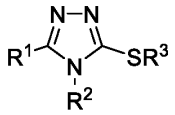
What is claimed:

1. The use of a compound in the manufacture of a medicament for the treatment of a disease or health condition that is ameliorated by inhibiting β-catenin (β-cat) or disrupting the interaction between β-cat and T-cell factor 4 (TCF4), wherein the compound has Formula **1**:



1

or a pharmaceutically acceptable salt thereof, wherein

R^1 is $-(CR^4_2)_mXR^5$;

R^2 is alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, aralkyl, heteroaralkyl, or heteroaryl;

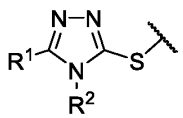
R^3 is $-(CR^6_2)_nR^7$;

R^4 for each occurrence is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aralkyl, and heteroaralkyl; or two instances of R^4 taken together with the carbon or carbons to which they are attached form a 3-7 membered cycloalkyl;

R^5 is hydrogen, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, or heteroaryl;

R^6 for each occurrence is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aralkyl, and heteroaralkyl; or two instances of R^6 taken together with the carbon or carbons to which they are attached form a 3-7 membered cycloalkyl;

R^7 is $-(C=O)R^8$, $-(C=O)OR^8$, or $-(C=O)N(R^8)_2$; or R^7 is a moiety having Formula **2**:



2

R^8 for each occurrence is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl,

aralkyl, and heteroaralkyl; or two R^8 taken together with the nitrogen to which they are attached form a 3-7 membered heterocycloalkyl; or R^6 and R^8 taken together with the atoms to which they are attached form a 4-7 membered optionally substituted cycloalkyl or a 4-7 membered optionally substituted heterocycloalkyl;

m is a whole number selected from 0-4;

n is a whole number selected from 0-4; and

X is -O-, -S-, or is absent.

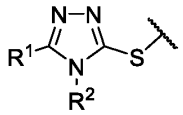
2. The use of claim 1, wherein m is 1 or 2; and X is -O- or is absent.

3. The use of claim 2, wherein R^5 is cycloalkyl or aryl.

4. The use of claim 1, wherein R^2 is cycloalkyl, aralkyl, or heteroaralkyl.

5. The use of claim 1, wherein R^2 is $-(CR^9_2)_pR^{10}$, wherein p is a whole number selected from 0-4; R^9 for each occurrence is independently hydrogen or alkyl; and R^{10} is cycloalkyl, aryl or heteroaryl.

6. The use of claim 1, wherein n is 1 or 2; R^6 for each occurrence is independently hydrogen or alkyl; R^7 is $-(C=O)R^8$, $-(C=O)OR^8$, or $-(C=O)N(R^8)_2$; or R^7 is a moiety having Formula **2**:

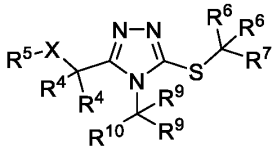


2

R^8 for each occurrence is independently selected from the group consisting of alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, aralkyl, and heteroaralkyl; or two R^8 taken together with the nitrogen to which they are attached form a 3-6 membered heterocycloalkyl; or R^6 and R^8 taken together with the atoms to which they are attached form a 5-6 membered cycloalkyl.

7. The use of claim 6, wherein R^8 for each occurrence is independently selected from the group consisting of alkyl, cycloalkyl, and aryl; or two instances of R^8 taken together with the nitrogen to which they are attached form a 5-6 membered heterocycloalkyl; or R^6 and R^8 taken together with the atoms to which they are attached form a 5-6 membered cycloalkyl.

8. The use of claim 1, wherein the compound has Formula **3**:



or a pharmaceutically acceptable salt thereof, wherein

R^4 for each occurrence is independently selected from the group consisting of hydrogen and alkyl;

R^5 is aryl or heteroaryl;

R^6 for each occurrence is independently selected from the group consisting of hydrogen and alkyl;

R^7 is -(C=O)R^8, -(C=O)OR^8, or -(C=O)N(R^8)$_2$; or R^7 is a moiety having Formula **4**:



4

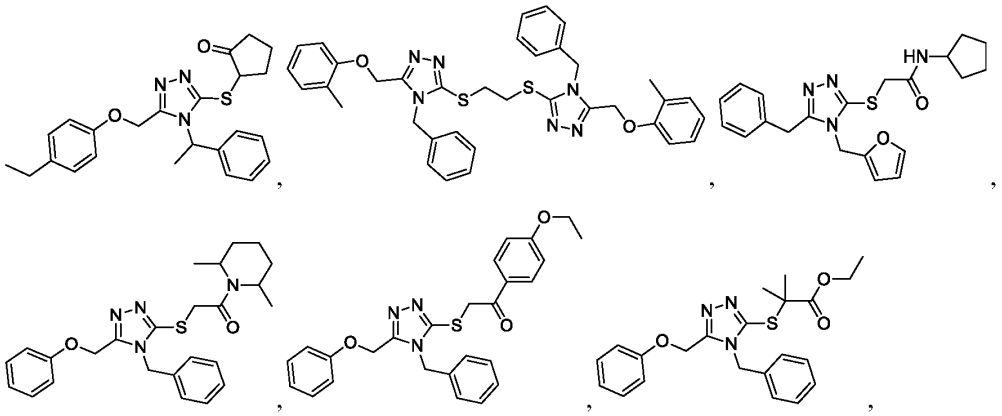
R^8 for each occurrence is independently selected from the group consisting of alkyl, cycloalkyl, and aryl; or two instances of R^8 taken together with the nitrogen to which they are attached form a 5-6 membered heterocycloalkyl; or R^6 and R^8 taken together with the atoms to which they are attached form a 5-6 membered cycloalkyl;

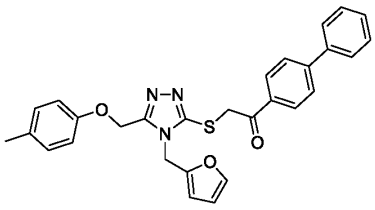
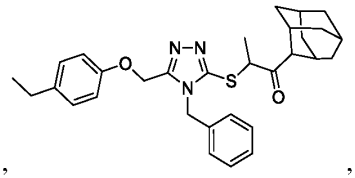
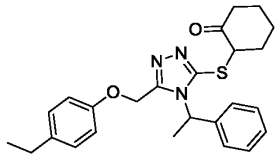
R^9 for each occurrence is independently selected from the group consisting of hydrogen and alkyl;

R^{10} is cycloalkyl, aryl or heteroaryl; and

X is -O- or absent.

9. The use of claim 1, wherein the compound is selected from the group consisting of:



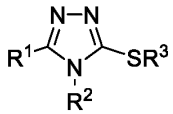


, and 

or a pharmaceutically acceptable salt thereof.

10. The use of claim 1, wherein the disease or health condition is selected from the group consisting of cancer, neurodegenerative, a metabolic disease, a cardiovascular disease, fibrosis, and a bone disease.

11. The use of claim 1, wherein the disease or health condition is a cancer selected from the group consisting of colorectal cancer, hepatocellular cancer, melanoma, liver cancer, breast cancer, prostate cancer, and leukemia.

12. A method of inhibiting β-cat or disrupting the interaction between β-cat and TCF4, the method comprising: contacting β-cat with a compound of Formula **1**:



1

or a pharmaceutically acceptable salt thereof, wherein

R^1 is $-(CR^4_2)_mXR^5$;

R^2 is alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, aralkyl, heteroaralkyl, or heteroaryl;

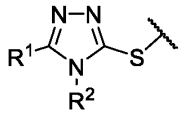
R^3 is $-(CR^6_2)_nR^7$;

R^4 for each occurrence is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aralkyl, and heteroaralkyl; or two instances of R^4 taken together with the carbon or carbons to which they are attached form a 3-7 membered cycloalkyl;

R^5 is hydrogen, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, or heteroaryl;

R^6 for each occurrence is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aralkyl, and heteroaralkyl; or two instances of R^6 taken together with the carbon or carbons to which they are attached form a 3-7 membered cycloalkyl;

R^7 is $-(C=O)R^8$, $-(C=O)OR^8$, or $-(C=O)N(R^8)_2$; or R^7 is a moiety having Formula **2**:



2

R^8 for each occurrence is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aralkyl, and heteroaralkyl; or two R^8 taken together with the nitrogen to which they are attached form a 3-7 membered heterocycloalkyl; or R^6 and R^8 taken together with the atoms to which they are attached form a 4-7 membered optionally substituted cycloalkyl or a 4-7 membered optionally substituted heterocycloalkyl;

m is a whole number selected from 0-4;

n is a whole number selected from 0-4; and

X is -O-, -S-, or is absent.

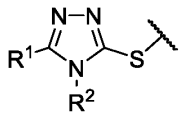
13. The method of claim 12, wherein m is 1 or 2; and X is -O- or is absent.

14. The method of claim 13, wherein R^5 is cycloalkyl or aryl.

15. The method of claim 12, wherein R^2 is cycloalkyl, aralkyl or heteroaralkyl.

16. The method of claim 12, wherein R^2 is $-(CR^9_2)_pR^{10}$, wherein p is a whole number selected from 0-4; R^9 for each occurrence is independently hydrogen or alkyl; and R^{10} is cycloalkyl, aryl or heteroaryl.

