BILE ACID RECYCLING INHIBITORS FOR TREATMENT OF PEDIATRIC CHOLESTATIC LIVER DISEASES

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 61/553,094, filed October 28, 2011, U.S. Provisional Application No. 61/607,487, filed March 6, 2012, U.S. Provisional Application No. 61/607,503, filed March 6, 2012, which are incorporated herein by reference in their entirety.

BACKGROUND OF THE INVENTION

[0002] Pediatric cholestatic liver diseases affect a small percentage of children, but therapy results in significant healthcare costs each year. Currently, many of the pediatric cholestatic liver diseases require invasive and costly treatments such as liver transplantation and surgery. An effective and less invasive treatment that is suitable for the pediatric population is not available.

[0003] It is well understood and accepted that the therapeutic needs of children are sufficiently different than those of adults as to require specific studies of medications in children. For example, oral administration of a solid dosage form of medication is painless and simple for most adult patients, but for the pediatric patient population, swallowing an oral solid dosage form produced for adults can be problematic. In addition, the drugs used in solid dosages often have an unpleasant taste. More importantly, oral administration of adult medication targeting cholestatic liver diseases may result in side effects such as diarrhea and intestinal discomfort. Such problems pose a safety risk and affect compliance. Effective and acceptable forms of pediatric medication for pediatric cholestastatic liver diseases are needed.

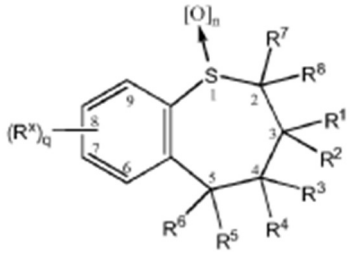
SUMMARY

[0004] The present invention refers to subject matter as defined in the attached set of claims. Provided herein are therapeutic compositions and methods for treating or ameliorating a pediatric cholestatic liver disease or pediatric cholestasis. In certain embodiments, provided herein are methods for treating or ameliorating a pediatric cholestatic liver disease comprising non-systemically administering to a pediatric patient a therapeutically effective amount of a composition comprising an Apical Sodium-dependent Bile Transporter Inhibitor (ASBTI) or a pharmaceutically acceptable salt thereof. In certain embodiments, provided herein are methods for treating or ameliorating a pediatric cholestatic liver disease comprising administering to an individual in need thereof a therapeutically effective amount of a composition comprising a non-systemically absorbed ASBTI or a pharmaceutically acceptable salt thereof. In certain embodiments, provided herein are methods for treating or ameliorating a pediatric cholestatic liver disease comprising non-systemically administering to a pediatric patient a therapeutically effective amount of a pediatric dosage form comprising an Apical Sodium-dependent Bile Transporter Inhibitor (ASBTI) or a pharmaceutically acceptable salt thereof. In certain embodiments, provided herein are methods for treating or ameliorating a pediatric cholestatic liver disease comprising administering to an individual in need thereof a therapeutically effective amount of a pediatric dosage form comprising a non-systemically absorbed ASBTI or a pharmaceutically acceptable salt thereof.

CLAIMS

WHAT IS CLAIMED IS:

1. Use of a composition comprising an Apical Sodium-dependent Bile Acid Transporter Inhibitor (ASBTI) or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable diluent, excipient or carrier, in the manufacture of a medicament for treating a pediatric cholestatic liver disease in a pediatric patient between 0 and 18 years of age, wherein less than 10% of the ASBTI is systemically absorbed, and wherein the ASBTI is a compound of Formula II:



Forumla II

wherein:

q is an integer from 1 to 4;

n is an integer from 0 to 2;

R^1 and R^2 are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, alkylaryl, arylalkyl, alkoxy, alkoxyalkyl, dialkylamino, alkylthio, (polyalkyl)aryl, and cycloalkyl, wherein alkyl, alkenyl, alkynyl, haloalkyl, alkylaryl, arylalkyl, alkoxy, alkoxyalkyl, dialkylamino, alkylthio, (polyalkyl)aryl, and cycloalkyl optionally are substituted with one or more substituents selected from the group consisting of OR^9, NR^9R^{10}, $N^+R^9R^{10}R^wA^-$, SR^9, $S^+R^9R^{10}A^-$, $P^+R^9R^{10}R^{11}$ A^-, $S(O)$ R^9, SO_2R^9, SO_3R^9, CO_2R^9, CN, halogen, oxo, and $CONR^9R^{10}$,

wherein alkyl, alkenyl, alkynyl, alkylaryl, alkoxy, alkoxyalkyl, (polyalkyl)aryl, and cycloalkyl optionally have one or more carbons replaced by O, NR^9, $N^+R^9R^{10}A^-$, S, SO, SO_2, $S^+R^9A^-$, $P^+R^9R^{10}$ A^-, or phenylene, wherein R^9, R^{10}, and R^w are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, arylalkyl, and alkylammoniumalkyl; or

R^1 and R^2 taken together with the carbon to which they are attached form C3-C10 cycloalkyl;

R^3 and R^4 are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, acyloxy, aryl, heterocycle, OR^9, NR^9R^{10}, SR^9, $S(O)R^9$, SO_2R^9, and SO_3R^9, wherein R^9 and R^{10} are as defined above; or

R^3 and R^4 together =O , $=NOR^{11}$, =S, $=NNR^{11}$ R^{12}, $=NR^9$, or $=CR^{11}$ R^{12},

wherein R^{11} and R^{12} are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, alkenylalkyl, alkynylalkyl, heterocycle, carboxyalkyl, carboalkoxyalkyl, cycloalkyl, cyanoalkyl, OR^9, NR^9R^{10}, SR^9, $S(O)$ R^9, SO_2R^9, SO_3R^9, CO_2R^9, CN, halogen, oxo, and $CONR^9R^{10}$, wherein R^9 and R^{10} are as defined above, provided that both R^3 and R^4 cannot be OH, NH_2, and SH, or

R^{11} and R^{12} together with the nitrogen or carbon atom to which they are attached form a cyclic ring; R^5 and R^6 are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, quarternary heteroaryl, OR^9, SR^9, $S(O)$ R^9, SO_2R^9, SO_3R^9, and $-L_z-K_z$;

wherein z is 1, 2 or 3; each L is independently a substituted or unsubstituted alkyl, a substituted or unsubstituted heteroalkyl, a substituted or unsubstituted alkoxy, a substituted or unsubstituted aminoalkyl group, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted cycloalkyl, or a substituted or unsubstituted heterocycloalkyl; each K is a non-protic charged group;

wherein alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, and quaternary heteroaryl can be substituted with one or more substituent groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, halogen, oxo, R^{15}, OR^{13}, $OR^{13}R^{14}$, $NR^{13}R^{14}$, SR^{13}, $S(O)R^{13}$, SO_2R^{13}, SO_3R^{13}, $NR^{13}OR^{14}$, $NR^{13}NR^{14}R^{15}$, NO_2, CO_2R^{13}, CN, OM, SO_2OM, $SO_2NR^{13}R^{14}$, $C(O)NR^{13}R^{14}$, C(O)OM , CR^{13}, $P(O)R^{13}R^{14}$, $P^+R^{13}R^{14}R^{15}A^-$, $P(OR^{13})OR^{14}$, $S^+R^{13}R^{14}A^-$, and $N^+R^9R^{11}R^{12}A^-$;

wherein:

A- is a pharmaceutically acceptable anion and M is a pharmaceutically acceptable cation, said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can be further substituted with one or more substituent groups selected from the group consisting of OR^7, NR^7R^8, $S(O)R^7$, SO_2R^7, SO_3R^7, CO_2R^7, CN, oxo, $CONR^7R^8$, $N^+R^7R^8R^9A^-$, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, $P(O)R^7R^8$, $P^+R^7R^8R^9A^-$, and $P(O)(OR^7)\ OR^8$ and

wherein said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can optionally have one or more carbons replaced by O, NR^7, $N^+R^7R^8A^-$, S, SO, SO_2 , $S^+R^7A^-$, PR^7, $P(O)\ R^7$, $P^+R^7R^8A^-$, or phenylene, and R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, polyalkyl, aryl, arylalkyl, cycloalkyl, heterocycle, heteroaryl, quaternary heterocycle, quaternary heteroaryl, quaternary heteroarylalkyl, and -G-T-V-W, wherein alkyl, alkenyl, alkynyl, arylalkyl, heterocycle, and polyalkyl optionally have one or more carbons replaced by O, NR^9, $N^+R^9R^{10}A^-$, S, SO, SO_2, $S^+R^9A^-$, PR, $P^+R^9R^{10}A^-$, $P(O)R^9$, phenylene, carbohydrate, C_2-C_7 polyol, amino acid, peptide, or polypeptide, and

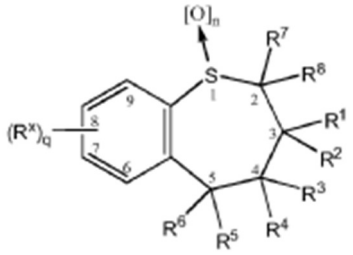
G, T and V are each independently a bond, -O-, -S-, -N(H)-, substituted or unsubstituted alkyl, -O-alkyl, -N(H)-alkyl, -C(O)N(H)-, -N(H)C(O)-, -N(H)C(O)N(H)-, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted alkenylalkyl, alkynylalkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted heterocycle, substituted or unsubstituted carboxyalkyl, substituted or unsubstituted carboalkoxyalkyl, or substituted or unsubstituted cycloalkyl, and W is quaternary heterocycle, quaternary heteroaryl, quaternary heteroarylalkyl, $N^+R^9R^{11}R^{12}A^-$, $P^+R^9R^{10}R^{11}\ A^-$, $OS(O)_2OM$, or $S^+R^9R^{10}A^-$, and

R^{13}, R^{14} and R^{15} are optionally substituted with one or more groups selected from the group consisting of sulfoalkyl, quaternary heterocycle, quaternary heteroaryl, OR^9, NR^9R^{10}, $N^+R^9R^{11}R^{12}A^-$, SR^9, $S(O)\ R^9$, SO_2R^9, SO_3R^9, oxo, CO_2R^9, CN, halogen, $CONR^9R^{10}$, SO_2OM, $SO_2NR^9R^{10}$, $PO(OR^{16})OR^{17}$, $P^+R^9R^{10}R^{11}A^-$, $S^+R^9R^{10}A^-$, and C(O)OM,

wherein R^{16} and R^{17} are independently selected from the substituents constituting R^9 and M; or

