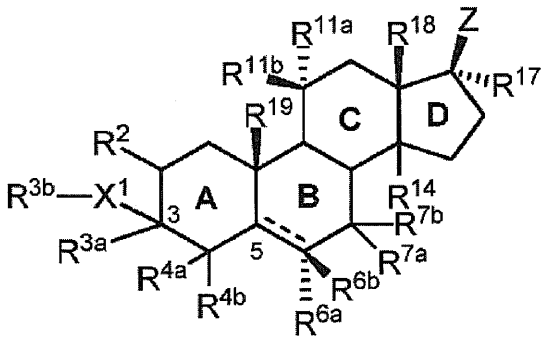
Summary

[0004] Described herein are methods of treating a sterol synthesis disorder such as SLOS or a sterol deficiency disorder. The methods of treatment can include treating a subject by administering to the subject an NMD A receptor modulating compound. Exemplary compounds are described herein.

[0005] Described herein is a method of treating a subject suffering from a sterol synthesis disorder (e.g., disorder of cholesterol biosynthesis; disorder characterized by a significant disruption of sterol biosynthesis) or a sterol deficiency disorder (e.g., abnormal levels of a sterol described herein; e.g., at least 1, e.g., at least 2 standard deviations below normal sterol levels), comprising administering to the subject an effective amount of an NMD A receptor modulating compound or pharmaceutically acceptable salt thereof.

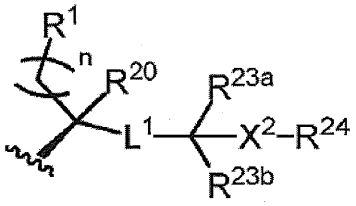
[0005a] In one aspect of the present disclosure, there is provided a compound of Formula **I** or pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a subject suffering from Smith-Lemli-Opitz Syndrome (SLOS):

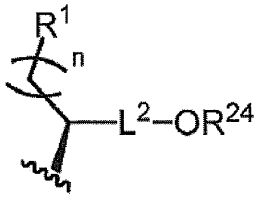


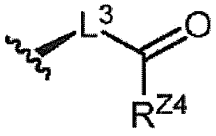
(I)

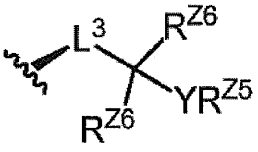
wherein:

Z is a group of the formula (i), (ii), (iii), (iv), or (v):

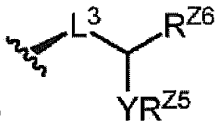

(i),


(ii),


(iii),


(iv),

or


(v)

L^1 and L^2 are selected from a group consisting of a bond, a substituted or unsubstituted C_1-C_6 alkylene, a substituted or unsubstituted C_2-C_6 alkenylene, substituted or unsubstituted C_2-C_6 alkynylene, a substituted or unsubstituted hetero C_1-C_6 alkylene, a substituted or unsubstituted hetero C_2-C_6 alkenylene, and a substituted or unsubstituted hetero C_2-C_6 alkynylene;

L^3 is a substituted or unsubstituted C_1-C_6 alkylene, a substituted or unsubstituted C_2-C_6 alkenylene, substituted or unsubstituted C_2-C_6 alkynylene, a substituted or unsubstituted hetero C_1-C_6 alkylene, a substituted or unsubstituted hetero C_2-C_6 alkenylene, or a substituted or unsubstituted hetero C_2-C_6 alkynylene;

each instance of X^1 and X^2 is independently -O-, -S-, -N(R^X)-, wherein each instance of R^x is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroalkyl, or an amino protecting group;

