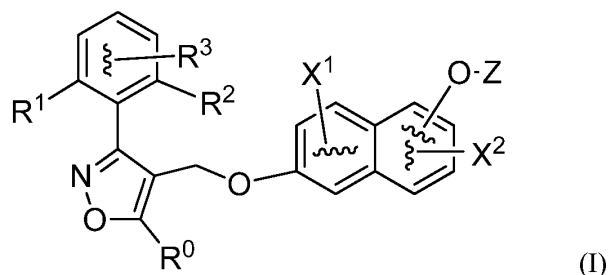


CLAIMS

1. A compound for modulating the activity of FXR having a structure of formula (I), a pharmaceutically acceptable salt, an ester or a stereoisomer thereof:



wherein:

R^1 , R^2 and R^3 are independently selected from H, halogen, unsubstituted or halogen substituted C_{1-6} alkyl and unsubstituted or halogen substituted C_{1-6} alkoxy, provided that at least one of R^1 , R^2 and R^3 is not hydrogen, R^0 is selected from unsubstituted or halogen substituted C_{1-6} alkyl, C_{3-6} cycloalkyl and C_{4-7} alkylcycloalkyl;

X^1 and X^2 are independently selected from H and halogen;

moiety $-O-Z$ attaches to the naphthalene ring, wherein Z is a residue selected from 5-10 membered aryl or 5-10 membered heteroaryl optionally having one or more hetero atoms selected from N, O and S, wherein the 5-10 membered aryl or 5-10 membered heteroaryl is substituted by R^4 and is optionally further substituted by R^5 ;

wherein R^4 is selected from $-COOH$, $-CH_2COOH$, $-NHSO_2CF_3$, $-SO_2NH-C_{1-6}$ alkyl, $-SO_3H$, $-CONHSO_2-C_{1-6}$ alkyl, $-CONHSO_2-C_{3-6}$ cycloalkyl, $-CONHSO_2-5-10$ membered aryl and $-CONHSO_2-5-10$ membered aryl substituted by C_{1-6} alkyl at the aryl, and wherein R^5 is selected from H, C_{1-6} alkyl, halogen, C_{1-6} haloalkyl, $-O-(C_{1-6}$ alkyl) and $-NH-(C_{1-6}$ alkyl).

2. The compound according to claim 1, wherein R^1 , R^2 and R^3 are independently selected from H, halogen and C_{1-3} perfluoroalkoxy, and R^0 is selected from isopropyl or cyclopropyl.

3. The compound according to claim 2, wherein R^1 , R^2 and R^3 are independently selected from H, Cl, F and $-O-CF_3$.

4. The compound according to claims 1, wherein both of R^1 and R^2 are Cl, and R^3 is selected from H, F or $-O-CH_3$; or R^1 is $-O-CF_3$, and both of R^2 and R^3 are H.

5. The compound according to claim 1, wherein Z is a phenyl which is substituted by R^4 and is optionally substituted by R^5 ; or Z is a 5-10 membered heteroaryl having one or more

hetero atoms selected from N, O and S, which is substituted by R⁴ and is optionally substituted by R⁵.

6. The compound according to claim 5, wherein Z is a 5-6 membered heteroaryl having one or more hetero atoms selected from N, O and S, which is substituted by R⁴ and is optionally substituted by R⁵.

7. The compound according to claim 1, wherein Z is a R⁴ and optionally R⁵ substituted pyridyl.

8. The compound according to any one of claims 1 to 7, wherein R⁴ is selected from -COOH, -CH₂COOH, -CONHSO₂-C₁₋₆ alkyl and -CONHSO₂-C₃₋₆ cycloalkyl.

