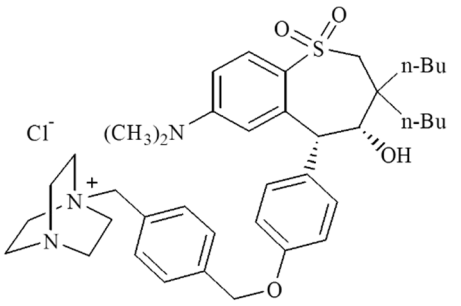
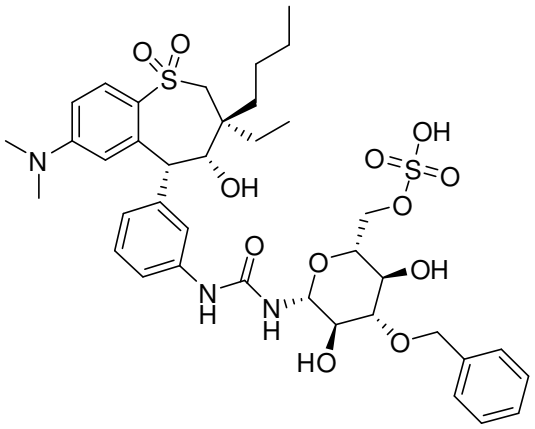
[0003a] In one aspect, the present disclosure refers to the use of a therapeutically effective amount of a composition comprising a minimally absorbed Apical Sodium-dependent Bile Acid Transporter Inhibitor (ASBTI) or a pharmaceutically acceptable salt or solvate thereof in the manufacture of a medicament for the treatment of a cholestatic liver disease or pruritis in an individual in need thereof, wherein the ASBTI is



,

or



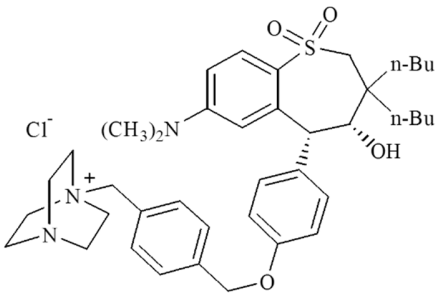
, or a pharmaceutically acceptable salt thereof, wherein the ASBTI decreases serum or hepatic bile acid levels in the individual by at least about 20% as compared to the levels prior to administration of the ASBTI.

[0003b] In another aspect, the present disclosure refers to the use of a therapeutically effective amount of a composition comprising a minimally absorbed Apical Sodium-dependent Bile Acid Transporter Inhibitor (ASBTI) or a pharmaceutically acceptable salt or solvate thereof in the manufacture of a medicament for the treatment of a liver disease in an individual in need thereof, wherein the liver disease is progressive familial intrahepatic cholestasis (PFIC), PFIC type 1, PFIC type 2, PFIC type 3, benign recurrent intrahepatic cholestasis (BRIC), BRIC type 1, BRIC type 2, BRIC type 3, Alagille syndrome, biliary atresia, post-Kasai biliary atresia, or post-liver transplantation biliary atresia, and wherein the ASBTI is:

CLAIMS

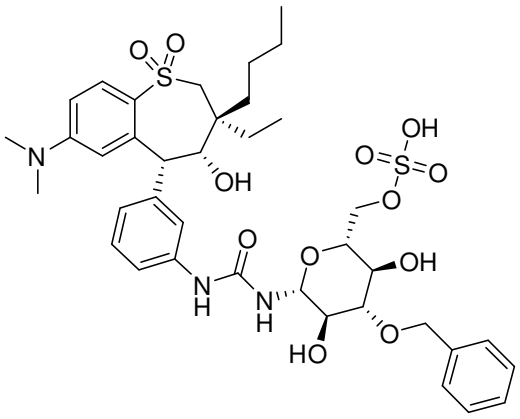
WHAT IS CLAIMED IS:

1. Use of a therapeutically effective amount of a composition comprising a minimally absorbed Apical Sodium-dependent Bile Acid Transporter Inhibitor (ASBTI) or a pharmaceutically acceptable salt or solvate thereof in the manufacture of a medicament for the treatment of a cholestatic liver disease or pruritis in an individual in need thereof, wherein the ASBTI is



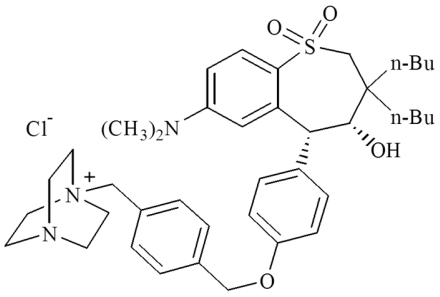
,

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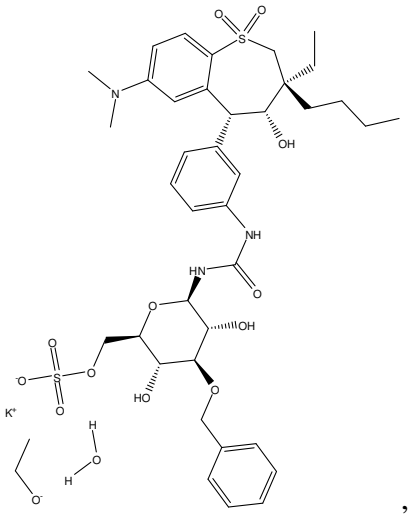
, or a pharmaceutically acceptable salt thereof, wherein the ASBTI decreases serum or hepatic bile acid levels in the individual by at least about 20% as compared to the levels prior to administration of the ASBTI.

2. The use in claim 1, wherein the compound is



, or an alternative pharmaceutically acceptable salt thereof.

3. The use in claim 1, wherein the compound is



, or an alternative pharmaceutically acceptable salt thereof.

4. The use in claim 1, wherein the ASBTI decreases the levels of serum bile acids or hepatic bile acids, reduces bilirubin, reduces liver enzymes, lowers intraenterocyte bile acids/salts, or reduces necrosis and/or damage to hepatocellular architecture.

5. The use in claim 1, wherein the ASBTI decreases elevated levels of lipoprotein X; elevated levels of AP (alkaline phosphatase); elevated levels of LAP (leukocyte alkaline phosphatase); elevated levels of gamma GT (gamma-glutamyl transpeptidase); elevated levels of 5'-nucleotidase; pruritus; elevated serum concentration of conjugated bilirubin; elevated serum concentrations of nonconjugated bilirubin or delta bilirubin; and presence of xanthomas.

6. The use in claim 1, wherein the cholestatic liver disease is an obstructive cholestasis, non-obstructive cholestasis, extrahepatic cholestasis, intrahepatic cholestasis, primary intrahepatic cholestasis, secondary intrahepatic cholestasis, progressive familial intrahepatic cholestasis (PFIC), PFIC type 1, PFIC type 2, PFIC type 3, benign recurrent intrahepatic cholestasis (BRIC), BRIC type 1, BRIC type 2, BRIC type 3, total parenteral nutrition associated cholestasis, paraneoplastic cholestasis, Stauffer syndrome, intrahepatic cholestasis of pregnancy, contraceptive-associated cholestasis, drug-associated cholestasis, infection-associated cholestasis, Dubin-Johnson Syndrome, primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC), gallstone disease, 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, or MRP2 deficiency syndrome.

7. The use in claim 1, wherein the cholestatic liver disease is intrahepatic cholestasis of pregnancy (ICP).

8. The use in claim 7, wherein the ICP is in the third trimester of pregnancy.

9. The use in claim 7, wherein the ICP is characterized by one or more of pruritis, biochemical cholestasis, or cholestatic liver disease.

10. The use in claim 7, wherein the individual has a genetic predisposition to ICP.

11. The use in claim 10, wherein the genetic predisposition to ICP comprises a heterogenous state for an MDR3 gene defect.

12. The use in claim 1, wherein the cholestatic liver disease is primary sclerosing cholangitis (PSC).

13. The use in claim 1, wherein the cholestatic liver disease is characterized by one or more symptoms selected from jaundice, pruritis, cirrhosis, hypercholemia, neonatal respiratory distress syndrome, lung pneumonia, increased serum 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.

14. The use in claim 1, wherein less than 10% of the ASBTI is systemically absorbed.

15. The use in claim 1, further comprises a second agent selected from ursodeoxycholic acid, chenodeoxycholic acid, cholic acid, taurocholic acid, ursocholic acid, glycocholic acid, glycodeoxycholic acid, taurodeoxycholic acid, taurocholate, glycochenodeoxycholic acid, and tauroursodeoxycholic acid.

16. The use in claim 1, wherein the ASBTI is to be administered before ingestion of food, optionally wherein the ASBTI is to be administered less than about 60 minutes or less than about 30 minutes before ingestion of food.

17. The use in claim 1, wherein the ASBTI is to be administered orally.

18. The use in claim 1, wherein the ASBTI is to be administered as an ileal-pH sensitive release or an enterically coated formulation.

19. The use in claim 1, further comprising a vitamin supplement.

20. The use in claim 19, wherein the vitamin supplement comprises a fat-soluble vitamin.

21. The use in claim 20, wherein the fat-soluble vitamin is vitamin A, D, E, or K.

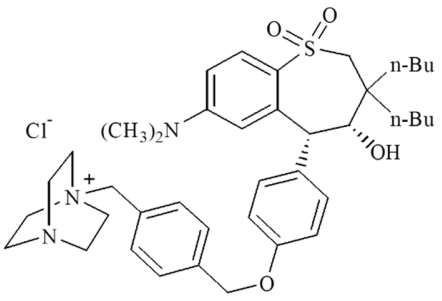
22. The use in claim 1, further comprising an agent selected from the group consisting of cholestyramine, antihistamine, rifampin, naloxone, Phenobarbital, dronabinol, methotrexate, corticosteroid, cyclosporine, and colchicines.

23. The use in claim 1, further comprising the use of partial external biliary diversion (PEBD).

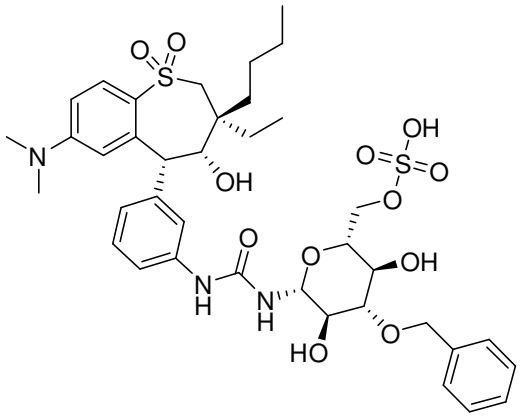
24. The use in claim 1, wherein the individual in need thereof is nonresponsive to ursodiol.

25. The use in claim 1, further comprising a bile acid sequestrant or binder.

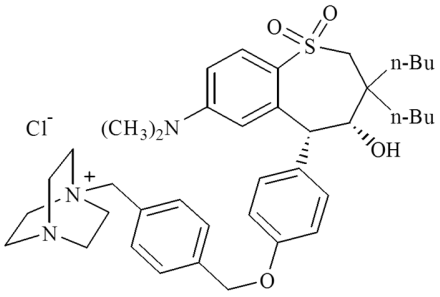
26. Use of a therapeutically effective amount of a composition comprising a minimally absorbed Apical Sodium-dependent Bile Acid Transporter Inhibitor (ASBTI) or a pharmaceutically acceptable salt or solvate thereof in the manufacture of a medicament for the treatment of a liver disease in an individual in need thereof, wherein the liver disease is progressive familial intrahepatic cholestasis (PFIC), PFIC type 1, PFIC type 2, PFIC type 3, benign recurrent intrahepatic cholestasis (BRIC), BRIC type 1, BRIC type 2, BRIC type 3, Alagille syndrome, biliary atresia, post-Kasai biliary atresia, or post-liver transplantation biliary atresia, and wherein the ASBTI is:



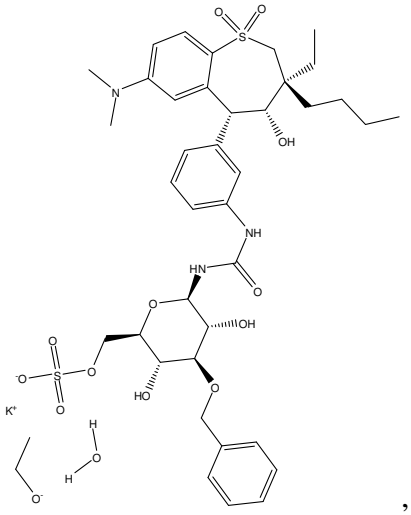
or


, or a pharmaceutically acceptable salt thereof.