R^1 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, halo, $-N_3$, $-NO_2$, -SCN, -CN, $-OR^{A1}$, $-SR^{A1}$, $-N(R^{A1})_2$, $-N{=}NR^{A1}$, $-N{=}C(R^{A1})_2$, $-N(OR^{A1})(R^{A1})$,-$C(=O)R^{A1}$, $-C(=O)OR^{A1}$, $-C(=O)SR^{A1}$, $-C(=O)N(R^{A1})_2$, $-C(=O)N(OR^{A1})(R^{A1})$, $-OC(=O)R^{A1}$, -$OC(=O)OR^{A1}$, $-OC(=O)SR^{A1}$, $-OC(=O)N(R^{A1})_2$, $-NR^{A1}C(=O)R^{A1}$, $-NR^{A1}C(=O)OR^{A1}$, -$NR^{A1}C(=O)SR^{A1}$, $-NR^{A1}C(=O)N(R^{A1})_2$, $-SC(=O)R^{A2}$, $-SC(=O)OR^{A1}$, $-SC(=O)SR^{A1}$, $-SC(=O)N(R^{A1})_2$,

$-OS(=O)_2R^{A2}$, $-OS(=O)_2OR^{A1}$, $-S-S(=O)_2R^{A2}$, $-S-S(=O)_2OR^{A1}$, $-S(=O)R^{A2}$, $-SO_2R^{A2}$,— $NR_{A1}SO_2R^{A2}$, or $-SO_2N(R^{A1})_2$, wherein R^{A1} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, a nitrogen protecting group when attached to a nitrogen atom, or two R^{A1} groups are joined to form an substituted or unsubstituted heterocyclic ring; and R^{A2} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl, or an R^{A1} group and an R^{A2} group are joined to form an substituted or unsubstituted heterocyclic ring;

each instance of R^2, R^{4a}, R^{4b}, R^{7a}, R^{7b}, R^{IIa}, and R^{IIb} is independently hydrogen, -OH, halo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, $-N_3$, $-NO_2$, -SCN, -CN, $-OR^{B1}$, $-SR^{B1}$, $-N(R^{B1})_2$, $-N=NR^{B1}$, $-N=C(R^{B1})_2$, $-N(OR^{B1})(R^{B1})$, $-C(=O)R^{B1}$, $-C(=O)OR^{B1}$, $-C(=O)SR^{B1}$, $-C(=O)N(R^{B1})_2$, $-C(=O)N(OR^{B1})(R^{B1})$,$-OC(=O)R^{B1}$, $-OC(=O)OR^{B1}$, $-OC(=O)SR^{B1}$, $-OC(=O)N(R^{B1})_2$, $-NR^{B1}C(=O)R^{B1}$, $-NR^{B1}C(=O)OR^{B1}$, $-NR^{B1}C(=O)SR^{B1}$, $-NR^{B1}C(=O)N(R^{B1})_2$, $-SC(=O)R^{B2}$, $-SC(=O)OR^{B1}$, $-SC(=O)SR^{B1}$, $-SC(=O)N(R^{B1})_2$, $-OS(=O)_2R^{B2}$, $-OS(=O)_2OR^{B1}$, $-S-S(=O)_2R^{B2}$, $-S-S(=O)_2OR^{B1}$, $-S(=O)R^{B2}$, $-SO_2R^{B2}$,— $NR^{B1}SO_2R^{B2}$, or $-SO_2N(R^{B1})_2$, wherein R^{B1} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, a nitrogen protecting group when attached to a nitrogen atom, or two R groups are joined to form an substituted or unsubstituted heterocyclic ring; and R^{B2} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl, or an R^{B1} group and an R^{B2} group are joined to form an substituted or unsubstituted heterocyclic ring; or optionally wherein each of R^{4a} and R^{4b}, and/or R^{7a} and R^{7b}, and/or R^{IIa} and R^{IIb} are joined to form an oxo (=O) group;