R^{14} and R^{15}, together with the nitrogen atom to which they are attached, form a cyclic ring; and
is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, alkylammoniumalkyl, and arylalkyl; and
R^7 and R^8 are independently selected from the group consisting of hydrogen and alkyl; and
one or more R^x are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, polyalkyl, acyloxy, aryl, arylalkyl, halogen, haloalkyl, cycloalkyl, heterocycle, heteroaryl, polyether, quaternary heterocycle, quaternary heteroaryl, OR^{13}, $NR^{13}R^{14}$, SR^{13}, $S(O)\ R^{13}$, $S(O)_2R^{13}$, SO_3R^{13}, $S^+R^{13}R^{14}A^-$, $NR^{13}OR^{14}$, $NR^{13}NR^{14}R^{15}$, NO_2, CO_2R^{13}, CN, OM, SO_2OM, $SO_2NR^{13}R^{14}$, $NR^{14}C(O)R^{13}$, $C(O)NR^{13}R^{14}$, $NR^{14}C(O)R^{13}$, C(O)OM, COR^{13}, OR^{18}, $S(O)_n\ NR^{18}$, $NR^{13}R^{18}$, $NR^{18}R^{14}$, $N^+R^9R^{11}R^{12}A^-$, $P^+R^9R^{11}R^{12}A^-$, amino acid, peptide, polypeptide, and carbohydrate;
wherein alkyl, alkenyl, alkynyl, cycloalkyl, aryl, polyalkyl, heterocycle, acyloxy, arylalkyl, haloalkyl, polyether, quaternary heterocycle, and quaternary heteroaryl can be further substituted with OR^9, NR^9R^{10}, $N^+R^9R^{11}R^{12}A^-$, SR^9, $S(O)R^9$, SO_2R^9, SO_3R^9, oxo, CO_2R^9, CN, halogen, $CONR^9R^{10}$, $S\ O_2\ OM$, $SO_2\ NR^9R^{10}$, $PO(OR^{16})OR^{17}$, $P^+R^9R^{11}\ R^{12}A^-$, $S^+R^9R^{10}A^-$, or C(O)M,
wherein W is O or NH, R^{31} is selected from
wherein R^{18} is selected from the group consisting of acyl, arylalkoxycarbonyl, arylalkyl, heterocycle, heteroaryl, alkyl,
wherein acyl, arylalkoxycarbonyl, arylalkyl, heterocycle, heteroaryl, alkyl, quaternary heterocycle, and quaternary heteroaryl optionally are substituted with one or more substituents selected from the group consisting of OR^9, NR^9R^{10}, $N^+R^9R^{11}R^{12}A$, SR^9, $S(O)R^9$, SO_2R^9, SO_3R^9, oxo, CO_3R^9, CN, halogen, $CONR^9R^{10}$, SO_3R^9, SO_2OM, $SO_2NR^9R^{10}$, $PO(OR^{16})OR^{17}$, and C(O)OM,
wherein in R^x, one or more carbons are optionally replaced by O, NR^{13}, $N^+R^{13}R^{14}A^-$, S, SO, SO_2, $S^+R^{13}A^-$, PR^{13}, $P(O)R^{13}$, $P^+R^{13}R^{14}A^-$, phenylene, amino acid, peptide, polypeptide, carbohydrate, polyether, or polyalkyl,
wherein in said polyalkyl, phenylene, amino acid, peptide, polypeptide, and carbohydrate, one or more carbons are optionally replaced by O, NR^9, $R^9R^{10}A^-$, S, SO, SO_2, $S^+R^9A^-$, PR^9, $P^+R^9R^{10}A^-$, or $P(O)R^9$;
wherein quaternary heterocycle and quaternary heteroaryl are optionally substituted with one or more groups selected from the group consisting of alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, heterocycle, arylalkyl, halogen, oxo, OR^{13}, $NR^{13}R^{14}$, SR^{13}, $S(O)\ R^{13}$, $SO_2\ R^{13}$, $S\ O_3\ R^{13}$, $NR^{13}OR^{14}$, $NR^{13}NR^{14}R^{15}$, NO_2, CO_2R^{13}, CN, OM, $SO_2\ OM$, $SO_2NR^{13}R^{14}$, $C(O)\ NR^{13}R^{14}$, C(O) OM, COR^{13}, $P(O)R^{13}R^{14}$ $P^+R^{13}R^{14}R^{15}A$, $P(OR^{13})OR^{14}$, $S^+R^{13}R^{14}A^-$, and $N^+R^9R^{11}R^{12}A$, provided that both R^5 and R^6 cannot be hydrogen or SH;
provided that when R^5 or R^6 is phenyl, only one of R^1 or R^2 is H;
provided that when q=l and R^x is styryl, anilido, or anilinocarbonyl, only one of R^5 or R^6 is alkyl; or a pharmaceutically acceptable salt or solvate thereof.

2. Use of a composition comprising an Apical Sodium-dependent Bile Acid Transporter Inhibitor (ASBTI) or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable diluent, excipient or carrier, in the manufacture of a medicament for treating pruritus in a pediatric patient between 0 and 18 years of age suffering from a pediatric cholestatic liver disease, wherein less than 10% of the ASBTI is systemically absorbed, and wherein the ASBTI is a compound of Formula II:



Forumla II

wherein:

q is an integer from 1 to 4;

n is an integer from 0 to 2;

R^1 and R^2 are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, alkylaryl, arylalkyl, alkoxy, alkoxyalkyl, dialkylamino, alkylthio, (polyalkyl)aryl, and cycloalkyl, wherein alkyl, alkenyl, alkynyl, haloalkyl, alkylaryl, arylalkyl, alkoxy, alkoxyalkyl, dialkylamino, alkylthio, (polyalkyl)aryl, and cycloalkyl optionally are substituted with one or more substituents selected from the group consisting of OR^9, NR^9R^{10}, $N^+R^9R^{10}R^wA^-$, SR^9, $S^+R^9R^{10}A^-$, $P^+R^9R^{10}R^{11}$ A^-, $S(O)$ R^9, SO_2R^9, SO_3R^9, CO_2R^9, CN, halogen, oxo, and $CONR^9R^{10}$,

wherein alkyl, alkenyl, alkynyl, alkylaryl, alkoxy, alkoxyalkyl, (polyalkyl)aryl, and cycloalkyl optionally have one or more carbons replaced by O, NR^9, $N^+R^9R^{10}A^-$, S, SO, SO_2, $S^+R^9A^-$, $P^+R^9R^{10}$ A^-, or phenylene, wherein R^9, R^{10}, and R^w are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, arylalkyl, and alkylammoniumalkyl; or

R^1 and R^2 taken together with the carbon to which they are attached form C3-C10 cycloalkyl;

R^3 and R^4 are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, acyloxy, aryl, heterocycle, OR^9, NR^9R^{10}, SR^9, $S(O)R^9$, SO_2R^9, and SO_3R^9, wherein R^9 and R^{10} are as defined above; or

R^3 and R^4 together =O , $=NOR^{11}$, =S, $=NNR^{11}$ R^{12}, $=NR^9$, or $=CR^{11}$ R^{12},

wherein R^{11} and R^{12} are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, alkenylalkyl, alkynylalkyl, heterocycle, carboxyalkyl, carboalkoxyalkyl, cycloalkyl, cyanoalkyl, OR^9, NR^9R^{10}, SR^9, $S(O)$ R^9, SO_2R^9, SO_3R^9, CO_2R^9, CN, halogen, oxo, and $CONR^9R^{10}$, wherein R^9 and R^{10} are as defined above, provided that both R^3 and R^4 cannot be OH, NH_2, and SH, or

R^{11} and R^{12} together with the nitrogen or carbon atom to which they are attached form a cyclic ring; R^5 and R^6 are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, quarternary heteroaryl, OR^9, SR^9, $S(O)$ R^9, SO_2R^9, SO_3R^9, and $-L_z-K_z$; wherein z is 1, 2 or 3; each L is independently a substituted or unsubstituted alkyl, a substituted or unsubstituted heteroalkyl, a substituted or unsubstituted alkoxy, a substituted or unsubstituted aminoalkyl

group, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted cycloalkyl, or a substituted or unsubstituted heterocycloalkyl; each K is a non-protic charged group;

wherein alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, and quaternary heteroaryl can be substituted with one or more substituent groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, halogen, oxo, R^{15}, OR^{13}, $OR^{13}R^{14}$, $NR^{13}R^{14}$, SR^{13}, $S(O)R^{13}$, SO_2R^{13}, SO_3R^{13}, $NR^{13}OR^{14}$, $NR^{13}NR^{14}R^{15}$, NO_2, CO_2R^{13}, CN, OM, SO_2OM, $SO_2NR^{13}R^{14}$, $C(O)NR^{13}R^{14}$, C(O)OM , CR^{13}, $P(O)R^{13}R^{14}$, $P^+R^{13}R^{14}R^{15}A^-$, $P(OR^{13})OR^{14}$, $S^+R^{13}R^{14}A^-$, and $N^+R^9R^{11}R^{12}A^-$;

wherein:

A- is a pharmaceutically acceptable anion and M is a pharmaceutically acceptable cation, said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can be further substituted with one or more substituent groups selected from the group consisting of OR^7, NR^7R^8, $S(O)R^7$, SO_2R^7, SO_3R^7, CO_2R^7, CN, oxo, $CONR^7R^8$, $N^+R^7R^8R^9A^-$, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, $P(O)R^7R^8$, $P^+R^7R^8R^9A^-$, and $P(O)(OR^7)\ OR^8$ and

wherein said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can optionally have one or more carbons replaced by O, NR^7, $N^+R^7R^8A^-$, S, SO, SO_2 , $S^+R^7A^-$, PR^7, $P(O)\ R^7$, $P^+R^7R^8A^-$, or phenylene, and R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, polyalkyl, aryl, arylalkyl, cycloalkyl, heterocycle, heteroaryl, quaternary heterocycle, quaternary heteroaryl, quaternary heteroarylalkyl, and -G-T-V-W, wherein alkyl, alkenyl, alkynyl, arylalkyl, heterocycle, and polyalkyl optionally have one or more carbons replaced by O, NR^9, $N^+R^9R^{10}A^-$, S, SO, SO_2, $S^+R^9A^-$, PR, $P^+R^9R^{10}A^-$, $P(O)R^9$, phenylene, carbohydrate, C_2-C_7 polyol, amino acid, peptide, or polypeptide, and

G, T and V are each independently a bond, -O-, -S-, -N(H)-, substituted or unsubstituted alkyl, -O-alkyl, -N(H)-alkyl, -C(O)N(H)-, -N(H)C(O)-, -N(H)C(O)N(H)-, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted alkenylalkyl, alkynylalkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted heterocycle, substituted or unsubstituted carboxyalkyl, substituted or unsubstituted carboalkoxyalkyl, or substituted or unsubstituted cycloalkyl, and W is quaternary heterocycle, quaternary heteroaryl, quaternary heteroarylalkyl, $N^+R^9R^{11}R^{12}A^-$, $P^+R^9R^{10}R^{11}\ A^-$, $OS(O)_2OM$, or $S^+R^9R^{10}A^-$, and