27. The use in claim 26, wherein the compound is


, or an alternative pharmaceutically acceptable salt thereof.

28. The use in claim 26, wherein the compound is


, or an alternative pharmaceutically acceptable salt thereof.

29. The use in claim 26, wherein less than 10% of the ASBTI is systemically absorbed.

30. The use in claim 26, further comprises a second agent selected from ursodeoxycholic acid, chenodeoxycholic acid, cholic acid, taurocholic acid, ursocholic acid, glycocholic acid, glycodeoxycholic acid, taurodeoxycholic acid, taurocholate, glycochenodeoxycholic acid, and tauroursodeoxycholic acid.

31. The use in claim 26, wherein the ASBTI is to be administered before ingestion of food, optionally wherein the ASBTI is to be administered less than about 60 minutes or less than about 30 minutes before ingestion of food.

32. The use in claim 26, wherein the ASBTI is to be administered orally.

33. The use in claim 26, wherein the ASBTI is to be administered as an ileal-pH sensitive release or an enterically coated formulation.

34. The use in claim 26, further comprising a vitamin supplement.

35. The use in claim 34, wherein the vitamin supplement comprises a fat-soluble vitamin.

36. The use in claim 35, wherein the fat-soluble vitamin is vitamin A, D, E, or K.

37. The use in claim 26, further comprising an agent selected from the group consisting of cholestyramine, antihistamine, rifampin, naloxone, Phenobarbital, dronabinol, methotrexate, corticosteroid, cyclosporine, and colchicines.

38. The use in claim 26, wherein the individual in need thereof is nonresponsive to ursodiol.

39. The use in claim 26, further comprising a bile acid sequestrant or binder.

40. The use in claim 26, wherein the liver disease is progressive familial intrahepatic cholestasis (PFIC).

41. The use in claim 26, wherein the liver disease is Alagille syndrome.

42. The use in claim 1, wherein the ASBTI decreases serum or hepatic bile acid levels in the individual by at least about 30% as compared to the levels prior to administration of the ASBTI.

43. The use in claim 1, wherein the ASBTI decreases serum or hepatic bile acid levels in the individual by at least about 40% as compared to the levels prior to administration of the ASBTI.

44. The use in claim 1, wherein the ASBTI decreases serum or hepatic bile acid levels in the individual by at least about 50% as compared to the levels prior to administration of the ASBTI.

45. The use in claim 26, wherein the ASBTI decreases serum or hepatic bile acid levels in the individual by at least about 30% as compared to the levels prior to administration of the ASBTI.

46. The use in claim 26, wherein the ASBTI decreases serum or hepatic bile acid levels in the individual by at least about 40% as compared to the levels prior to administration of the ASBTI.

47. The use in claim 26, wherein the ASBTI decreases serum or hepatic bile acid levels in the individual by at least about 50% as compared to the levels prior to administration of the ASBTI.

48. The use of any of claims 1-47, wherein the ASBTI is to be administered at a dosage between 1 µg/kg/day and 10 mg/kg/day.

49. The use of claim 48, wherein the ASBTI is to be administered at a dosage from 5 µg/kg/day to 1 mg/kg/day.

50. The use of claim 48, wherein the ASBTI is to be administered at a dosage from 10 µg/kg/day to 300 µg/kg/day.

51. The use of any of claims 1-50, wherein the ASBTI is to be administered at a dosage comprising from 0.5 mg/day to 40 mg/day of the ASBTI.

52. The use of any of claims 1-51, wherein the individual has a defective BSEP expression and/or function.

53. The use of any of claims 1-52, wherein the individual has a mutation in ABCB11 gene.

54. The use of any of claims 1-52, wherein the individual has a mutation in ABCB4 gene.