R^{3a} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

R^{3b} is hydrogen, $-C(=O)R^{C1}$, $-C(=O)OR^{C1}$, $-C(=O)SR^{C1}$, $-C(=O)N(R^{C1})_2$, $-S(=O)_2R^{C2}$, $-S(=O)_2OR^{C1}$, $-P(=O)_2R^{C2}$, $-P(=O)_2OR^{C1}$, $-P(=O)(OR^{C1})_2$, $-P(=O)(R^{C2})_2$, or $-P(=O)(R^{C2})(OR^{C1})$, wherein R^{C1} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, a nitrogen protecting group when attached to a nitrogen atom, or two R^{C1} groups are joined to form an substituted or unsubstituted heterocyclic ring; and R^{C2} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

each of R^{6a} and R^{6b} is independently hydrogen, halo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, or substituted or unsubstituted alkynyl, and ------ represents a single or double bond, provided if a double bond is present in Ring B, then one of R^{6a} or R^{6b} is absent, and provided if a single bond is present in Ring B, then the hydrogen at C5 is in the *alpha* or *beta* position;

R^{14} is hydrogen or substituted or unsubstituted alkyl;

R^{17} is hydrogen, halo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, or $-OR^{D1}$, wherein R^{D1} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, or an oxygen protecting group; each instance of R^{18}, R^{19}, and R^{20} is independently hydrogen or substituted or unsubstituted alkyl;

and each instance of R^{23a} and R^{23b} is independently hydrogen, halogen, or substituted or unsubstituted alkyl, or R^{23a} and R^{23b} are joined together to form substituted or unsubstituted C_3-C_6 cycloalkyl;

R^{24} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstitued alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstitued aryl, substituted or unsubstituted heteroaryl, -$C(=O)R^{E1}$, -$C(=O)OR^{E1}$, -$C(=O)SR^{E1}$, -$C(=O)N(R^{E1})_2$, -$S(=O)_2R^{E2}$, -$S(=O)_2OR^{E1}$, -$P(=O)_2R^{E2}$, -$P(=O)_2OR^{E1}$, -$P(=O)(OR^{E1})_2$, -$P(=O)(R^{E2})_2$, or -$P(=O)(R^{E2})(OR^{E1})$, wherein R^{E1} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, a nitrogen protecting group when attached to a nitrogen atom, or two R^{E1} groups are joined to form an substituted or unsubstituted heterocyclic ring; and R^{E2} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

Y is -O-, -S-, or -NR^{Z5}-;

R^{Z4} is independently substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -OR^{Z5}, -SR^{Z5}, or -$N(R^{Z5})_2$;

each instance of R^{Z5} is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, a nitrogen protecting group when attached to a nitrogen atom, or two R^{Z5} groups are joined to form a substituted or unsubstituted heterocyclic ring; and

each instance of R^{Z6} is independently hydrogen or substituted or unsubstituted alkyl, or two R^{Z6} groups are joined to form a C_{3-6} carbocyclic ring; and

the subscript n is 0, 1, 2, or 3.

[0006] As used herein, "normal sterol level" varies by age, and is defined, as described in as Bjorkhem et al., . of Lipid Res. 2001, 42: 366-371 ; for example, within 2 standard deviations of the values provided in Table 2 (e.g., within 2 standard deviations, within 1.5 standard deviations, or within 1 standard deviation). Normal and abnormal sterol levels (e.g., 24(S)-hydroxycholesterol and 27(S)-hydroxycholesterol) for example in various age groups, have been reported in e.g., Bjorkhem et al., . of Lipid Res. 2001, 42: 366-371 ; Bretillon et al., . Lipid Res. 2000, 41: 840-845; Bjorkhem et al., . Lipid Res. 1998, 39: 1594-1600; Lutjohann et al., Proc. Natl. Acad. Sci. USA 1996, 93: 9799-9804, the contents of each of which are incorporated herein by reference.

[0007] In some embodiments, the subject suffers from a sterol synthesis disorder and a 24(S)-hydroxycholesterol deficiency disorder.

