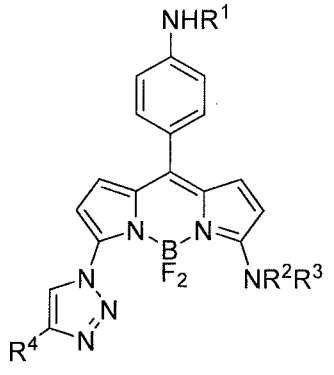


(V),

or a pharmaceutically acceptable salt thereof.

7. The compound of claim 1, wherein the compound is conjugated to a chemical reactive moiety selected from biotin, diazirine, acryloyl, haloacetyl, diaaziridine, N-hydroxysuccinimide ester, imidoester, pentafluorophenyl ester, hydroxymethyl phosphine, maleimide, pyridyldisulfide, thiosulfonate, vinylsulfone, hydrazide, alkoxyamine, aryl azide, benzophenone, isocyanate, alkyne or ketone.

8. A method for a solid phase synthesis of a compound of Formula (I) or a pharmaceutically acceptable salt thereof:



(I)

wherein:

R^1 is H or $CO(C_1\text{-}C_6)$alkyl, wherein $CO(C_1\text{-}C_6)$alkyl is optionally substituted at any position with 1-3 substituents selected from halogen, hydroxyl, O-acetyl, NH-acetyl, or $-NH_2$;

R^2 and R^3 are each, independently, H, $(C_1\text{-}C_{10})$alkyl, $(C_6\text{-}C_{10})$aryl$(C_0\text{-}C_6)$alkyl, $(C_3\text{-}C_{10})$heteroaryl, $(C_3\text{-}C_8)$cycloalkyl, $(C_2\text{-}C_{10})$alkynyl or $(C_2\text{-}C_{10})$alkenyl;

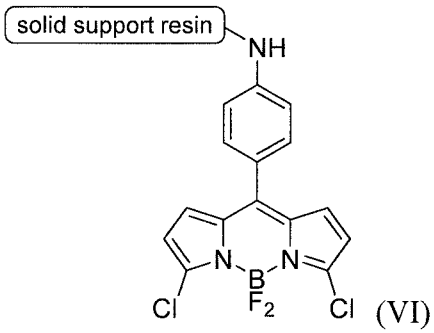
wherein $(C_1\text{-}C_{10})$alkyl, $(C_6\text{-}C_{10})$aryl$(C_0\text{-}C_6)$alkyl, $(C_3\text{-}C_{10})$heteroaryl, $(C_3\text{-}C_8)$cycloalkyl, $(C_2\text{-}C_{10})$alkynyl and $(C_2\text{-}C_{10})$alkenyl are optionally substituted at any position with 1-5 substituents selected from $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, NH_2, $-NH(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_1\text{-}C_6$ haloalkyl), $-NH(CO)(C_1\text{-}C_6$ alkoxy), $-NH(CO)(C_1\text{-}C_6$ haloalkoxy), $-NH(CO)(C_2\text{-}C_6$ alkenyl), $-Si(C_1\text{-}C_6$ alkyl), $-SO_2(C_1\text{-}C_6$ alkyl), $-SH$, $-B(OH)_2$, $-OTosyl$, $-CO(C_1\text{-}C_6$ alkoxyl), $-COH$, $-COOH$, $-CO(C_1\text{-}C_6$ alkyl) or halogen;

or R^2 and R^3 are taken together to form a ring, wherein the ring is optionally substituted with 1-5 additional substituents selected from halogen or $(C_1\text{-}C_6)$alkyl; and

R^4 is $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_8)$cycloalkyl, $(C_6\text{-}C_{10})$aryl, $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, or $(C_3\text{-}C_{10})$heteroaryl, further wherein R^4 is optionally substituted at any position with 1-5 substituents selected from $(C_1\text{-}C_{10})$alkyl, $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, $(C_3\text{-}C_8)$cycloalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_6\text{-}C_{10})$aryloxy, $(C_6\text{-}C_{10})$aryl, amino, $-NH(CO)(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_2\text{-}C_6$ alkenyl), $-NH(CO)(C_2\text{-}C_6$ alkynyl), $-NH(CO)(C_1\text{-}C_6$ haloalkyl), halo, OCF_3, CF_3, hydroxyl, or a halogen radioisotope;