R^{13}, R^{14} and R^{15} are optionally substituted with one or more groups selected from the group consisting of sulfoalkyl, quaternary heterocycle, quaternary heteroaryl, OR^9, NR^9R^{10}, $N^+R^9R^{11}R^{12}A^-$, SR^9, $S(O)\ R^9$, SO_2R^9, SO_3R^9, oxo, CO_2R^9, CN, halogen, $CONR^9R^{10}$, SO_2OM, $SO_2NR^9R^{10}$, $PO(OR^{16})OR^{17}$, $P^+R^9R^{10}R^{11}A^-$, $S^+R^9R^{10}A^-$, and C(O)OM,

wherein R^{16} and R^{17} are independently selected from the substituents constituting R^9 and M; or

R^{14} and R^{15}, together with the nitrogen atom to which they are attached, form a cyclic ring; and

is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle,

ammoniumalkyl, alkylammoniumalkyl, and arylalkyl; and

R^7 and R^8 are independently selected from the group consisting of hydrogen and alkyl; and

one or more R^x are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, polyalkyl, acyloxy, aryl, arylalkyl, halogen, haloalkyl, cycloalkyl, heterocycle, heteroaryl, polyether, quaternary heterocycle, quaternary heteroaryl, OR^{13}, $NR^{13}R^{14}$, SR^{13}, $S(O)\ R^{13}$, $S(O)_2R^{13}$, SO_3R^{13}, $S^+R^{13}R^{14}A^-$, $NR^{13}OR^{14}$, $NR^{13}NR^{14}R^{15}$, NO_2, CO_2R^{13}, CN, OM, SO_2OM, $SO_2NR^{13}R^{14}$, $NR^{14}C(O)R^{13}$, $C(O)NR^{13}R^{14}$, $NR^{14}C(O)R^{13}$, C(O)OM, COR^{13}, OR^{18}, $S(O)_n\ NR^{18}$, $NR^{13}R^{18}$, $NR^{18}R^{14}$, $N^+R^9R^{11}R^{12}A^-$, $P^+R^9R^{11}R^{12}A^-$, amino acid, peptide, polypeptide, and carbohydrate;

wherein alkyl, alkenyl, alkynyl, cycloalkyl, aryl, polyalkyl, heterocycle, acyloxy, arylalkyl, haloalkyl, polyether, quaternary heterocycle, and quaternary heteroaryl can be further substituted with OR^9, NR^9R^{10}, $N^+R^9R^{11}R^{12}A^-$, SR^9, $S(O)R^9$, SO_2R^9, SO_3R^9, oxo, CO_2R^9, CN, halogen, $CONR^9R^{10}$, $S\ O_2\ OM$, $SO_2\ NR^9R^{10}$, $PO(OR^{16})OR^{17}$, $P^+R^9R^{11}\ R^{12}A^-$, $S^+R^9R^{10}A^-$, or C(O)M,

wherein W is O or NH, R^{31} is selected from

wherein R^{18} is selected from the group consisting of acyl, arylalkoxycarbonyl, arylalkyl, heterocycle, heteroaryl, alkyl,

wherein acyl, arylalkoxycarbonyl, arylalkyl, heterocycle, heteroaryl, alkyl, quaternary heterocycle, and quaternary heteroaryl optionally are substituted with one or more substituents selected from the group consisting of OR^9, NR^9R^{10}, $N^+R^9R^{11}R^{12}A$, SR^9, $S(O)R^9$, SO_2R^9, SO_3R^9, oxo, CO_3R^9, CN, halogen, $CONR^9R^{10}$, SO_3R^9, SO_2OM, $SO_2NR^9R^{10}$, $PO(OR^{16})OR^{17}$, and C(O)OM,

wherein in R^x, one or more carbons are optionally replaced by O, NR^{13}, $N^+R^{13}R^{14}A^-$, S, SO, SO_2, $S^+R^{13}A^-$, PR^{13}, $P(O)R^{13}$, $P^+R^{13}R^{14}A^-$, phenylene, amino acid, peptide, polypeptide, carbohydrate, polyether, or polyalkyl,

wherein in said polyalkyl, phenylene, amino acid, peptide, polypeptide, and carbohydrate, one or more carbons are optionally replaced by O, NR^9, $R^9R^{10}A^-$, S, SO, SO_2, $S^+R^9A^-$, PR^9, $P^+R^9R^{10}A^-$, or $P(O)R^9$;

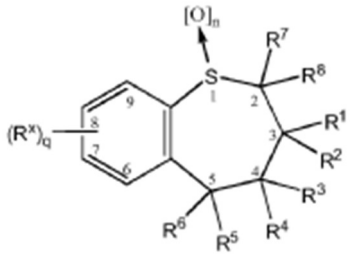
wherein quaternary heterocycle and quaternary heteroaryl are optionally substituted with one or more groups selected from the group consisting of alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, heterocycle, arylalkyl, halogen, oxo, OR^{13}, $NR^{13}R^{14}$, SR^{13}, $S(O)\ R^{13}$, $SO_2\ R^{13}$, $S\ O_3\ R^{13}$, $NR^{13}OR^{14}$, $NR^{13}NR^{14}R^{15}$, NO_2, CO_2R^{13}, CN, OM, $SO_2\ OM$, $SO_2NR^{13}R^{14}$, $C(O)\ NR^{13}R^{14}$, C(O) OM, COR^{13}, $P(O)R^{13}R^{14}$ $P^+R^{13}R^{14}R^{15}A$, $P(OR^{13})OR^{14}$, $S^+R^{13}R^{14}A^-$, and $N^+R^9R^{11}R^{12}A$, provided that both R^5 and R^6 cannot be hydrogen or SH;

provided that when R^5 or R^6 is phenyl, only one of R^1 or R^2 is H;

provided that when q=l and R^x is styryl, anilido, or anilinocarbonyl, only one of R^5 or R^6 is alkyl; or a pharmaceutically acceptable salt or solvate thereof.

3. Use of composition comprising an Apical Sodium-dependent Bile Acid Transporter Inhibitor (ASBTI) or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable diluent, excipient or carrier, in the manufacture of a medicament for treating pediatric hypercholemia in a pediatric patient

between 0 and 18 years of age, wherein less than 10% of the ASBTI is systemically absorbed, and wherein the ASBTI is a compound of Formula II:



Forumla II

wherein:

q is an integer from 1 to 4;

n is an integer from 0 to 2;

R^1 and R^2 are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, alkylaryl, arylalkyl, alkoxy, alkoxyalkyl, dialkylamino, alkylthio, (polyalkyl)aryl, and cycloalkyl, wherein alkyl, alkenyl, alkynyl, haloalkyl, alkylaryl, arylalkyl, alkoxy, alkoxyalkyl, dialkylamino, alkylthio, (polyalkyl)aryl, and cycloalkyl optionally are substituted with one or more substituents selected from the group consisting of OR^9, NR^9R^{10}, $N^+R^9R^{10}R^wA^-$, SR^9, $S^+R^9R^{10}A^-$, $P^+R^9R^{10}R^{11}$ A^-, S(O) R^9, SO_2R^9, SO_3R^9, CO_2R^9, CN, halogen, oxo, and $CONR^9R^{10}$,

wherein alkyl, alkenyl, alkynyl, alkylaryl, alkoxy, alkoxyalkyl, (polyalkyl)aryl, and cycloalkyl optionally have one or more carbons replaced by O, NR^9, $N^+R^9R^{10}A^-$, S, SO, SO_2, $S^+R^9A^-$, $P^+R^9R^{10}$ A^-, or phenylene, wherein R^9, R^{10}, and R^w are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, arylalkyl, and alkylammoniumalkyl; or

R^1 and R^2 taken together with the carbon to which they are attached form C3-C10 cycloalkyl;

R^3 and R^4 are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, acyloxy, aryl, heterocycle, OR^9, NR^9R^{10}, SR^9, $S(O)R^9$, SO_2R^9, and SO_3R^9, wherein R^9 and R^{10} are as defined above; or

R^3 and R^4 together =O , $=NOR^{11}$, =S, $=NNR^{11}$ R^{12}, $=NR^9$, or $=CR^{11}$ R^{12},

wherein R^{11} and R^{12} are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, alkenylalkyl, alkynylalkyl, heterocycle, carboxyalkyl, carboalkoxyalkyl, cycloalkyl, cyanoalkyl, OR^9, NR^9R^{10}, SR^9, S(O) R^9, SO_2R^9, SO_3R^9, CO_2R^9, CN, halogen, oxo, and $CONR^9R^{10}$, wherein R^9 and R^{10} are as defined above, provided that both R^3 and R^4 cannot be OH, NH_2, and SH, or

R^{11} and R^{12} together with the nitrogen or carbon atom to which they are attached form a cyclic ring; R^5 and R^6 are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, quarternary heteroaryl, OR^9, SR^9, S(O) R^9, SO_2R^9, SO_3R^9, and $-L_z-K_z$; wherein z is 1, 2 or 3; each L is independently a substituted or unsubstituted alkyl, a substituted or unsubstituted heteroalkyl, a substituted or unsubstituted alkoxy, a substituted or unsubstituted aminoalkyl group, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted cycloalkyl, or a substituted or unsubstituted heterocycloalkyl; each K is a non-protic charged group;

wherein alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, and quaternary heteroaryl can be substituted with one or more substituent groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, halogen, oxo, R^{15}, OR^{13}, $OR^{13}R^{14}$, $NR^{13}R^{14}$, SR^{13}, $S(O)R^{13}$, SO_2R^{13}, SO_3R^{13}, $NR^{13}OR^{14}$, $NR^{13}NR^{14}R^{15}$, NO_2, CO_2R^{13}, CN, OM, SO_2OM, $SO_2NR^{13}R^{14}$, $C(O)NR^{13}R^{14}$, C(O)OM , CR^{13}, $P(O)R^{13}R^{14}$, $P^+R^{13}R^{14}R^{15}A^-$, $P(OR^{13})OR^{14}$, $S^+R^{13}R^{14}A^-$, and $N^+R^9R^{11}R^{12}A^-$;

wherein:

A- is a pharmaceutically acceptable anion and M is a pharmaceutically acceptable cation, said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can be further substituted with one or more substituent groups selected from the group consisting of OR^7, NR^7R^8, $S(O)R^7$, SO_2R^7, SO_3R^7, CO_2R^7, CN, oxo, $CONR^7R^8$, $N^+R^7R^8R^9A^-$, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, $P(O)R^7R^8$, $P^+R^7R^8R^9A^-$, and $P(O)(OR^7)\ OR^8$ and

wherein said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can optionally have one or more carbons replaced by O, NR^7, $N^+R^7R^8A^-$, S, SO, SO_2 , $S^+R^7A^-$, PR^7, $P(O)\ R^7$, $P^+R^7R^8A^-$, or phenylene, and R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, polyalkyl, aryl, arylalkyl, cycloalkyl, heterocycle, heteroaryl, quaternary heterocycle, quaternary heteroaryl, quaternary heteroarylalkyl, and -G-T-V-W, wherein alkyl, alkenyl, alkynyl, arylalkyl, heterocycle, and polyalkyl optionally have one or more carbons replaced by O, NR^9, $N^+R^9R^{10}A^-$, S, SO, SO_2, $S^+R^9A^-$, PR, $P^+R^9R^{10}A^-$, $P(O)R^9$, phenylene, carbohydrate, C_2-C_7 polyol, amino acid, peptide, or polypeptide, and

G, T and V are each independently a bond, -O-, -S-, -N(H)-, substituted or unsubstituted alkyl, -O-alkyl, -N(H)-alkyl, -C(O)N(H)-, -N(H)C(O)-, -N(H)C(O)N(H)-, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted alkenylalkyl, alkynylalkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted heterocycle, substituted or unsubstituted carboxyalkyl, substituted or unsubstituted carboalkoxyalkyl, or substituted or unsubstituted cycloalkyl, and W is quaternary heterocycle, quaternary heteroaryl, quaternary heteroarylalkyl, $N^+R^9R^{11}R^{12}A^-$, $P^+R^9R^{10}R^{11}\ A^-$, $OS(O)_2OM$, or $S^+R^9R^{10}A^-$, and

R^{13}, R^{14} and R^{15} are optionally substituted with one or more groups selected from the group consisting of sulfoalkyl, quaternary heterocycle, quaternary heteroaryl, OR^9, NR^9R^{10}, $N^+R^9R^{11}R^{12}A^-$, SR^9, $S(O)\ R^9$, SO_2R^9, SO_3R^9, oxo, CO_2R^9, CN, halogen, $CONR^9R^{10}$, SO_2OM, $SO_2NR^9R^{10}$, $PO(OR^{16})OR^{17}$, $P^+R^9R^{10}R^{11}A^-$, $S^+R^9R^{10}A^-$, and C(O)OM,

wherein R^{16} and R^{17} are independently selected from the substituents constituting R^9 and M; or

R^{14} and R^{15}, together with the nitrogen atom to which they are attached, form a cyclic ring; and

is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, alkylammoniumalkyl, and arylalkyl; and

R^7 and R^8 are independently selected from the group consisting of hydrogen and alkyl; and

one or more R^x are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, polyalkyl,

acyloxy, aryl, arylalkyl, halogen, haloalkyl, cycloalkyl, heterocycle, heteroaryl, polyether, quaternary heterocycle, quaternary heteroaryl, OR^{13}, $NR^{13}R^{14}$, SR^{13}, S(O) R^{13}, $S(O)_2R^{13}$, SO_3R^{13}, $S^+R^{13}R^{14}A^-$, $NR^{13}OR^{14}$, $NR^{13}NR^{14}R^{15}$, NO_2, CO_2R^{13}, CN, OM, SO_2OM, $SO_2NR^{13}R^{14}$, $NR^{14}C(O)R^{13}$, $C(O)NR^{13}R^{14}$, $NR^{14}C(O)R^{13}$, C(O)OM, COR^{13}, OR^{18}, $S(O)_n$ NR^{18}, $NR^{13}R^{18}$, $NR^{18}R^{14}$, $N^+R^9R^{11}R^{12}A^-$, $P^+R^9R^{11}R^{12}A^-$, amino acid, peptide, polypeptide, and carbohydrate;

wherein alkyl, alkenyl, alkynyl, cycloalkyl, aryl, polyalkyl, heterocycle, acyloxy, arylalkyl, haloalkyl, polyether, quaternary heterocycle, and quaternary heteroaryl can be further substituted with OR^9, NR^9R^{10}, $N^+R^9R^{11}R^{12}A^-$, SR^9, $S(O)R^9$, SO_2R^9, SO_3R^9, oxo, CO_2R^9, CN, halogen, $CONR^9R^{10}$, SO_2OM, $SO_2NR^9R^{10}$, $PO(OR^{16})OR^{17}$, $P^+R^9R^{11}R^{12}A^-$, $S^+R^9R^{10}A^-$, or C(O)M,

wherein W is O or NH, R^{31} is selected from

wherein R^{18} is selected from the group consisting of acyl, arylalkoxycarbonyl, arylalkyl, heterocycle, heteroaryl, alkyl,

wherein acyl, arylalkoxycarbonyl, arylalkyl, heterocycle, heteroaryl, alkyl, quaternary heterocycle, and quaternary heteroaryl optionally are substituted with one or more substituents selected from the group consisting of OR^9, NR^9R^{10}, $N^+R^9R^{11}R^{12}A$, SR^9, $S(O)R^9$, SO_2R^9, SO_3R^9, oxo, CO_3R^9, CN, halogen, $CONR^9R^{10}$, SO_3R^9, SO_2OM, $SO_2NR^9R^{10}$, $PO(OR^{16})OR^{17}$, and C(O)OM,

wherein in R^x, one or more carbons are optionally replaced by O, NR^{13}, $N^+R^{13}R^{14}A^-$, S, SO, SO_2, $S^+R^{13}A^-$, PR^{13}, $P(O)R^{13}$, $P^+R^{13}R^{14}A^-$, phenylene, amino acid, peptide, polypeptide, carbohydrate, polyether, or polyalkyl,

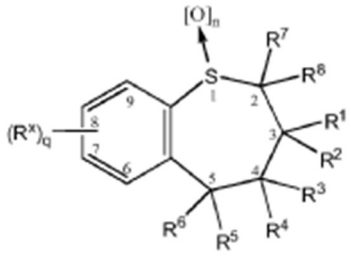
wherein in said polyalkyl, phenylene, amino acid, peptide, polypeptide, and carbohydrate, one or more carbons are optionally replaced by O, NR^9, $R^9R^{10}A^-$, S, SO, SO_2, $S^+R^9A^-$, PR^9, $P^+R^9R^{10}A^-$, or $P(O)R^9$;

wherein quaternary heterocycle and quaternary heteroaryl are optionally substituted with one or more groups selected from the group consisting of alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, heterocycle, arylalkyl, halogen, oxo, OR^{13}, $NR^{13}R^{14}$, SR^{13}, S(O) R^{13}, SO_2 R^{13}, $S O_3$ R^{13}, $NR^{13}OR^{14}$, $NR^{13}NR^{14}R^{15}$, NO_2, CO_2R^{13}, CN, OM, SO_2 OM, $SO_2NR^{13}R^{14}$, C(O) $NR^{13}R^{14}$, C(O) OM, COR^{13}, $P(O)R^{13}R^{14}$ $P^+R^{13}R^{14}R^{15}A$, $P(OR^{13})OR^{14}$, $S^+R^{13}R^{14}A^-$, and $N^+R^9R^{11}R^{12}A$, provided that both R^5 and R^6 cannot be hydrogen or SH;

provided that when R^5 or R^6 is phenyl, only one of R^1 or R^2 is H;

provided that when q=l and R^x is styryl, anilido, or anilinocarbonyl, only one of R^5 or R^6 is alkyl; or a pharmaceutically acceptable salt or solvate thereof.

4. Use of a composition comprising an Apical Sodium-dependent Bile Acid Transporter Inhibitor (ASBTI) or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable diluent, excipient or carrier, in the manufacture of a medicament for decreasing the level of serum bile acids or hepatic bile acids in a pediatric patient suffering from a pediatric cholestatic liver disease, wherein the pediatric patient is between 0 and 18 years of age, wherein less than 10% of the ASBTI is systemically absorbed, and wherein the ASBTI is a compound of Formula II:



Forumla II

wherein:

q is an integer from 1 to 4;

n is an integer from 0 to 2;

R^1 and R^2 are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, alkylaryl, arylalkyl, alkoxy, alkoxyalkyl, dialkylamino, alkylthio, (polyalkyl)aryl, and cycloalkyl, wherein alkyl, alkenyl, alkynyl, haloalkyl, alkylaryl, arylalkyl, alkoxy, alkoxyalkyl, dialkylamino, alkylthio, (polyalkyl)aryl, and cycloalkyl optionally are substituted with one or more substituents selected from the group consisting of OR^9, NR^9R^{10}, $N^+R^9R^{10}R^wA^-$, SR^9, $S^+R^9R^{10}A^-$, $P^+R^9R^{10}R^{11}$ A^-, $S(O)$ R^9, SO_2R^9, SO_3R^9, CO_2R^9, CN, halogen, oxo, and $CONR^9R^{10}$,

wherein alkyl, alkenyl, alkynyl, alkylaryl, alkoxy, alkoxyalkyl, (polyalkyl)aryl, and cycloalkyl optionally have one or more carbons replaced by O, NR^9, $N^+R^9R^{10}A^-$, S, SO, SO_2, $S^+R^9A^-$, $P^+R^9R^{10}$ A^-, or phenylene, wherein R^9, R^{10}, and R^w are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, arylalkyl, and alkylammoniumalkyl; or

R^1 and R^2 taken together with the carbon to which they are attached form C3-C10 cycloalkyl;

R^3 and R^4 are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, acyloxy, aryl, heterocycle, OR^9, NR^9R^{10}, SR^9, $S(O)R^9$, SO_2R^9, and SO_3R^9, wherein R^9 and R^{10} are as defined above; or

R^3 and R^4 together =O , $=NOR^{11}$, =S, $=NNR^{11}$ R^{12}, $=NR^9$, or $=CR^{11}$ R^{12},

wherein R^{11} and R^{12} are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, alkenylalkyl, alkynylalkyl, heterocycle, carboxyalkyl, carboalkoxyalkyl, cycloalkyl, cyanoalkyl, OR^9, NR^9R^{10}, SR^9, $S(O)$ R^9, SO_2R^9, SO_3R^9, CO_2R^9, CN, halogen, oxo, and $CONR^9R^{10}$, wherein R^9 and R^{10} are as defined above, provided that both R^3 and R^4 cannot be OH, NH_2, and SH, or