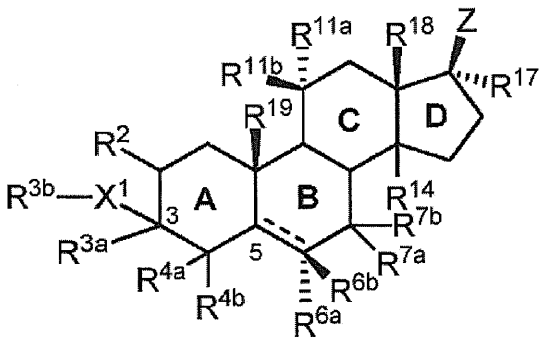
[0008] In some embodiments, the sterol deficiency disorder is characterized by the presence of 24(S)-hydroxycholesterol in the plasma of the subject at significantly reduced levels (e.g., at least 1 or 2 standard deviations below) compared with the plasma of a subject not suffering from a sterol deficiency disorder).

[0009] In some embodiments, the metabolic processing of 24(S)-hydroxycholesterol is low as compared with a subject not suffering from the disorder.

[0010] In some embodiments, the compound is 24(S)-hydroxycholesterol. In some embodiments, the compound is not a product of nature. In some embodiments, the sterol is 24(S)-hydroxycholesterol, 25-hydroxycholesterol, or 27(S)-hydroxycholesterol.

Claims

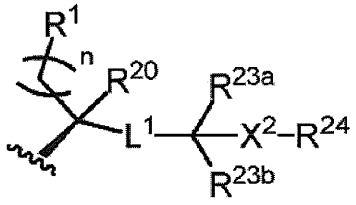
1. Use of a compound of Formula **I** or pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a subject suffering from Smith-Lemli-Opitz Syndrome (SLOS):



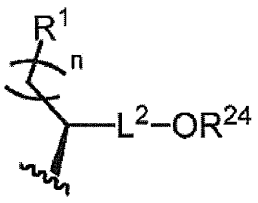
(I)

wherein:

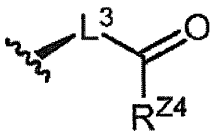
Z is a group of the formula (i), (ii), (iii), (iv), or (v):



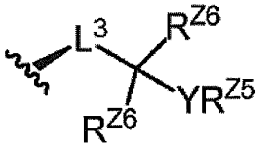
(i),



(ii),

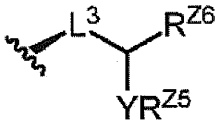


(iii),



(iv),

or



(v)

L^1 and L^2 are selected from a group consisting of a bond, a substituted or unsubstituted C_1-C_6 alkylene, a substituted or unsubstituted C_2-C_6 alkenylene, substituted or unsubstituted C_2-C_6 alkynylene, a substituted or unsubstituted hetero C_1-C_6 alkylene, a substituted or unsubstituted hetero C_2-C_6 alkenylene, and a substituted or unsubstituted hetero C_2-C_6 alkynylene;

L^3 is a substituted or unsubstituted C_1-C_6 alkylene, a substituted or unsubstituted C_2-C_6 alkenylene, substituted or unsubstituted C_2-C_6 alkynylene, a substituted or unsubstituted hetero C_1-C_6 alkylene, a substituted or unsubstituted hetero C_2-C_6 alkenylene, or a substituted or unsubstituted hetero C_2-C_6 alkynylene;

each instance of X^1 and X^2 is independently -O-, -S-, -N(R^X)-, wherein each instance of R^x is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroalkyl, or an amino protecting group;