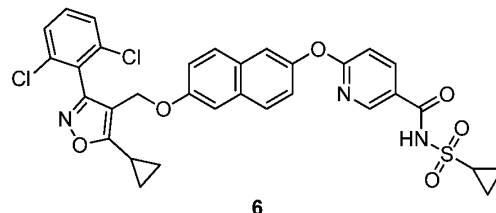
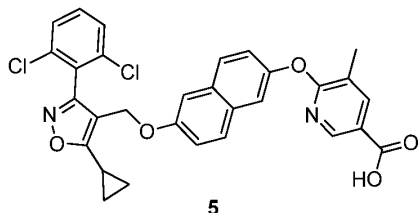
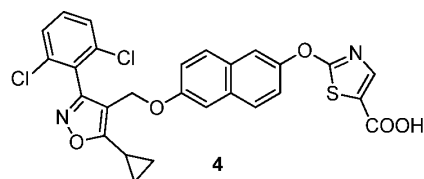
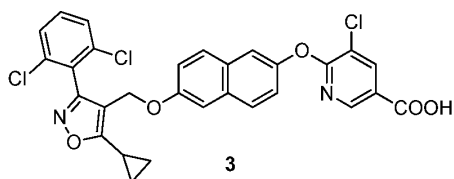
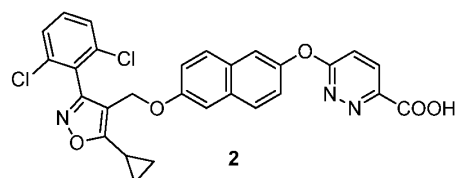
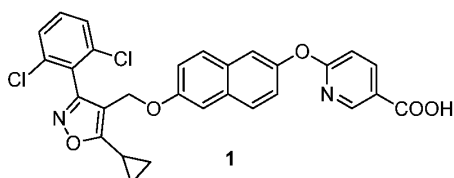
10 9. The compound according to claim 8, wherein R^4 is $-\text{COOH}$ or $-\text{CH}_2\text{COOH}$; preferably, R^4 is $-\text{COOH}$.