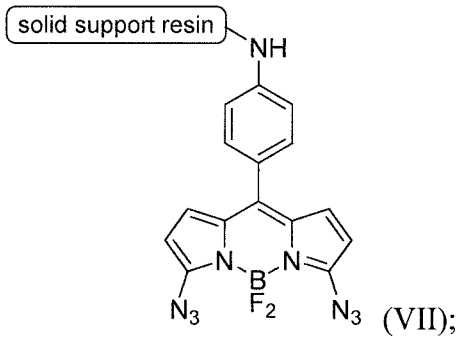
the method comprising:

(a) reacting a compound of Formula (VI):



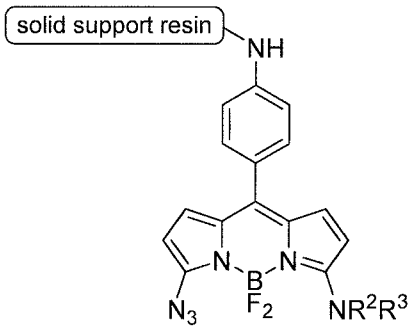
(VI)

with an azide under conditions sufficient to form a bis(azido)BODIPY compound of formula (VII):



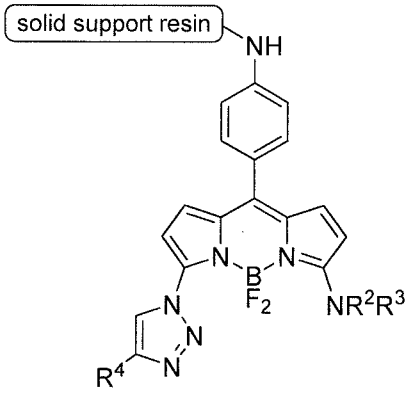
(VII);

(b) reacting the compound of Formula (VII) with an amine of the formula R^2R^3NH under conditions sufficient to form a compound of Formula (VIII):



(VIII);

(c) reacting the compound of Formula (VIII) with an alkyne of the formula R^4–C≡CH in the presence of a copper (I) catalyst under conditions sufficient to form a compound of Formula (IX):



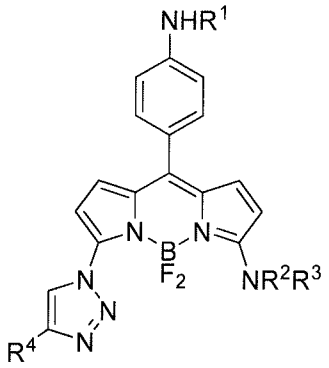
(IX);

(d) removing the solid support resin from the compound of Formula (IX) to form an unbound BODIPY compound where R^1 in Formula (I) is H; and

(e) optionally reacting the unbound BODIPY compound of step d) with an acid chloride of the formula R^1COCl to form a compound of Formula (I) where R^1 is $CO(C_1\text{-}C_6)$alkyl optionally substituted with 1-3 substituents selected from halogen, O-acetyl, or N-acetyl.

9. The method of claim 8, wherein when step (e) is performed, the method comprises an additional step of treating the reaction mixture with a base under conditions sufficient to saponify an ester or amide linkage, wherein R^1 is $CO(C_1\text{-}C_6)$alkyl optionally substituted with 1-3 hydroxyl or $-NH_2$ substituents.

10. A method for a solution phase synthesis of a compound of Formula (I) or a pharmaceutically acceptable salt thereof:



(I)

wherein:

R^1 is H or $CO(C_1\text{-}C_6)$alkyl, wherein $CO(C_1\text{-}C_6)$alkyl is optionally substituted at any position with 1-3 substituents selected from halogen, hydroxyl, O-acetyl, NH-acetyl, or $-NH_2$;

R^2 and R^3 are each, independently, H, $(C_1\text{-}C_{10})$alkyl, $(C_6\text{-}C_{10})$aryl$(C_0\text{-}C_6)$alkyl, $(C_3\text{-}C_{10})$heteroaryl, $(C_3\text{-}C_8)$cycloalkyl, $(C_2\text{-}C_{10})$alkynyl or $(C_2\text{-}C_{10})$alkenyl;