R^1 is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, halo, $-N_3$, $-NO_2$, -SCN, -CN, $-OR^{A1}$, $-SR^{A1}$, $-N(R^{A1})_2$, $-N{=}NR^{A1}$, $-N{=}C(R^{A1})_2$, $-N(OR^{A1})(R^{A1})$,-$C(=O)R^{A1}$, $-C(=O)OR^{A1}$, $-C(=O)SR^{A1}$, $-C(=O)N(R^{A1})_2$, $-C(=O)N(OR^{A1})(R^{A1})$, $-OC(=O)R^{A1}$, -$OC(=O)OR^{A1}$, $-OC(=O)SR^{A1}$, $-OC(=O)N(R^{A1})_2$, $-NR^{A1}C(=O)R^{A1}$, $-NR^{A1}C(=O)OR^{A1}$, -$NR^{A1}C(=O)SR^{A1}$, $-NR^{A1}C(=O)N(R^{A1})_2$, $-SC(=O)R^{A2}$, $-SC(=O)OR^{A1}$, $-SC(=O)SR^{A1}$, $-SC(=O)N(R^{A1})_2$, $-OS(=O)_2R^{A2}$, $-OS(=O)_2OR^{A1}$, $-S\text{-}S(=O)_2R^{A2}$, $-S\text{-}S(=O)_2OR^{A1}$, $-S(=O)R^{A2}$, $-SO_2R^{A2}$,— $NR_{A1}SO_2R^{A2}$, or $-SO_2N(R^{A1})_2$, wherein R^{A1} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, a nitrogen protecting group when attached to a nitrogen atom, or two R^{A1} groups are joined to form an substituted or unsubstituted heterocyclic ring; and R^{A2} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl, or an R^{A1} group and an R^{A2} group are joined to form an substituted or unsubstituted heterocyclic ring;

each instance of R^2, R^{4a}, R^{4b}, R^{7a}, R^{7b}, R^{IIa}, and R^{IIb} is independently hydrogen, -OH, halo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, $-N_3$, $-NO_2$, -SCN, -CN, $-OR^{B1}$, $-SR^{B1}$, -$N(R^{B1})_2$, $-N{=}NR^{B1}$, $-N{=}C(R^{B1})_2$, $-N(OR^{B1})(R^{B1})$, $-C(=O)R^{B1}$, $-C(=O)OR^{B1}$, $-C(=O)SR^{B1}$, -$C(=O)N(R^{Bl})_2$, $-C(=O)N(OR^{B1})(R^{B1})$,-$OC(=O)R^{B1}$, $-OC(=O)OR^{B1}$, $-OC(=O)SR^{B1}$, $-OC(=O)N(R^{B1})_2$,

$-NR^{B1}C(=O)R^{B1}$, $-NR^{B1}C(=O)OR^{B1}$, $-NR^{B1}C(=O)SR^{B1}$, $-NR^{B1}C(=O)N(R^{B1})_2$, $-SC(=O)R^{B2}$, $-SC(=O)OR^{B1}$, $-SC(=O)SR^{B1}$, $-SC(=O)N(R^{B1})_2$, $-OS(=O)_2R^{B2}$, $-OS(=O)_2OR^{B1}$, $-S-S(=O)_2R^{B2}$, $-S-S(=O)_2OR^{B1}$, $-S(=O)R^{B2}$, $-SO_2R^{B2}$,— $NR^{B1}SO_2R^{B2}$, or $-SO_2N(R^{B1})_2$, wherein R^{B1} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, a nitrogen protecting group when attached to a nitrogen atom, or two R groups are joined to form an substituted or unsubstituted heterocyclic ring; and R^{B2} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl, or an R^{B1} group and an R^{B2} group are joined to form an substituted or unsubstituted heterocyclic ring; or optionally wherein each of R^{4a} and R^{4b}, and/or R^{7a} and R^{7b}, and/or R^{11a} and R^{11b} are joined to form an oxo (=O) group;

R^{3a} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

R^{3b} is hydrogen, $-C(=O)R^{C1}$, $-C(=O)OR^{C1}$, $-C(=O)SR^{C1}$, $-C(=O)N(R^{C1})_2$, $-S(=O)_2R^{C2}$, $-S(=O)_2OR^{C1}$, $-P(=O)_2R^{C2}$, $-P(=O)_2OR^{C1}$, $-P(=O)(OR^{C1})_2$, $-P(=O)(R^{C2})_2$, or $-P(=O)(R^{C2})(OR^{C1})$, wherein R^{C1} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, a nitrogen protecting group when attached to a nitrogen atom, or two R^{C1} groups are joined to form an substituted or unsubstituted heterocyclic ring; and R^{C2} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

each of R^{6a} and R^{6b} is independently hydrogen, halo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, or substituted or unsubstituted alkynyl, and ====== represents a single or double bond, provided if a double bond is present in Ring B, then one of R^{6a} or R^{6b} is absent, and provided if a single bond is present in Ring B, then the hydrogen at C5 is in the *alpha* or *beta* position;