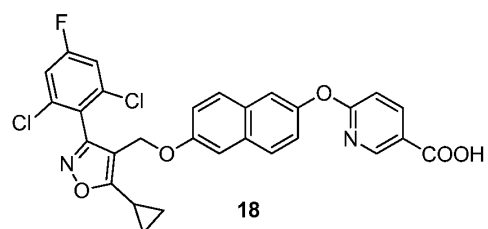
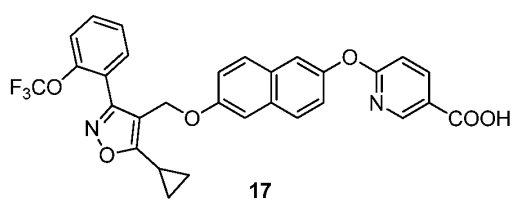
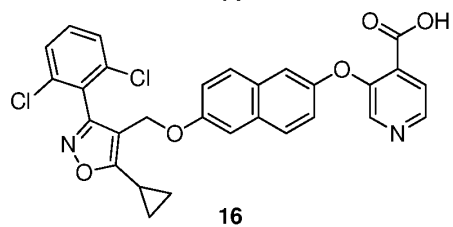
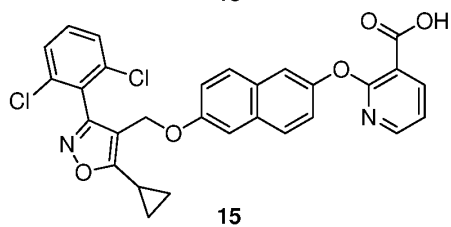
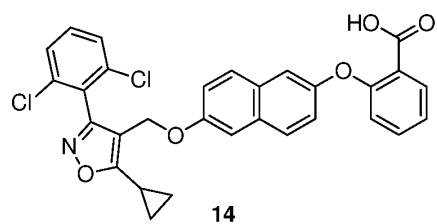
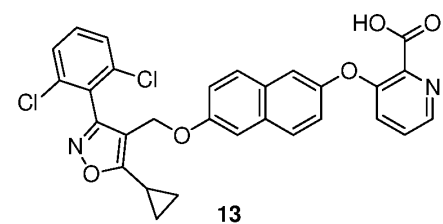
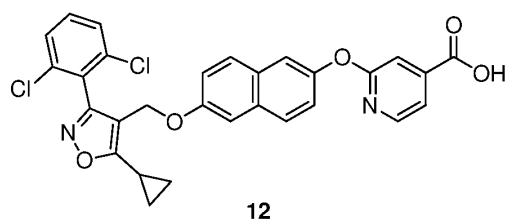
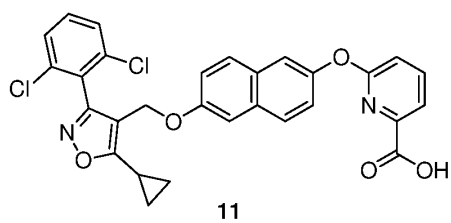
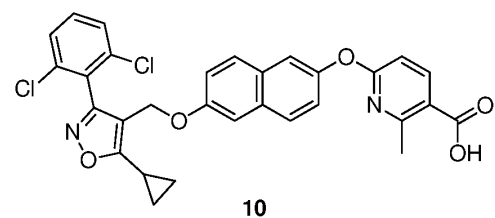
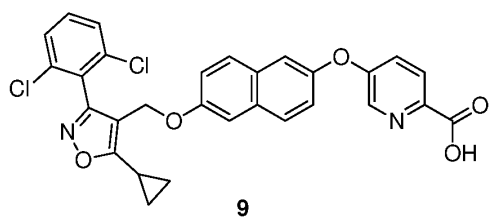
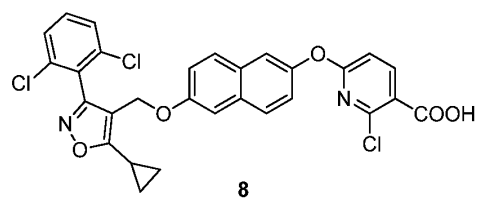
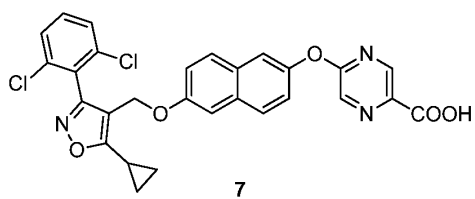
10. The compound according to claim 1, wherein R⁵ is selected from H, C₁₋₃ alkyl and halogen.