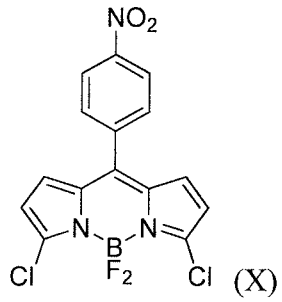
wherein $(C_1\text{-}C_{10})$alkyl, $(C_6\text{-}C_{10})$aryl$(C_0\text{-}C_6)$alkyl, $(C_3\text{-}C_{10})$heteroaryl, $(C_3\text{-}C_8)$cycloalkyl, $(C_2\text{-}C_{10})$alkynyl and $(C_2\text{-}C_{10})$alkenyl are optionally substituted at any position with 1-5 substituents selected from $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, NH_2, $-NH(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_1\text{-}C_6$ haloalkyl), $-NH(CO)(C_1\text{-}C_6$ alkoxy), $-NH(CO)(C_1\text{-}C_6$ haloalkoxy), $-NH(CO)(C_2\text{-}C_6$ alkenyl), $-Si(C_1\text{-}C_6$ alkyl), $-SO_2(C_1\text{-}C_6$ alkyl), $-SH$, $-B(OH)_2$, $-OTosyl$, $-CO(C_1\text{-}C_6$ alkoxyl), $-COH$, $-COOH$, $-CO(C_1\text{-}C_6$ alkyl) or halogen;

or R^2 and R^3 are taken together to form a ring, wherein the ring is optionally substituted with 1-5 additional substituents selected from halogen or $(C_1\text{-}C_6)$alkyl; and

R^4 is $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_8)$cycloalkyl, $(C_6\text{-}C_{10})$aryl, $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, or $(C_3\text{-}C_{10})$heteroaryl, further wherein R^4 is optionally substituted at any position with 1-5 substituents selected from $(C_1\text{-}C_{10})$alkyl, $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, $(C_3\text{-}C_8)$cycloalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_6\text{-}C_{10})$aryloxy, $(C_6\text{-}C_{10})$aryl, amino, $-NH(CO)(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_2\text{-}C_6$ alkenyl), $-NH(CO)(C_2\text{-}C_6$ alkynyl), $-NH(CO)(C_1\text{-}C_6$ haloalkyl), halo, OCF_3, CF_3, hydroxyl, or a halogen radioisotope;

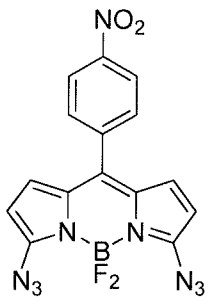
the method comprising:

(a) reacting a compound of Formula (X):



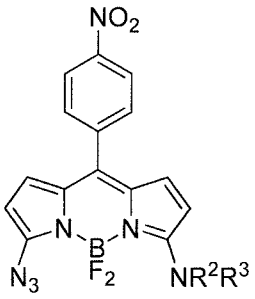
(X)

with an azide under conditions sufficient to form a bis(azido)BODIPY compound of formula (XI):



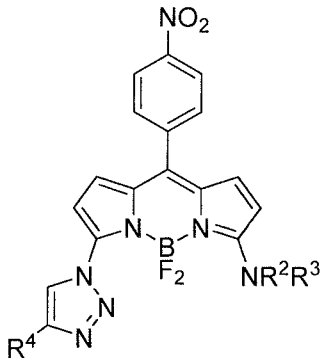
(XI);

(b) reacting the compound of Formula (XI) with an amine of the formula R^2R^3NH under conditions sufficient to form a compound of Formula (XII):



(XII);

(c) reacting the compound of Formula (XII) with an alkyne of the formula R^4–C≡CH in the presence of a copper (I) catalyst under conditions sufficient to form a compound of Formula (XIII):



(XIII);