R^{11} and R^{12} together with the nitrogen or carbon atom to which they are attached form a cyclic ring; R^5 and R^6 are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, quarternary heteroaryl, OR^9, SR^9, $S(O)$ R^9, SO_2R^9, SO_3R^9, and $-L_z-K_z$; wherein z is 1, 2 or 3; each L is independently a substituted or unsubstituted alkyl, a substituted or unsubstituted heteroalkyl, a substituted or unsubstituted alkoxy, a substituted or unsubstituted aminoalkyl group, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted cycloalkyl, or a substituted or unsubstituted heterocycloalkyl; each K is a non-protic charged group;

wherein alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, and quaternary heteroaryl can be substituted with one or more substituent groups independently selected from the group

consisting of alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, halogen, oxo, R^{15}, OR^{13}, $OR^{13}R^{14}$, $NR^{13}R^{14}$, SR^{13}, $S(O)R^{13}$, SO_2R^{13}, SO_3R^{13}, $NR^{13}OR^{14}$, $NR^{13}NR^{14}R^{15}$, NO_2, CO_2R^{13}, CN, OM, SO_2OM, $SO_2NR^{13}R^{14}$, $C(O)NR^{13}R^{14}$, C(O)OM , CR^{13}, $P(O)R^{13}R^{14}$, $P^+R^{13}R^{14}R^{15}A^-$, $P(OR^{13})OR^{14}$, $S^+R^{13}R^{14}A^-$, and $N^+R^9R^{11}R^{12}A^-$;

wherein:

A- is a pharmaceutically acceptable anion and M is a pharmaceutically acceptable cation, said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can be further substituted with one or more substituent groups selected from the group consisting of OR^7, NR^7R^8, $S(O)R^7$, SO_2R^7, SO_3R^7, CO_2R^7, CN, oxo, $CONR^7R^8$, $N^+R^7R^8R^9A^-$, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, $P(O)R^7R^8$, $P^+R^7R^8R^9A^-$, and $P(O)(OR^7)\ OR^8$ and

wherein said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can optionally have one or more carbons replaced by O, NR^7, $N^+R^7R^8A^-$, S, SO, SO_2 , $S^+R^7A^-$, PR^7, $P(O)\ R^7$, $P^+R^7R^8A^-$, or phenylene, and R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, polyalkyl, aryl, arylalkyl, cycloalkyl, heterocycle, heteroaryl, quaternary heterocycle, quaternary heteroaryl, quaternary heteroarylalkyl, and -G-T-V-W, wherein alkyl, alkenyl, alkynyl, arylalkyl, heterocycle, and polyalkyl optionally have one or more carbons replaced by O, NR^9, $N^+R^9R^{10}A^-$, S, SO, SO_2, $S^+R^9A^-$, PR, $P^+R^9R^{10}A^-$, $P(O)R^9$, phenylene, carbohydrate, C_2-C_7 polyol, amino acid, peptide, or polypeptide, and

G, T and V are each independently a bond, -O-, -S-, -N(H)-, substituted or unsubstituted alkyl, -O-alkyl, -N(H)-alkyl, -C(O)N(H)-, -N(H)C(O)-, -N(H)C(O)N(H)-, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted alkenylalkyl, alkynylalkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted heterocycle, substituted or unsubstituted carboxyalkyl, substituted or unsubstituted carboalkoxyalkyl, or substituted or unsubstituted cycloalkyl, and W is quaternary heterocycle, quaternary heteroaryl, quaternary heteroarylalkyl, $N^+R^9R^{11}R^{12}A^-$, $P^+R^9R^{10}R^{11}\ A^-$, $OS(O)_2OM$, or $S^+R^9R^{10}A^-$, and

R^{13}, R^{14} and R^{15} are optionally substituted with one or more groups selected from the group consisting of sulfoalkyl, quaternary heterocycle, quaternary heteroaryl, OR^9, NR^9R^{10}, $N^+R^9R^{11}R^{12}A^-$, SR^9, $S(O)\ R^9$, SO_2R^9, SO_3R^9, oxo, CO_2R^9, CN, halogen, $CONR^9R^{10}$, SO_2OM, $SO_2NR^9R^{10}$, $PO(OR^{16})OR^{17}$, $P^+R^9R^{10}R^{11}A^-$, $S^+R^9R^{10}A^-$, and C(O)OM,

wherein R^{16} and R^{17} are independently selected from the substituents constituting R^9 and M; or

R^{14} and R^{15}, together with the nitrogen atom to which they are attached, form a cyclic ring; and

is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, alkylammoniumalkyl, and arylalkyl; and

R^7 and R^8 are independently selected from the group consisting of hydrogen and alkyl; and

one or more R^x are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, polyalkyl, acyloxy, aryl, arylalkyl, halogen, haloalkyl, cycloalkyl, heterocycle, heteroaryl, polyether, quaternary heterocycle, quaternary heteroaryl, OR^{13}, $NR^{13}R^{14}$, SR^{13}, $S(O)\ R^{13}$, $S(O)\ _2R^{13}$, SO_3R^{13}, $S^+R^{13}R^{14}A^-$,

$NR^{13}OR^{14}$, $NR^{13}NR^{14}R^{15}$, NO_2, CO_2R^{13}, CN, OM, SO_2OM, $SO_2NR^{13}R^{14}$, $NR^{14}C(O)R^{13}$, $C(O)NR^{13}R^{14}$, $NR^{14}C(O)R^{13}$, C(O)OM, COR^{13}, OR^{18}, $S(O)_n$ NR^{18}, $NR^{13}R^{18}$, $NR^{18}R^{14}$, $N^+R^9R^{11}R^{12}A^-$, $P^+R^9R^{11}R^{12}A^-$, amino acid, peptide, polypeptide, and carbohydrate;

wherein alkyl, alkenyl, alkynyl, cycloalkyl, aryl, polyalkyl, heterocycle, acyloxy, arylalkyl, haloalkyl, polyether, quaternary heterocycle, and quaternary heteroaryl can be further substituted with OR^9, NR^9R^{10}, $N^+R^9R^{11}R^{12}A^-$, SR^9, $S(O)R^9$, SO_2R^9, SO_3R^9, oxo, CO_2R^9, CN, halogen, $CONR^9R^{10}$, S O_2 OM, SO_2 NR^9R^{10}, $PO(OR^{16})OR^{17}$, $P^+R^9R^{11}$ $R^{12}A^-$, $S^+R^9R^{10}A^-$, or C(O)M,

wherein W is O or NH, R^{31} is selected from

wherein R^{18} is selected from the group consisting of acyl, arylalkoxycarbonyl, arylalkyl, heterocycle, heteroaryl, alkyl,

wherein acyl, arylalkoxycarbonyl, arylalkyl, heterocycle, heteroaryl, alkyl, quaternary heterocycle, and quaternary heteroaryl optionally are substituted with one or more substituents selected from the group consisting of OR^9, NR^9R^{10}, $N^+R^9R^{11}R^{12}A$, SR^9, $S(O)R^9$, SO_2R^9, SO_3R^9, oxo, CO_3R^9, CN, halogen, $CONR^9R^{10}$, SO_3R^9, SO_2OM, $SO_2NR^9R^{10}$, $PO(OR^{16})OR^{17}$, and C(O)OM,

wherein in R^x, one or more carbons are optionally replaced by O, NR^{13}, $N^+R^{13}R^{14}A^-$, S, SO, SO_2, $S^+R^{13}A^-$, PR^{13}, $P(O)R^{13}$, $P^+R^{13}R^{14}A^-$, phenylene, amino acid, peptide, polypeptide, carbohydrate, polyether, or polyalkyl,

wherein in said polyalkyl, phenylene, amino acid, peptide, polypeptide, and carbohydrate, one or more carbons are optionally replaced by O, NR^9, $R^9R^{10}A^-$, S, SO, SO_2, $S^+R^9A^-$, PR^9, $P^+R^9R^{10}A^-$, or $P(O)R^9$;

wherein quaternary heterocycle and quaternary heteroaryl are optionally substituted with one or more groups selected from the group consisting of alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, heterocycle, arylalkyl, halogen, oxo, OR^{13}, $NR^{13}R^{14}$, SR^{13}, $S(O)$ R^{13}, SO_2 R^{13}, S O_3 R^{13}, $NR^{13}OR^{14}$, $NR^{13}NR^{14}R^{15}$, NO_2, CO_2R^{13}, CN, OM, SO_2 OM, $SO_2NR^{13}R^{14}$, C(O) $NR^{13}R^{14}$, C(O) OM, COR^{13}, $P(O)R^{13}R^{14}$ $P^+R^{13}R^{14}R^{15}A$,$P(OR^{13})OR^{14}$, $S^+R^{13}R^{14}A^-$, and $N^+R^9R^{11}R^{12}A$, provided that both R^5 and R^6 cannot be hydrogen or SH;

provided that when R^5 or R^6 is phenyl, only one of R^1 or R^2 is H;

provided that when q=l and R^x is styryl, anilido, or anilinocarbonyl, only one of R^5 or R^6 is alkyl; or a pharmaceutically acceptable salt or solvate thereof.

5. The use of any one of claims 1, 2 or 4, wherein the pediatric cholestatic liver disease is progressive familial intrahepatic cholestasis (PFIC), PFIC type 1, PFIC type 2, PFIC type 3, Alagille syndrome, Dubin-Johnson Syndrome, biliary atresia, post-Kasai biliary atresia, post-liver transplantation biliary atresia, post-liver transplantation cholestasis, post-liver transplantation associated liver disease, intestinal failure associated liver disease, bile acid mediated liver injury, pediatric primary sclerosing cholangitis, MRP2 deficiency syndrome, neonatal sclerosing cholangitis, a pediatric obstructive cholestasis, a pediatric non-obstructive cholestasis, a pediatric extrahepatic cholestasis, a pediatric intrahepatic cholestasis, a pediatric primary intrahepatic cholestasis, a pediatric secondary intrahepatic cholestasis, benign recurrent intrahepatic

cholestasis (BRIC), BRIC type 1, BRIC type 2, BRIC type 3, total parenteral nutrition associated cholestasis, paraneoplastic cholestasis, Stauffer syndrome, drug-associated cholestasis, infection-associated cholestasis, or gallstone disease.

6. The use of any one of claims 1, 2, 4 or 5, wherein the pediatric cholestatic liver disease is characterized by one or more symptoms selected from jaundice, pruritus, cirrhosis, hypercholemia, neonatal respiratory distress syndrome, lung pneumonia, increased serum concentration of bile acids, increased hepatic concentration of bile acids, increased serum concentration of bilirubin, hepatocellular injury, liver scarring, liver failure, hepatomegaly, xanthomas, malabsorption, splenomegaly, diarrhea, pancreatitis, hepatocellular necrosis, giant cell formation, hepatocellular carcinoma, gastrointestinal bleeding, portal hypertension, hearing loss, fatigue, loss of appetite, anorexia, peculiar smell, dark urine, light stools, steatorrhea, failure to thrive, and renal failure.