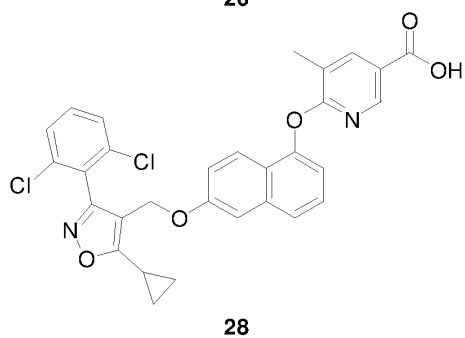
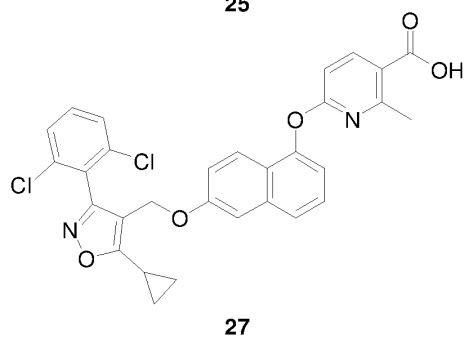
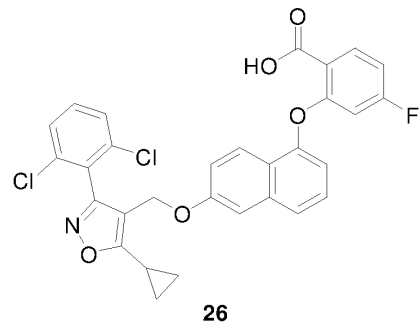
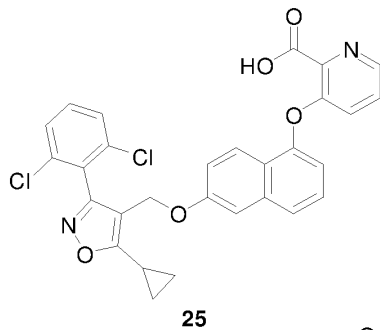
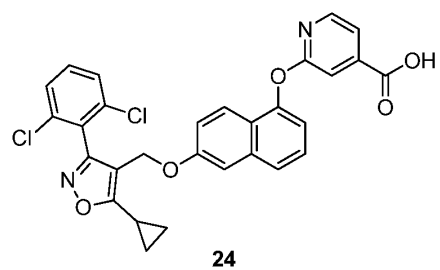
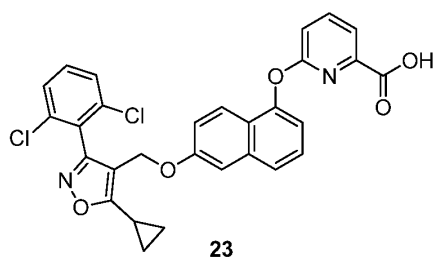
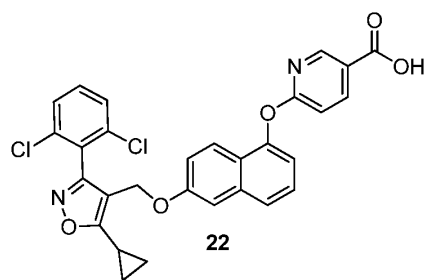
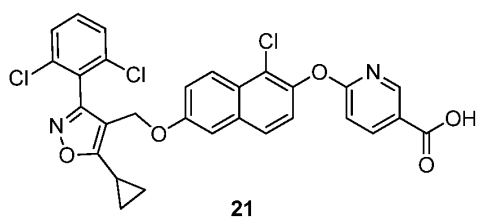
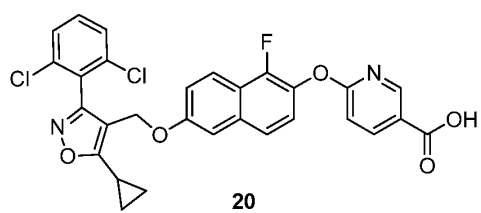
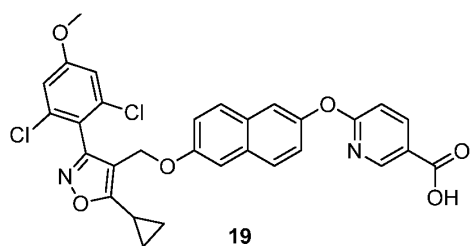
11. The compound according to claim 1, wherein Z is pyridyl; R⁴ is -COOH; and R⁵ is H
15 or halogen.