R^{14} is hydrogen or substituted or unsubstituted alkyl;

R^{17} is hydrogen, halo, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, or $-OR^{D1}$, wherein R^{D1} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, or an oxygen protecting group; each instance of R^{18}, R^{19}, and R^{20} is independently hydrogen or substituted or unsubstituted alkyl;

and each instance of R^{23a} and R^{23b} is independently hydrogen, halogen, or substituted or unsubstituted alkyl, or R^{23a} and R^{23b} are joined together to form substituted or unsubstituted C_3-C_6 cycloalkyl;

R^{24} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstitued alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstitued aryl, substituted or unsubstituted heteroaryl, $-C(=O)R^{E1}$, $-C(=O)OR^{E1}$, $-C(=O)SR^{E1}$, $-C(=O)N(R^{E1})_2$, $-S(=O)_2R^{E2}$, $-S(=O)_2OR^{E1}$, $-P(=O)_2R^{E2}$, $-P(=O)_2OR^{E1}$, $-P(=O)(OR^{E1})_2$, $-P(=O)(R^{E2})_2$, or $-P(=O)(R^{E2})(OR^{E1})$, wherein R^{E1} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, a nitrogen protecting group when attached to a nitrogen atom, or two R^{E1} groups are joined to form an substituted or unsubstituted heterocyclic ring; and R^{E2} is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

Y is -O-, -S-, or $-NR^{Z5}$-;

R^{Z4} is independently substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, $-OR^{Z5}$, $-SR^{Z5}$, or $-N(R^{Z5})_2$;

each instance of R^{Z5} is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, a nitrogen protecting group when attached to a nitrogen atom, or two R^{Z5} groups are joined to form a substituted or unsubstituted heterocyclic ring; and

each instance of R^{Z6} is independently hydrogen or substituted or unsubstituted alkyl, or two R^{Z6} groups are joined to form a C_{3-6} carbocyclic ring; and

the subscript n is 0, 1, 2, or 3.

2. The use of claim 1, wherein the compound has an EC_{50} of 10 μM or less.

3. The use of claim 1, wherein the compound is present at an effective plasma concentration of 10 to 800 ng/mL of plasma.

4. The use of claim 1, wherein the compound is present at an effective plasma concentration of at least 10 ng/mL of plasma.

5. The use of claim 1, wherein the medicament is to be administered to the subject, wherein the administration to the subject normalizes concentrations of oxysterols in circulation relative to a subject not administered with the compound or administered with a placebo.

6. The use of claim 1, wherein the medicament is to be administered to the subject, wherein the administration to the subject elevates levels of cholesterol in tissues and plasma relative to a subject not administered with the compound or administered with a placebo.

7. The use of claim 1, wherein the subject is an infant.

8. The use of claim 1, wherein the subject is less than 21 years old.

9. The use of claim 1, wherein the subject is less than 15 years old.

10. The use of claim 1, wherein the subject is less than 12 years old.

11. The use of claim 1, wherein the subject is less than 8 years old.

12. The use of claim 1, wherein the subject is less than 4 years old.

13. The use of claim 1, wherein the subject is less than 1 year old.

14. The use of claim 1, wherein the medicament is to be administered to the subject, and an additional therapy is to be further administered.

15. The use of claim 14, within the additional therapy is dietary cholesterol therapy (e.g., cholesterol supplementation, statin treatment (e.g., 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (e.g., HMG Co A reductase inhibitors), e.g., simvastatin), bile acid supplementation or downstream hormone supplementation, medical therapies, surgical interventions, antioxidants, or gene therapy.