17. The method of claim 12, wherein n is 1; R^6 for each occurrence is independently hydrogen or alkyl; R^7 is $-(C=O)R^8$, $-(C=O)OR^8$, or $-(C=O)N(R^8)_2$; or R^7 is a moiety having Formula **2**:

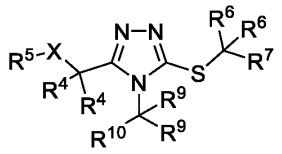


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R^8 for each occurrence is independently selected from the group consisting of alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, aralkyl, and heteroaralkyl; or two R^8 taken together with the nitrogen to which they are attached form a 3-6 membered heterocycloalkyl; or R^6 and R^8 taken together with the atoms to which they are attached form a 5-6 membered cycloalkyl.

18. The method of 17, wherein R^8 for each occurrence is independently selected from the group consisting of alkyl, cycloalkyl, and aryl; or two instances of R^8 taken together with the nitrogen to which they are attached form a 5-6 membered heterocycloalkyl; or R^6 and R^8 taken together with the atoms to which they are attached form a 5-6 membered cycloalkyl.

19. The method of claim 12, wherein the compound has Formula **3**:



3

or a pharmaceutically acceptable salt thereof, wherein

R^4 for each occurrence is independently selected from the group consisting of hydrogen and alkyl;

R^5 is aryl or heteroaryl;

R^6 for each occurrence is independently selected from the group consisting of hydrogen and alkyl;

R^7 is -(C=O)R^8, -(C=O)OR^8, or -(C=O)N(R^8)$_2$; or R^7 is a moiety having Formula **4**:



4

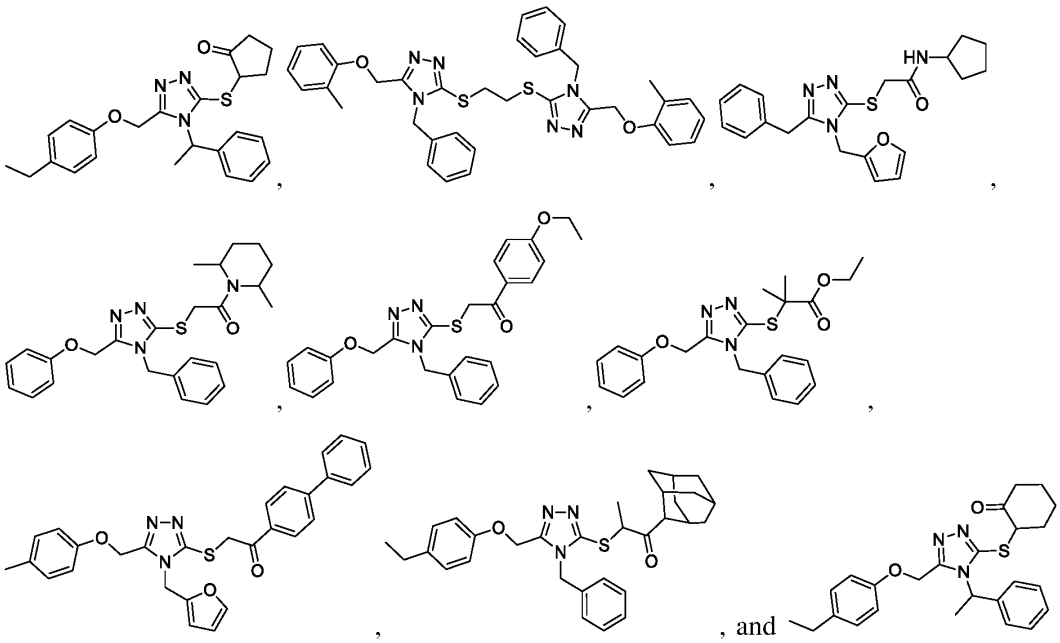
R^8 for each occurrence is independently selected from the group consisting of alkyl, cycloalkyl, and aryl; or two instances of R^8 taken together with the nitrogen to which they are attached form a 5-6 membered heterocycloalkyl; or R^6 and R^8 taken together with the atoms to which they are attached form a 5-6 membered cycloalkyl;

R^9 for each occurrence is independently selected from the group consisting of hydrogen and alkyl;

R^{10} is cycloalkyl, aryl or heteroaryl; and

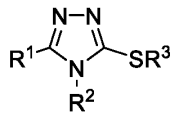
X is -O- or absent.

20. The method of claim 12, wherein the compound is selected from the group consisting of:



or a pharmaceutically acceptable salt thereof.