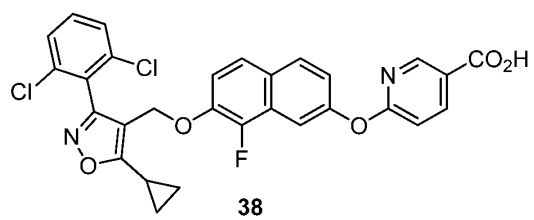
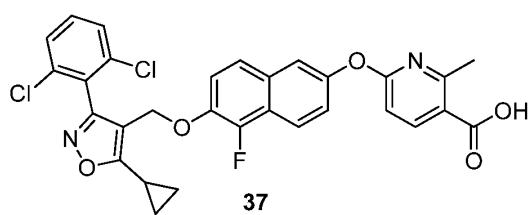
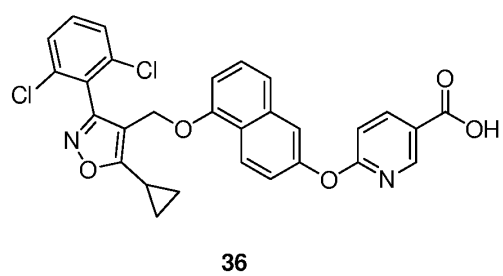
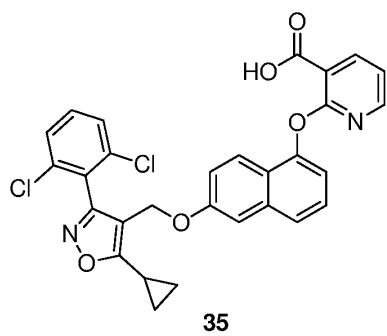
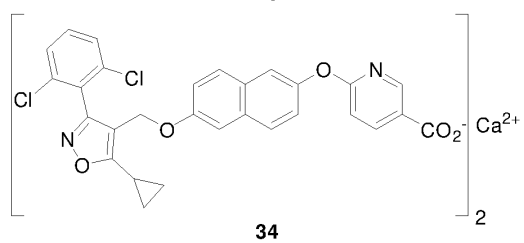
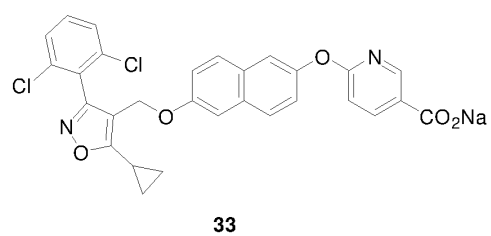
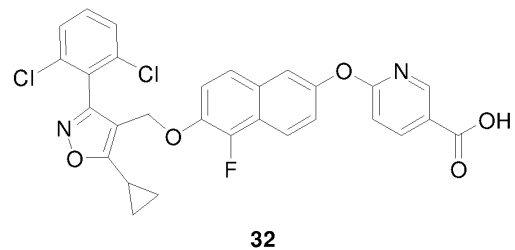
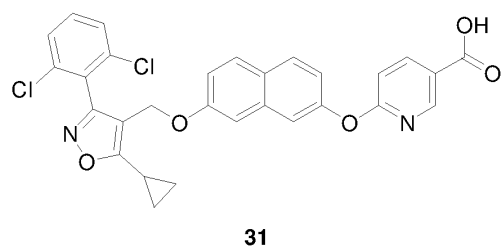
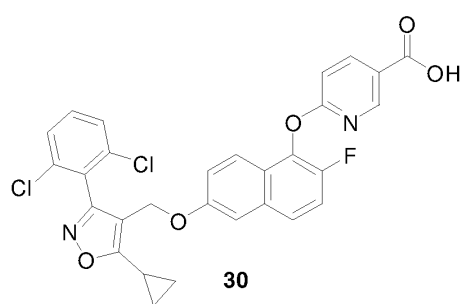
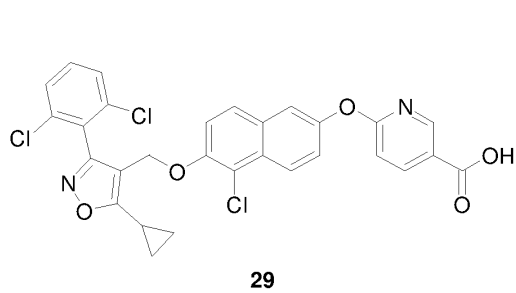
12. The compound according to claim 1, wherein the halogen is fluoro or chloro.