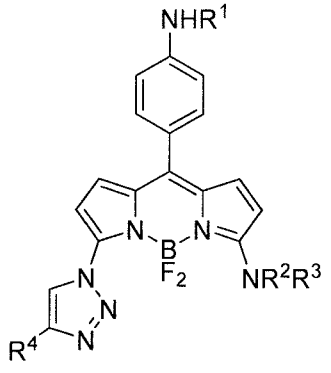
(d) reducing the NO_2 group in the compound of Formula (XIII) to form a BODIPY compound where R_1 in Formula (I) is H; and

(e) optionally reacting the BODIPY compound of step d) with an acid chloride of the formula R^1COCl to form a compound of Formula (I) where R^1 is $CO(C_1$-$C_6)$alkyl optionally substituted with 1-3 substituents selected from halogen, O-acetyl, or N-acetyl.

11. The method of claim 10, wherein when step (e) is performed, the method comprises an additional step of treating the reaction mixture with a base under conditions sufficient to saponify an ester or amide linkage, wherein R_1 is $CO(C_1$-$C_6)$alkyl optionally substituted with 1-3 hydroxyl or $-NH_2$ substituents.

12. A method for detecting human serum albumin (HSA) in a sample of a biological fluid, comprising:

a) contacting a sample of biological fluid thought to contain HSA with the compound of claim 1 represented by Formula (I)or a pharmaceutically acceptable salt thereof:



(I)

wherein:

R^1 is H or $CO(C_1\text{-}C_6)$alkyl, wherein $CO(C_1\text{-}C_6)$alkyl is optionally substituted at any position with 1-3 substituents selected from halogen, hydroxyl, O-acetyl, NH-acetyl, or $-NH_2$;

R^2 and R^3 are each, independently, H, $(C_1\text{-}C_{10})$alkyl, $(C_6\text{-}C_{10})$aryl$(C_0\text{-}C_6)$alkyl, $(C_3\text{-}C_{10})$heteroaryl, $(C_3\text{-}C_8)$cycloalkyl, $(C_2\text{-}C_{10})$alkynyl or $(C_2\text{-}C_{10})$alkenyl;

wherein $(C_1\text{-}C_{10})$alkyl, $(C_6\text{-}C_{10})$aryl$(C_0\text{-}C_6)$alkyl, $(C_3\text{-}C_{10})$heteroaryl, $(C_3\text{-}C_8)$cycloalkyl, $(C_2\text{-}C_{10})$alkynyl and $(C_2\text{-}C_{10})$alkenyl are optionally substituted at any position with 1-5 substituents selected from $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, NH_2, $-NH(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_1\text{-}C_6$ haloalkyl), $-NH(CO)(C_1\text{-}C_6$ alkoxy), $-NH(CO)(C_1\text{-}C_6$ haloalkoxy), $-NH(CO)(C_2\text{-}C_6$ alkenyl), $-Si(C_1\text{-}C_6$ alkyl), $-SO_2(C_1\text{-}C_6$ alkyl), $-SH$, $-B(OH)_2$, $-OTosyl$, $-CO(C_1\text{-}C_6$ alkoxyl), $-COH$, $-COOH$, $-CO(C_1\text{-}C_6$ alkyl) or halogen;

or R^2 and R^3 are taken together to form a ring, wherein the ring is optionally substituted with 1-5 additional substituents selected from halogen or $(C_1\text{-}C_6)$alkyl; and

R^4 is $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_8)$cycloalkyl, $(C_6\text{-}C_{10})$aryl, $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, or $(C_3\text{-}C_{10})$heteroaryl, further wherein R^4 is optionally substituted at any position with 1-5 substituents selected from $(C_1\text{-}C_{10})$alkyl, $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, $(C_3\text{-}C_8)$cycloalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_6\text{-}C_{10})$aryloxy, $(C_6\text{-}C_{10})$aryl, amino, $-NH(CO)(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_2\text{-}C_6$ alkenyl), $-NH(CO)(C_2\text{-}C_6$ alkynyl), $-NH(CO)(C_1\text{-}C_6$ haloalkyl), halo, OCF_3, CF_3, hydroxyl, or a halogen radioisotope;

to form an incubation media;