7. The use of any one of claims 1-6, wherein the composition decreases serum bile acid or hepatic bile acid levels in the patient by at least 20%.

8. The use of any one of claims 1-7, wherein the composition reduces xanthoma, serum lipoprotein X, liver enzymes, bilirubin, intraenterocyte bile acids/salts, or necrosis and/or damage to hepatocellular architecture.

9. The use of any one of claims 1-8, wherein the composition is a pediatric dosage form.

10. The use of claim 9, wherein the pediatric dosage form is selected from a solution, syrup, suspension, elixir, powder for reconstitution as suspension or solution, dispersible/effervescent tablet, chewable tablet, gummy candy, lollipop, freezer pops, troches, oral thin strips, orally disintegrating tablet, sachet, soft gelatin capsule, and sprinkle oral powder or granules.

11. The use of any one of claims 1-10, wherein the dosage of the ASBTI is between 1 µg/kg/day and 10 mg/kg/day.

12. The use of any one of claims 1-10, wherein the dosage of the ASBTI is any dosage from 5 µg/kg/day to 1 mg/kg/day.

13. The use of any one of claims 1-10, wherein the dosage of the ASBTI comprises from 0.001 mg/kg to 10 mg/kg.

14. The use of any one of claims 1-10, wherein the dosage comprises from 0.001 mg/day to 5000 mg/day of the ASBTI.

15. The use of any one of claims 1 -14, wherein the pediatric patient is between 6 months to 12 years old.

16. The use of claim 1, wherein:

q is 1;

n is 2;

R^x is $N(CH_3)_2$;

R^7 and R^8 are independently H;

R^1 and R^2 is alkyl;

R^3 is H, and R^4 is OH;

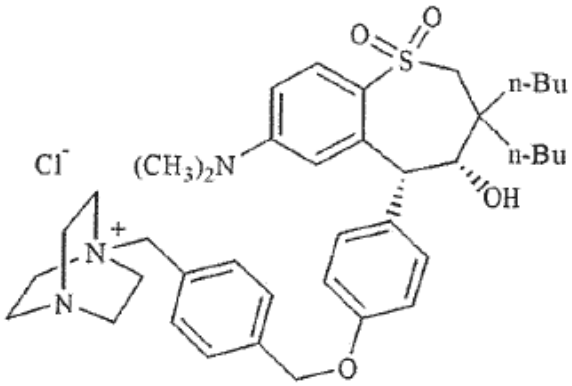
R^5 is H, and R^6 is selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, quarternary heteroaryl, OR^9, SR^9, $S(O)R^9$, SO_2R^9, SO_3R^9, and — L_z-K_z, wherein z is 1, 2 or 3; each L is independently a substituted or unsubstituted alkyl, a substituted or unsubstituted heteroalkyl, a substituted or unsubstituted alkoxy, a substituted or unsubstituted aminoalkyl group, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted cycloalkyl, or a substituted or unsubstituted heterocycloalkyl; each K is a non-protic charged group;

wherein alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, and quaternary heteroaryl can be substituted with one or more substituent groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, halogen, oxo, R^{15}, OR^{13}, $OR^{13}R^{14}$, $NR^{13}R^{14}$, SR^{13}, $S(O)R^{13}$, SO_2R^{13}, SO_3R^{13}, $NR^{13}OR^{14}$, $NR^{13}NR^{14}R^{15}$, NO_2, CO_2R^{13}, CN, OM, SO_2OM, $SO_2NR^{13}R^{14}$, $C(O)NR^{13}R^{14}$, C(O)OM , CR^{13}, $P(O)R^{13}R^{14}$, $P^+R^{13}R^{14}R^{15}A^-$, $P(OR^{13})OR^{14}$, $S^+R^{13}R^{14}A^-$, and $N^+R^9R^{11}R^{12}A^-$; wherein A- is a pharmaceutically acceptable anion and M is a pharmaceutically acceptable cation, said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can be further substituted with one or more substituent groups selected from the group consisting of OR^7, NR^7R^8, $S(O)R^7$, SO_2R^7, SO_3R^7, CO_2R^7, CN, oxo, $CONR^7R^8$, $N^+R^7R^8R^9A^-$, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, $P(O)R^7R^8$, $P^+R^7R^8R^9A^-$, and $P(O)(OR^7)OR^8$ and wherein said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can optionally have one or more carbons replaced by O, NR^7, $N^+R^7R^8A^-$, S, SO, SO_2 , $S^+R^7A^-$, PR^7, $P(O)R^7$,

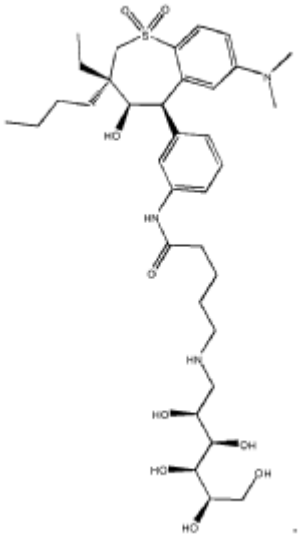
$P^+R^7R^8A^-$, or phenylene, and R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, polyalkyl, aryl, arylalkyl, cycloalkyl, heterocycle, heteroaryl, quaternary heterocycle, quaternary heteroaryl, quaternary heteroarylalkyl, and -G-T-V-W,
wherein alkyl, alkenyl, alkynyl, arylalkyl, heterocycle, and polyalkyl optionally have one or more carbons replaced by O, NR^9, $N^+R^9R^{10}A^-$, S, SO, SO_2, $S^+R^9A^-$, PR, $P^+R^9R^{10}A^-$, $P(O)R^9$, phenylene, carbohydrate, C_2-C_7 polyol, amino acid, peptide, or polypeptide, and
G, T and V are each independently a bond, -O-, -S-, -N(H)-, substituted or unsubstituted alkyl, -O-alkyl, -N(H)-alkyl, -C(O)N(H)-, -N(H)C(O)-, -N(H)C(O)N(H)-, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted alkenylalkyl, alkynylalkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted heterocycle, substituted or unsubstituted carboxyalkyl, substituted or unsubstituted carboalkoxyalkyl, or substituted or unsubstituted cycloalkyl, and
W is quaternary heterocycle, quaternary heteroaryl, quaternary heteroarylalkyl, $N^+R^9R^{11}R^{12}A^-$, $P^+R^9R^{10}R^{11}A^-$, $OS(O)_2OM$, or $S^+R^9R^{10}A^-$, and

R^9 and R^{10} are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, arylalkyl, and alkylammoniumalkyl;
R^{11} and R^{12} are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, alkenylalkyl, alkynylalkyl, heterocycle, carb oxyalkyl, carb oalkoxyalkyl, cyclo alkyl, cyanoalkyl, OR^9, NR^9R^{10}, SR^9, S(O) R^9, SO_2R^9, SO_3R^9, CO_2R^9, CN, halogen, oxo, and $CONR^9R^{10}$, wherein R^9 and R^{10} are as defined above, provided that both R^3 and R^4 cannot be OH, NH_2, and SH, or
R^{11} and R^{12} together with the nitrogen or carbon atom to which they are attached form a cyclic ring; R^{13}, R^{14} and R^{15} are optionally substituted with one or more groups selected from the group consisting of sulfoalkyl, quaternary heterocycle, quaternary heteroaryl, OR^9, NR^9R^{10}, $N^+R^9R^{11}R^{12}A^-$, SR^9, S(O) R^9, SO_2R^9, SO_3R^9, oxo, CO_2R^9, CN, halogen, $CONR^9R^{10}$, SO_2OM, $SO_2NR^9R^{10}$, $PO(OR^{16})OR^{17}$, $P^+R^9R^{10}R^{11}A^-$, $S^+R^9R^{10}A^-$, and C(O)OM,
wherein R^{16} and R^{17} are independently selected from the substituents constituting R^9 and M; or
R^{14} and R^{15}, together with the nitrogen atom to which they are attached, form a cyclic ring; and is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, alkylammoniumalkyl, and arylalkyl;
or a pharmaceutically acceptable salt, or solvate thereof.

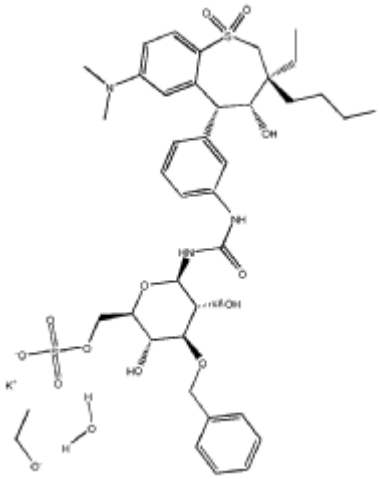
17. The use of claim 1, wherein the compound of Formula II is



18. The use of claim 1, wherein the compound of Formula II is

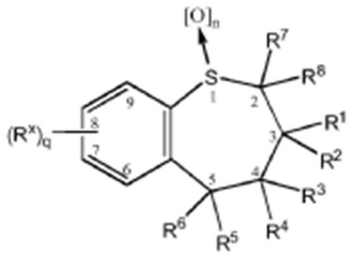


19. The use of claim 1, wherein the compound of Formula II



20. The use of any one of claims 1-19, wherein the composition further comprises a bile acid sequestrant or binder.

21. A pediatric dosage form comprising a pediatric dosage of a non-systemically absorbed Apical Sodium-dependent Bile Acid Transporter Inhibitor (ASBTI) or a pharmaceutically acceptable salt thereof, wherein the ASBTI is a compound of Formula II:



Formula II

wherein:

q is an integer from 1 to 4;

n is an integer from 0 to 2;

R^1 and R^2 are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, alkylaryl, arylalkyl, alkoxy, alkoxyalkyl, dialkylamino, alkylthio, (polyalkyl)aryl, and cycloalkyl, wherein alkyl, alkenyl, alkynyl, haloalkyl, alkylaryl, arylalkyl, alkoxy, alkoxyalkyl, dialkylamino, alkylthio, (polyalkyl)aryl, and cycloalkyl optionally are substituted with one or more substituents selected from the group consisting of OR^9, NR^9R^{10}, $N^+R^9R^{10}R^wA^-$, SR^9, $S^+R^9R^{10}A^-$, $P^+R^9R^{10}R^{11}$ A^-, S(O) R^9, SO_2R^9, SO_3R^9, CO_2R^9, CN, halogen, oxo, and $CONR^9R^{10}$,

wherein alkyl, alkenyl, alkynyl, alkylaryl, alkoxy, alkoxyalkyl, (polyalkyl)aryl, and cycloalkyl optionally have one or more carbons replaced by O, NR^9, $N^+R^9R^{10}A^-$, S, SO, SO_2, $S^+R^9A^-$, $P^+R^9R^{10}$ A^-, or phenylene, wherein R^9, R^{10}, and R^w are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, arylalkyl, and alkylammoniumalkyl; or