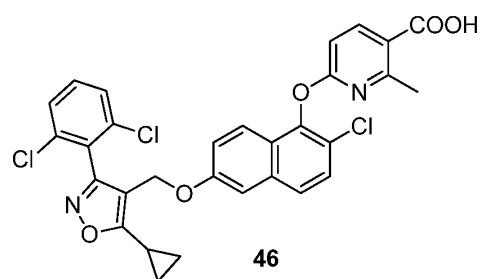
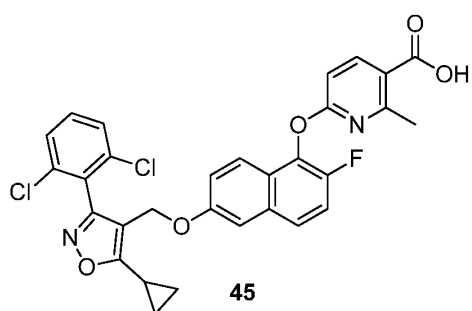
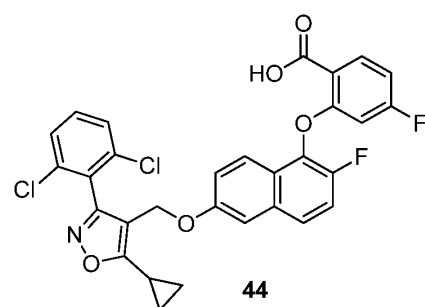
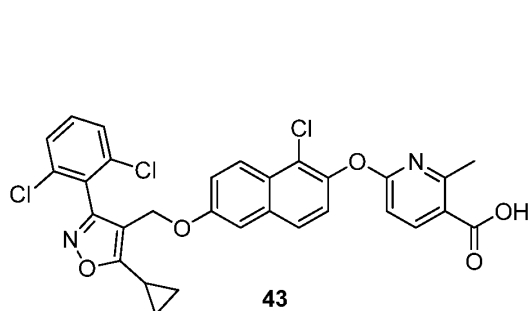
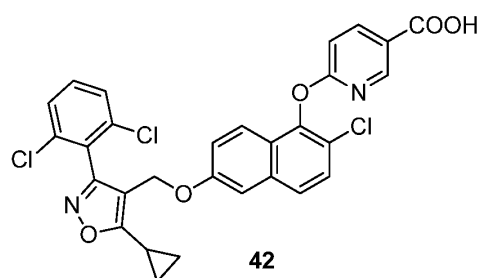
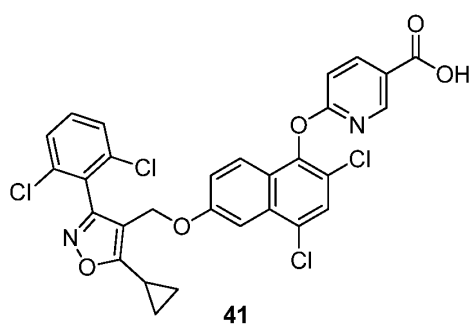
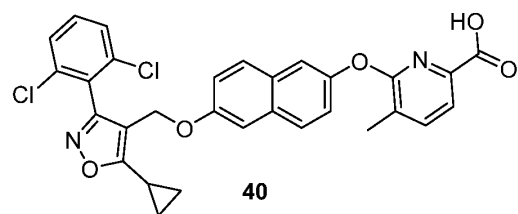
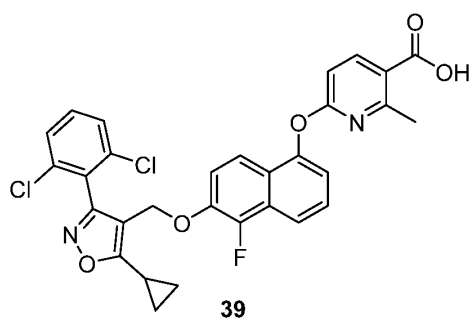
13. The compound according to claim 1, wherein the compound is of one of the following structures:

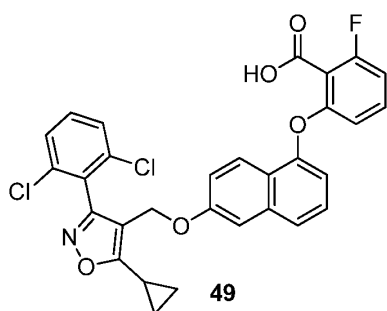
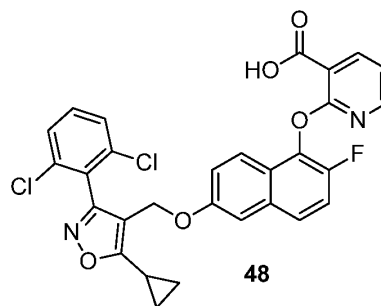
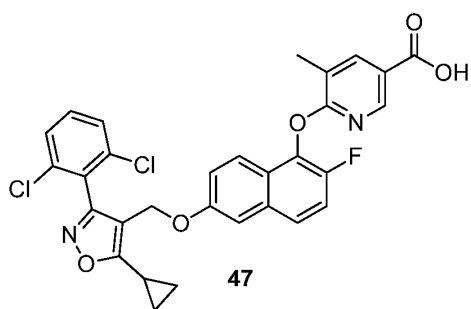




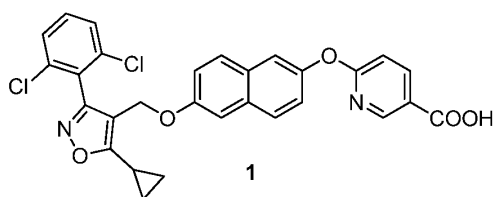




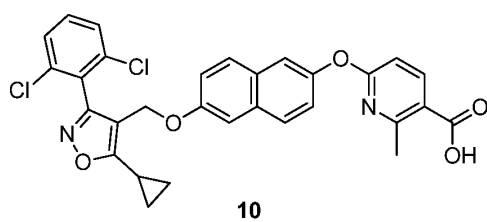




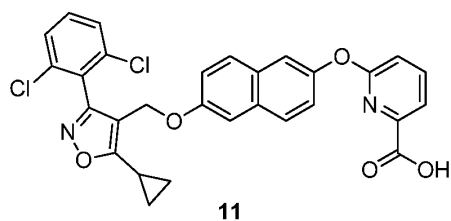
14. The compound according to claim 1, wherein the compound has the following structure:



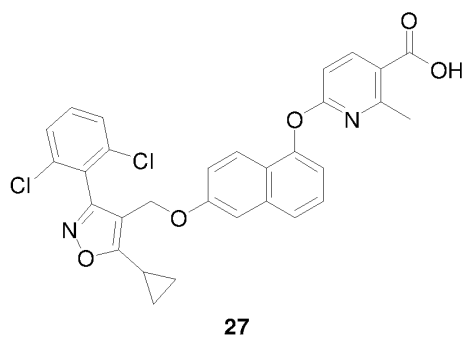
15. The compound according to claim 1, wherein the compound has the following structure:



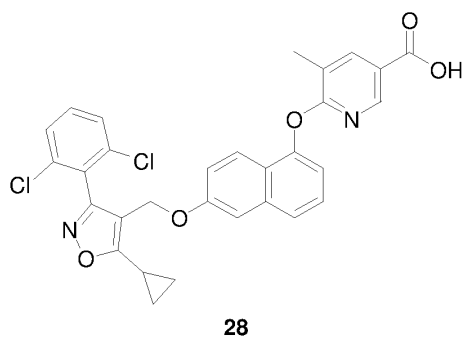
16. The compound according to claim 1, wherein the compound has the following structure:



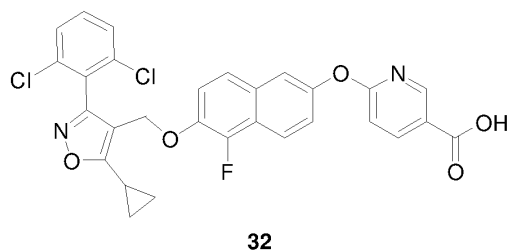
17. The compound according to claim 1, wherein the compound has the following structure:



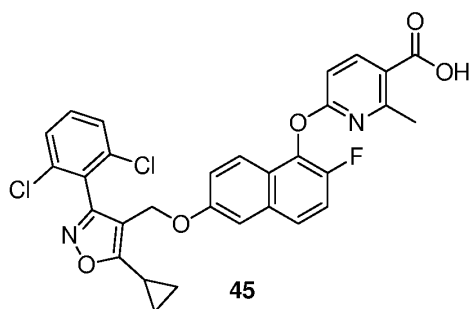
18. The compound according to claim 1, wherein the compound has the following structure:



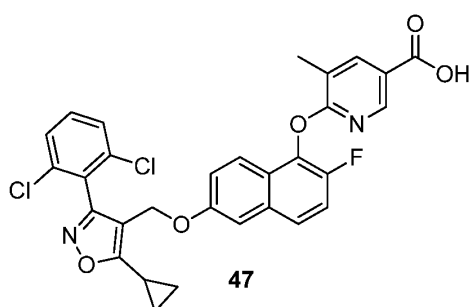
19. The compound according to claim 1, wherein the compound has the following structure:



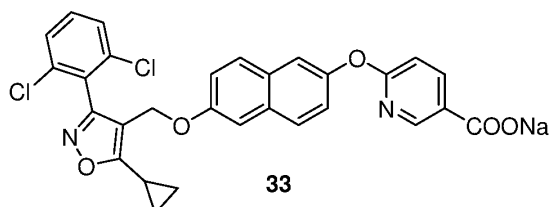
20. The compound according to claim 1, wherein the compound has the following structure:



21. The compound according to claim 1, wherein the compound has the following structure:



22. The compound according to claim 1, wherein the compound has the following structure:



23. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1 to 21 or a pharmaceutically acceptable salt, an ester or a stereoisomer thereof, and a pharmaceutically acceptable auxiliary material.

24. The pharmaceutical composition according to claim 23, wherein the pharmaceutical composition further comprises a second therapeutic agent being useful in the treatment of nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), primary biliary cirrhosis (PBC), cholestasis liver tree, chronic liver disease, hepatitis C infection, alcoholic liver disease, hepatic fibrosis, primary sclerosing cholangitis (PSC), gallstones, bile duct atresia, lower urinary tract symptoms and benign prostatic hyperplasia (BPH), ureteral calculi, obesity, type 2 diabetes, atherosclerosis, atherosclerosis, liver damage caused by

hypercholesterolemia or hyperlipidemia.

25. A method for treating a condition or disease mediated by FXR in a subject suffering therefrom, comprising administering to the subject a therapeutically effective amount of the compounds of any one of claims 1 to 21 or a pharmaceutically acceptable salt, an ester or a stereoisomer thereof, or a pharmaceutical composition of claim 23 or 24, and optionally in combination with a second therapeutic agent.

26. Use of the compounds of any one of claims 1 to 21 or a pharmaceutically acceptable salt, an ester or a stereoisomer thereof, or a pharmaceutical composition of claim 23 or 24, for the preparation of a medicament for the treatment of a condition mediated by FXR in a subject.

27. The use according to claim 26, wherein said condition is nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), primary biliary cirrhosis (PBC), cholestasis liver tree, chronic liver disease, hepatitis C infection, alcoholic liver disease, hepatic fibrosis, primary sclerosing cholangitis (PSC), gallstones, bile duct atresia, lower urinary tract symptoms and benign prostatic hyperplasia (BPH), ureteral calculi, obesity, type 2 diabetes, atherosclerosis, atherosclerosis, liver damage caused by hypercholesterolemia or hyperlipidemia.