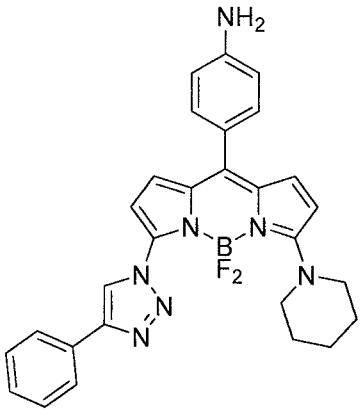
b) incubating the incubation media of step a) under conditions sufficient to form an incubated mixture; and

c) analyzing the mixture of step b) by fluorescence microscopy, wherein an increase in the fluorescence signal of the mixture relative to the fluorescence signal of the compound of

Formula (I) not in the presence of a sample containing HSA is indicative of the presence of HSA.

13. The method of claim 12, wherein a measure of intensity of the fluorescence signal is proportional to the concentration of the HSA present in the sample.

14. The method of claim 12, wherein the compound of Formula (I) has the structure of formula (II):

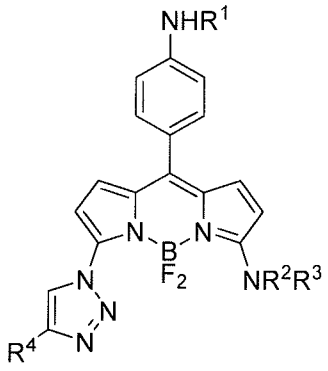


(II),

or a pharmaceutically acceptable salt thereof.

15. A method for visualizing live neurons in a cell culture, comprising:

a) contacting a cell culture with the compound of claim 1 represented by Formula (I) or a pharmaceutically acceptable salt thereof:



(I)

wherein:

R^1 is H or $CO(C_1\text{-}C_6)$alkyl, wherein $CO(C_1\text{-}C_6)$alkyl is optionally substituted at any position with 1-3 substituents selected from halogen, hydroxyl, O-acetyl, NH-acetyl, or $-NH_2$;

R^2 and R^3 are each, independently, H, $(C_1\text{-}C_{10})$alkyl, $(C_6\text{-}C_{10})$aryl$(C_0\text{-}C_6)$alkyl, $(C_3\text{-}C_{10})$heteroaryl, $(C_3\text{-}C_8)$cycloalkyl, $(C_2\text{-}C_{10})$alkynyl or $(C_2\text{-}C_{10})$alkenyl;

wherein $(C_1\text{-}C_{10})$alkyl, $(C_6\text{-}C_{10})$aryl$(C_0\text{-}C_6)$alkyl, $(C_3\text{-}C_{10})$heteroaryl, $(C_3\text{-}C_8)$cycloalkyl, $(C_2\text{-}C_{10})$alkynyl and $(C_2\text{-}C_{10})$alkenyl are optionally substituted at any position with 1-5 substituents selected from $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, NH_2, $-NH(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_1\text{-}C_6$ haloalkyl), $-NH(CO)(C_1\text{-}C_6$ alkoxy), $-NH(CO)(C_1\text{-}C_6$ haloalkoxy), $-NH(CO)(C_2\text{-}C_6$ alkenyl), $-Si(C_1\text{-}C_6$ alkyl), $-SO_2(C_1\text{-}C_6$ alkyl), $-SH$, $-B(OH)_2$, $-OTosyl$, $-CO(C_1\text{-}C_6$ alkoxyl), $-COH$, $-COOH$, $-CO(C_1\text{-}C_6$ alkyl) or halogen;

or R^2 and R^3 are taken together to form a ring, wherein the ring is optionally substituted with 1-5 additional substituents selected from halogen or $(C_1\text{-}C_6)$alkyl; and