R^1 and R^2 taken together with the carbon to which they are attached form C3-C10 cycloalkyl;

R^3 and R^4 are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, acyloxy, aryl, heterocycle, OR^9, NR^9R^{10}, SR^9, $S(O)R^9$, SO_2R^9, and SO_3R^9, wherein R^9 and R^{10} are as defined above; or

R^3 and R^4 together =O , $=NOR^{11}$, =S, $=NNR^{11}$ R^{12}, $=NR^9$, or $=CR^{11}$ R^{12},

wherein R^{11} and R^{12} are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, alkenylalkyl, alkynylalkyl, heterocycle, carboxyalkyl, carboalkoxyalkyl, cycloalkyl, cyanoalkyl, OR^9, NR^9R^{10}, SR^9, S(O) R^9, SO_2R^9, SO_3R^9, CO_2R^9, CN, halogen, oxo, and $CONR^9R^{10}$, wherein R^9 and R^{10} are as defined above, provided that both R^3 and R^4 cannot be OH, NH_2, and SH, or

R^{11} and R^{12} together with the nitrogen or carbon atom to which they are attached form a cyclic ring; R^5 and R^6 are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, quarternary heteroaryl, OR^9, SR^9, S(O) R^9, SO_2R^9, SO_3R^9, and $-L_z-K_z$; wherein z is 1, 2 or 3; each L is independently a substituted or unsubstituted alkyl, a substituted or unsubstituted heteroalkyl, a substituted or unsubstituted alkoxy, a substituted or unsubstituted aminoalkyl group, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted cycloalkyl, or a substituted or unsubstituted heterocycloalkyl; each K is a non-protic charged

group;

wherein alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, and quaternary heteroaryl can be substituted with one or more substituent groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, halogen, oxo, R^{15}, OR^{13}, $OR^{13}R^{14}$, $NR^{13}R^{14}$, SR^{13}, $S(O)R^{13}$, SO_2R^{13}, SO_3R^{13}, $NR^{13}OR^{14}$, $NR^{13}NR^{14}R^{15}$, NO_2, CO_2R^{13}, CN, OM, SO_2OM, $SO_2NR^{13}R^{14}$, $C(O)NR^{13}R^{14}$, C(O)OM , CR^{13}, $P(O)R^{13}R^{14}$, $P^+R^{13}R^{14}R^{15}A^-$, $P(OR^{13})OR^{14}$, $S^+R^{13}R^{14}A^-$, and $N^+R^9R^{11}R^{12}A^-$;

wherein:

A- is a pharmaceutically acceptable anion and M is a pharmaceutically acceptable cation, said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can be further substituted with one or more substituent groups selected from the group consisting of OR^7, NR^7R^8, $S(O)R^7$, SO_2R^7, SO_3R^7, CO_2R^7, CN, oxo, $CONR^7R^8$, $N^+R^7R^8R^9A^-$, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, $P(O)R^7R^8$, $P^+R^7R^8R^9A^-$, and $P(O)(OR^7)OR^8$ and

wherein said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can optionally have one or more carbons replaced by O, NR^7, $N^+R^7R^8A^-$, S, SO, SO_2 , $S^+R^7A^-$, PR^7, $P(O)R^7$, $P^+R^7R^8A^-$, or phenylene, and R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, polyalkyl, aryl, arylalkyl, cycloalkyl, heterocycle, heteroaryl, quaternary heterocycle, quaternary heteroaryl, quaternary heteroarylalkyl, and -G-T-V-W, wherein alkyl, alkenyl, alkynyl, arylalkyl, heterocycle, and polyalkyl optionally have one or more carbons replaced by O, NR^9, $N^+R^9R^{10}A^-$, S, SO, SO_2, $S^+R^9A^-$, PR, $P^+R^9R^{10}A^-$, $P(O)R^9$, phenylene, carbohydrate, C_2-C_7 polyol, amino acid, peptide, or polypeptide, and

G, T and V are each independently a bond, -O-, -S-, -N(H)-, substituted or unsubstituted alkyl, -O-alkyl, -N(H)-alkyl, -C(O)N(H)-, -N(H)C(O)-, -N(H)C(O)N(H)-, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted alkenylalkyl, alkynylalkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted heterocycle, substituted or unsubstituted carboxyalkyl, substituted or unsubstituted carboalkoxyalkyl, or substituted or unsubstituted cycloalkyl, and W is quaternary heterocycle, quaternary heteroaryl, quaternary heteroarylalkyl, $N^+R^9R^{11}R^{12}A^-$, $P^+R^9R^{10}R^{11}$ A-, $OS(O)_2OM$, or $S^+R^9R^{10}A^-$, and

R^{13}, R^{14} and R^{15} are optionally substituted with one or more groups selected from the group consisting of sulfoalkyl, quaternary heterocycle, quaternary heteroaryl, OR^9, NR^9R^{10}, $N^+R^9R^{11}R^{12}A^-$, SR^9, $S(O)R^9$, SO_2R^9, SO_3R^9, oxo, CO_2R^9, CN, halogen, $CONR^9R^{10}$, SO_2OM, $SO_2NR^9R^{10}$, $PO(OR^{16})OR^{17}$, $P^+R^9R^{10}R^{11}A^-$, $S^+R^9R^{10}A^-$, and C(O)OM,

wherein R^{16} and R^{17} are independently selected from the substituents constituting R^9 and M; or

R^{14} and R^{15}, together with the nitrogen atom to which they are attached, form a cyclic ring; and

is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, alkylammoniumalkyl, and arylalkyl; and

R^7 and R^8 are independently selected from the group consisting of hydrogen and alkyl; and

one or more R^x are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, polyalkyl, acyloxy, aryl, arylalkyl, halogen, haloalkyl, cycloalkyl, heterocycle, heteroaryl, polyether, quaternary heterocycle, quaternary heteroaryl, OR^{13}, $NR^{13}R^{14}$, SR^{13}, $S(O)\ R^{13}$, $S(O)_2R^{13}$, SO_3R^{13}, $S^+R^{13}R^{14}A$-, $NR^{13}OR^{14}$, $NR^{13}NR^{14}R^{15}$, NO_2, CO_2R^{13}, CN, OM, SO_2OM, $SO_2NR^{13}R^{14}$, $NR^{14}C(O)R^{13}$, $C(O)NR^{13}R^{14}$, $NR^{14}C(O)R^{13}$, C(O)OM, COR^{13}, OR^{18}, $S(O)_n\ NR^{18}$, $NR^{13}R^{18}$, $NR^{18}R^{14}$, $N^+R^9R^{11}R^{12}A^-$, $P^+R^9R^{11}R^{12}A^-$, amino acid, peptide, polypeptide, and carbohydrate;

wherein alkyl, alkenyl, alkynyl, cycloalkyl, aryl, polyalkyl, heterocycle, acyloxy, arylalkyl, haloalkyl, polyether, quaternary heterocycle, and quaternary heteroaryl can be further substituted with OR^9, NR^9R^{10}, $NVR^9R^{11}R^{12}A$-, BR^9, $S(O)R^9$, SO_2R^9, SO_3R^9, oxo, CO_2R^9, CN, halogen, $CONR^9R^{10}$, $S\ O_2\ OM$, $SO_2\ NR^9R^{10}$, $PO(OR^{16})OR^{17}$, $P^+R^9R^{11}\ R^{12}A$-, $S^+R^9R^{10}A$-, or C(O)M,

wherein W is O or NH, R^{31} is selected from

wherein R^{18} is selected from the group consisting of acyl, arylalkoxycarbonyl, arylalkyl, heterocycle, heteroaryl, alkyl,

wherein acyl, arylalkoxycarbonyl, arylalkyl, heterocycle, heteroaryl, alkyl, quaternary heterocycle, and quaternary heteroaryl optionally are substituted with one or more substituents selected from the group consisting of OR^9, NR^9R^{10}, $N^+R^9R^{11}R^{12}A$, SR^9, $S(O)R^9$, SO_2R^9, SO_3R^9, oxo, CO_3R^9, CN, halogen, $CONR^9R^{10}$, SO_3R^9, SO_2OM, $SO_2NR^9R^{10}$, $PO(OR^{16})OR^{17}$, and C(O)OM,

wherein in R^x, one or more carbons are optionally replaced by O, NR^{13}, $N^+R^{13}R^{14}A$-, S, SO, SO_2, $S^+R^{13}A$-, PR^{13}, $P(O)R^{13}$, $P^+R^{13}R^{14}A$-, phenylene, amino acid, peptide, polypeptide, carbohydrate, polyether, or polyalkyl,

wherein in said polyalkyl, phenylene, amino acid, peptide, polypeptide, and carbohydrate, one or more carbons are optionally replaced by O, NR^9, $R^9R^{10}A$-, S, SO, SO_2, S^+R^9A-, PR^9, $P^+R^9R^{10}A$-, or $P(O)R^9$;

wherein quaternary heterocycle and quaternary heteroaryl are optionally substituted with one or more groups selected from the group consisting of alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, heterocycle, arylalkyl, halogen, oxo, OR^{13}, $NR^{13}R^{14}$, SR^{13}, $S(O)\ R^{13}$, $SO_2\ R^{13}$, $S\ O_3\ R^{13}$, $NR^{13}OR^{14}$, $NR^{13}NR^{14}R^{15}$, NO_2, CO_2R^{13}, CN, OM, $SO_2\ OM$, $SO_2NR^{13}R^{14}$, $C(O)\ NR^{13}R^{14}$, C(O) OM, COR^{13}, $P(O)R^{13}R^{14}$ $P^+R^{13}R^{14}R^{15}A$, $P(OR^{13})OR^{14}$, $S^+R^{13}R^{14}A$-, and $N^+R^9R^{11}R^{12}A$, provided that both R^5 and R^6 cannot be hydrogen or SH;

provided that when R^5 or R^6 is phenyl, only one of R^1 or R^2 is H;

provided that when q=l and R^x is styryl, anilido, or anilinocarbonyl, only one of R^5 or R^6 is alkyl; or a pharmaceutically acceptable salt or solvate thereof.