21. A method of treating a disease or health condition that is ameliorated by inhibiting β-cat or disrupting the interaction between β-cat and TCF4 in a subject in need thereof, the method comprising administering a therapeutically effective amount of a compound of Formula **1**:



1

or a pharmaceutically acceptable salt thereof, wherein

R^1 is $-(CR^4_2)_mXR^5$;

R^2 is alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, aralkyl, heteroaralkyl, or heteroaryl;

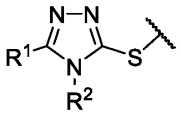
R^3 is $-(CR^6_2)_nR^7$;

R^4 for each occurrence is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aralkyl, and heteroaralkyl; or two instances of R^4 taken together with the carbon or carbons to which they are attached form a 3-7 membered cycloalkyl;

R^5 is hydrogen, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, or heteroaryl;

R^6 for each occurrence is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aralkyl, and heteroaralkyl; or two instances of R^6 taken together with the carbon or carbons to which they are attached form a 3-7 membered cycloalkyl;

R^7 is $-(C=O)R^8$, $-(C=O)OR^8$, or $-(C=O)N(R^8)_2$; or R^7 is a moiety having Formula **2**:



2

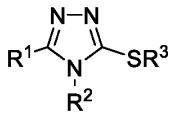
R^8 for each occurrence is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aralkyl, and heteroaralkyl; or two R^8 taken together with the nitrogen to which they are attached form a 3-7 membered heterocycloalkyl; or R^6 and R^8 taken together with the atoms to which they are attached form a 4-7 membered optionally substituted cycloalkyl or a 4-7 membered optionally substituted heterocycloalkyl;

m is a whole number selected from 0-4;

n is a whole number selected from 0-4; and

X is -O-, -S-, or is absent.

22. A compound for use in treating a disease or health condition that is ameliorated by inhibiting β-cat or disrupting the interaction between β-cat and TCF4, wherein the compound has Formula **1**:



1

or a pharmaceutically acceptable salt thereof, wherein

R^1 is $-(CR^4_2)_mXR^5$;

R^2 is alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, aralkyl, heteroaralkyl, or heteroaryl;

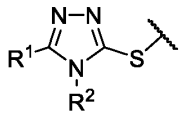
R^3 is $(CR^6_2)_nR^7$;

R^4 for each occurrence is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aralkyl, and heteroaralkyl; or two instances of R^4 taken together with the carbon or carbons to which they are attached form a 3-7 membered cycloalkyl;

R^5 is hydrogen, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, or heteroaryl;

R^6 for each occurrence is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aralkyl, and heteroaralkyl; or two instances of R^6 taken together with the carbon or carbons to which they are attached form a 3-7 membered cycloalkyl;

R^7 is $-(C=O)R^8$, $-(C=O)OR^8$, or $-(C=O)N(R^8)_2$; or R^7 is a moiety having Formula **2**:



2

R^8 for each occurrence is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aralkyl, and heteroaralkyl; or two R^8 taken together with the nitrogen to which they are attached form a 3-7 membered heterocycloalkyl; or R^6 and R^8 taken together with the atoms to which they are attached form a 4-7 membered cycloalkyl or 4-7 membered heterocycloalkyl;

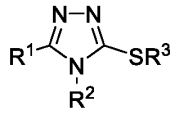
m is a whole number selected from 0-4;

n is a whole number selected from 0-4; and

X is -O-, -S-, or is absent.

23. The compound for use according to claim 22, wherein the disease or health condition is selected from the group consisting of cancer, neurodegenerative, a metabolic disease, a cardiovascular disease, fibrosis, and a bone disease.

24. A compound for use in therapy, wherein the compound has Formula **1**:



1

or a pharmaceutically acceptable salt thereof, wherein

R^1 is $-(CR^4_2)_mXR^5$;

R^2 is alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, aralkyl, heteroaralkyl, or heteroaryl;

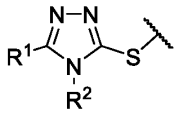
R^3 is $-(CR^6_2)_nR^7$;

R^4 for each occurrence is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aralkyl, and heteroaralkyl; or two instances of R^4 taken together with the carbon or carbons to which they are attached form a 3-7 membered cycloalkyl;

R^5 is hydrogen, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, or heteroaryl;

R^6 for each occurrence is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aralkyl, and heteroaralkyl; or two instances of R^6 taken together with the carbon or carbons to which they are attached form a 3-7 membered cycloalkyl;

R^7 is $-(C=O)R^8$, $-(C=O)OR^8$, or $-(C=O)N(R^8)_2$; or R^7 is a moiety having Formula **2**:



2

R^8 for each occurrence is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aralkyl, and heteroaralkyl; or two R^8 taken together with the nitrogen to which they are attached form a 3-7 membered heterocycloalkyl; or R^6 and R^8 taken together with the atoms to which they are attached form a 4-7 membered optionally substituted cycloalkyl or a 4-7 membered optionally substituted heterocycloalkyl;

m is a whole number selected from 0-4;

n is a whole number selected from 0-4; and

X is -O-, -S-, or is absent.