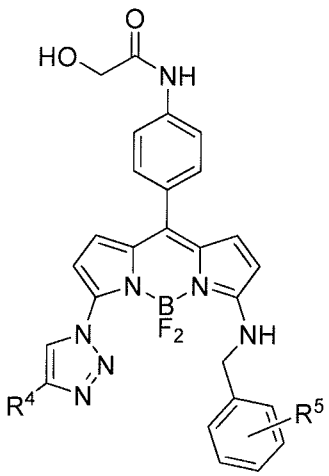
R^4 is $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_8)$cycloalkyl, $(C_6\text{-}C_{10})$aryl, $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, or $(C_3\text{-}C_{10})$heteroaryl, further wherein R^4 is optionally substituted at any position with 1-5 substituents selected from $(C_1\text{-}C_{10})$alkyl, $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, $(C_3\text{-}C_8)$cycloalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_6\text{-}C_{10})$aryloxy, $(C_6\text{-}C_{10})$aryl, amino, $-NH(CO)(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_2\text{-}C_6$ alkenyl), $-NH(CO)(C_2\text{-}C_6$ alkynyl), $-NH(CO)(C_1\text{-}C_6$ haloalkyl), halo, OCF_3, CF_3, hydroxyl, or a halogen radioisotope;

to form an incubation media;

b) incubating the incubation media of step a) under conditions sufficient to stain the live neurons; and

c) visualizing the stained live neurons of step b) with fluorescence microscopy.

16. The method of claim 15, wherein the compound of Formula (I) is a compound having the structure of Formula (XIV) or a pharmaceutically acceptable salt thereof:



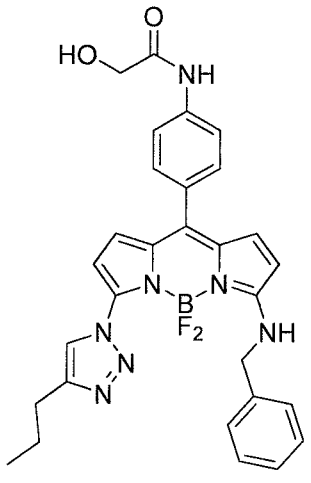
(XIV);

wherein:

R^4 is $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_8)$cycloalkyl, $(C_6\text{-}C_{10})$aryl, $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, or $(C_3\text{-}C_{10})$heteroaryl, further wherein R^4 is optionally substituted at any position with 1-5 substituents selected from $(C_1\text{-}C_{10})$alkyl, $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, $(C_3\text{-}C_8)$cycloalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_6\text{-}C_{10})$aryloxy, $(C_6\text{-}C_{10})$aryl, amino, $-NH(CO)(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_2\text{-}C_6$ alkenyl), $-NH(CO)(C_2\text{-}C_6$ alkynyl), $-NH(CO)(C_1\text{-}C_6$ haloalkyl), halo, OCF_3, CF_3, hydroxyl, or a halogen radioisotope; and

R^5 is present at any position with 1-5 substituents selected from H, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, NH_2, $-NH(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_1\text{-}C_6$ alkyl), $-NH(CO)(C_1\text{-}C_6$ haloalkyl), $-NH(CO)(C_1\text{-}C_6$ alkoxy), $-NH(CO)(C_1\text{-}C_6$ haloalkoxy), $-NH(CO)(C_2\text{-}C_6$ alkenyl), $-Si(C_1\text{-}C_6$ alkyl), $-SO_2(C_1\text{-}C_6$ alkyl), $-SH$, $-B(OH)_2$, $-OTosyl$, $-CO(C_1\text{-}C_6$ alkoxyl), $-COH$, $-COOH$, $-CO(C_1\text{-}C_6$ alkyl) or halogen.

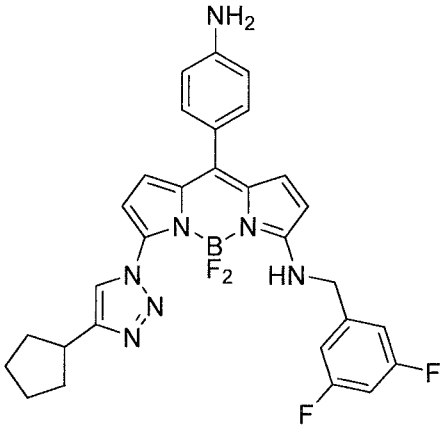
17. The method of claim 16, wherein the compound of Formula (I) has the structure of Formula (V):



(V),

or a pharmaceutically acceptable salt thereof.

18. The compound of claim 1, having the structure of Formula (XVI):



(XVI),

or a pharmaceutically acceptable salt thereof.

19. The compound of claim 1, wherein the halogen radioisotope is ^{18}F.