22. The pediatric dosage form of claim 21, wherein the pediatric dosage form is selected from a solution, syrup, suspension, elixir, powder for reconstitution as suspension or solution, dispersible/effervescent tablet, chewable tablet, gummy candy, lollipop, freezer pops, troches, oral thin strips, orally disintegrating tablet, sachet, soft gelatin capsule, and sprinkle oral powder or granules.

23. The pediatric dosage form of claim 21 or 22, wherein the dosage of the ASBTI is between 1 μg/kg/day and 10 mg/kg/day.

24. The pediatric dosage form of claim 21 or 22, wherein the dosage of the ASBTI is any dosage from 5 μg/kg/day to 5 mg/kg/day.

25. The pediatric dosage form of claim 21 or 22, wherein the dosage of the ASBTI is any dosage from 0.4 mg/kg/day to 5 mg/kg/day.

26. The pediatric dosage form of claim 21 or 22, wherein the dosage comprises between 0.1 to 20 mg of the ASBTI.

27. The pediatric dosage form of claim 21, wherein:
q is 1;
n is 2;
R^x is $N(CH_3)_2$;
R^7 and R^8 are independently H;
R^1 and R^2 is alkyl;
R^3 is H, and R^4 is OH;
R^5 is H, and R^6 is selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, quarternary heteroaryl, OR^9, SR^9, $S(O)R^9$, SO_2R^9, SO_3R^9, and $-L_z-K_z$;
wherein z is 1, 2 or 3; each L is independently a substituted or unsubstituted alkyl, a substituted or unsubstituted heteroalkyl, a substituted or unsubstituted alkoxy, a substituted or unsubstituted aminoalkyl group, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted cycloalkyl, or a substituted or unsubstituted heterocycloalkyl; each K is a non-protic charged group;
wherein alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, and quaternary heteroaryl can be substituted with one or more substituent groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, halogen, oxo, R^{15}, OR^{13}, $OR^{13}R^{14}$, $NR^{13}R^{14}$, SR^{13}, $S(O)R^{13}$, SO_2R^{13}, SO_3R^{13}, $NR^{13}OR^{14}$, $NR^{13}NR^{14}R^{15}$, NO_2, CO_2R^{13}, CN, OM, SO_2OM, $SO_2NR^{13}R^{14}$, $C(O)NR^{13}R^{14}$, $C(O)OM$, CR^{13}, $P(O)R^{13}R^{14}$, $P^+R^{13}R^{14}R^{15}A^-$, $P(OR^{13})OR^{14}$, $S^+R^{13}R^{14}A^-$, and $N^+R^9R^{11}R^{12}A^-$,
wherein A- is a pharmaceutically acceptable anion and M is a pharmaceutically acceptable cation, said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can be further substituted with one or more substituent groups selected from the group consisting of OR^7, NR^7R^8, $S(O)R^7$, SO_2R^7,

SO_3R^7, CO_2R^7, CN, oxo, $CONR^7R^8$, $N^+R^7R^8R^9A^-$, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, $P(O)R^7R^8$, $P^+R^7R^8R^9A^-$, and $P(O)(OR^7)$ OR^8 and wherein said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can optionally have one or more carbons replaced by O, NR^7, $N^+R^7R^8A^-$, S, SO, SO_2 , $S^+R^7A^-$, PR^7, $P(O)$ R^7, $P^+R^7R^8A^-$, or phenylene, and R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, polyalkyl, aryl, arylalkyl, cycloalkyl, heterocycle, heteroaryl, quaternary heterocycle, quaternary heteroaryl, quaternary heteroarylalkyl, and -G-T-V-W, wherein alkyl, alkenyl, alkynyl, arylalkyl, heterocycle, and polyalkyl optionally have one or more carbons replaced by O, NR^9, $N^+R^9R^{10}A^-$, S, SO, SO_2, $S^+R^9A^-$, PR, $P^+R^9R^{10}A^-$, $P(O)R^9$, phenylene, carbohydrate, C_2-C_7 polyol, amino acid, peptide, or polypeptide, and

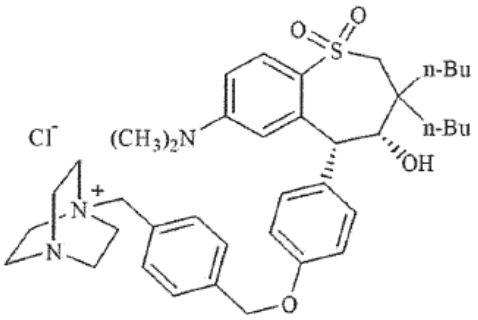
G, T and V are each independently a bond, -O-, -S-, -N(H)-, substituted or unsubstituted alkyl, -O-alkyl, -N(H)-alkyl, -C(O)N(H)-, -N(H)C(O)-, -N(H)C(O)N(H)-, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted alkenylalkyl, alkynylalkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted heterocycle, substituted or unsubstituted carboxyalkyl, substituted or unsubstituted carboalkoxyalkyl, or substituted or unsubstituted cycloalkyl, and W is quaternary heterocycle, quaternary heteroaryl, quaternary heteroarylalkyl, $N^+R^9R^{11}R^{12}A^-$, $P^+R^9R^{10}R^{11}A^-$,

, $OS(O)_2OM$, or $S^+R^9R^{10}A^-$, and

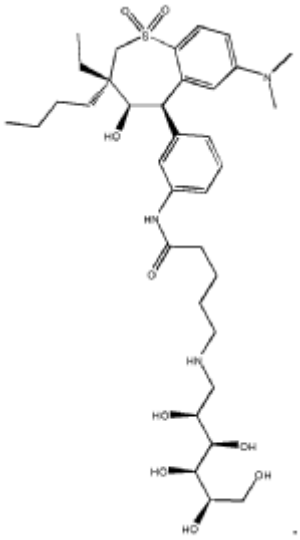
R^9 and R^{10} are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, arylalkyl, and alkylammoniumalkyl;

R^{11} and R^{12} are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, alkenylalkyl, alkynylalkyl, heterocycle, carb oxyalkyl, carboalkoxyalkyl, cyclo alkyl, cyanoalkyl, OR^9, NR^9R^{10}, SR^9, $S(O)$ R^9, SO_2R^9, SO_3R^9, CO_2R^9, CN, halogen, oxo, and $CONR^9R^{10}$, wherein R^9 and R^{10} are as defined above, provided that both R^3 and R^4 cannot be OH, NH_2, and SH, or
R^{11} and R^{12} together with the nitrogen or carbon atom to which they are attached form a cyclic ring; R^{13}, R^{14} and R^{15} are optionally substituted with one or more groups selected from the group consisting of sulfoalkyl, quaternary heterocycle, quaternary heteroaryl, OR^9, NR^9R^{10}, $N^+R^9R^{11}R^{12}A^-$, SR^9, $S(O)$ R^9, SO_2R^9, SO_3R^9, oxo, CO_2R^9, CN, halogen, $CONR^9R^{10}$, SO_2OM, $SO_2NR^9R^{10}$, $PO(OR^{16})OR^{17}$, $P^+R^9R^{10}R^{11}A^-$, $S^+R^9R^{10}A^-$, and C(O)OM,
wherein R^{16} and R^{17} are independently selected from the substituents constituting R^9 and M; or
R^{14} and R^{15}, together with the nitrogen atom to which they are attached, form a cyclic ring; and is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, alkylammoniumalkyl, and arylalkyl;
or a pharmaceutically acceptable salt, or solvate thereof.

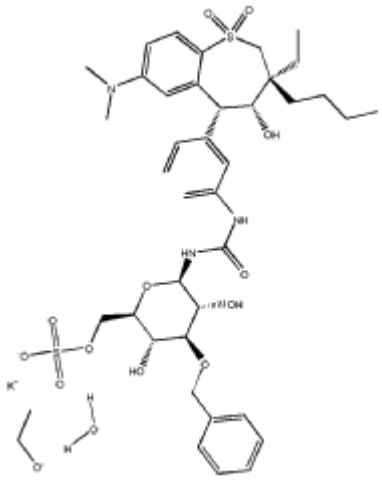
28. The pediatric dosage form of claim 21, wherein the compound of Formula II is



29. The pediatric dosage form of claim 21, wherein the compound of Formula II is

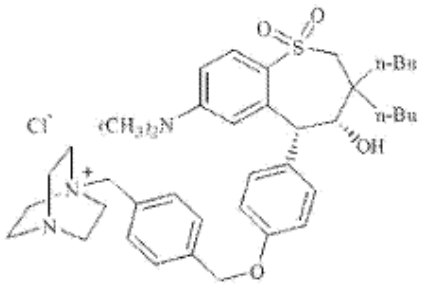


30. The pediatric dosage form of claim 21, wherein the compound of Formula II



31. The pediatric dosage form of any of claim 21 -30, wherein the pediatric dosage further comprises a bile acid sequestrant or binder.

32. The use of any one of claims 1-16, wherein the ASBTI is a compound selected from the group consisting of:



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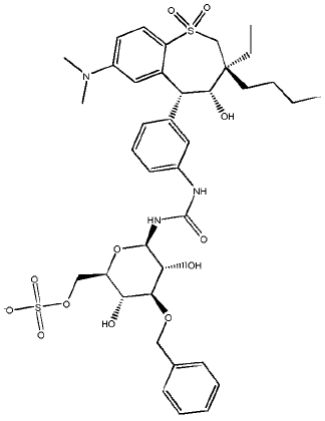
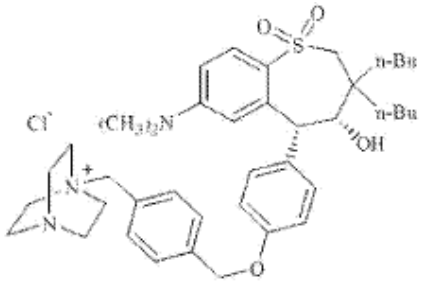


, and

1,1-dioxo-3,3-dibuty1-5-pheny1-7-methylthio-8-(N-{(R)-α-[N-((S)-1-carboxypropyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine.

33. The pediatric dosage form of any one of claims 21-30, wherein the ASBTI is a compound selected from the group consisting of:



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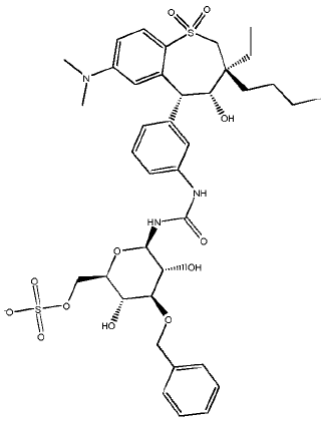

, and

1,1-dioxo-3,3-dibuty1-5-pheny1-7-methylthio-8-(N-{(R)-α-[N-((S)-1-carboxypropyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine.