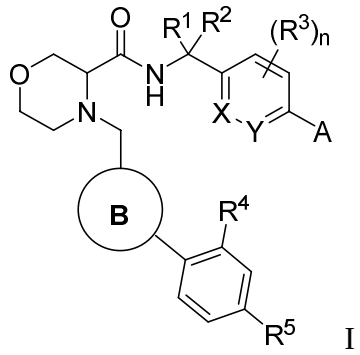
CLAIMS

1. A compound of the Formula I:



I

or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or optical isomer thereof, wherein;

A is OR', C(O)R', CO_2R', C(O)N(R')$_2$, C(O)N(R')S(O)$_2$R', S(O)$_2$R', S(O)$_2$OR', SO_2N(R')$_2$, C_{1-8} alkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;

Ring B is aryl or heteroaryl;

X and Y are each independently CR'' or N, wherein at least one of X and Y is CH;

R^1 and R^2 are each independently H, C_{1-6} alkyl, C_{1-6} alkoxy, or R^1 and R^2, together with the carbon atom to which they are attached, form a C_{3-6} cycloalkane-1,1-diyl ring;

each R^3 is independently selected from H, OR', COOR', C(O)R', halo, or C_{1-6} alkyl;

R^4 is H, C_{1-6} alkyl, C_{1-3} alkoxy optionally substituted with 1-3 fluorine atoms, halo, CN, NO_2, OR', CO_2R', or C(O)R';

R^5 is OR', OC(O)R', OC(O)OR', CO_2R', CON(R')$_2$, SO_2N(R')$_2$, SO_2R', OSO_2R', or OSO_2N(R')$_2$;

each R' is independently H, C_{1-6} alkyl, or C_{3-6} cycloalkyl;

each R" is H, C_{1-6} alkyl, halo, or OR'; and

n is 0, 1, 2, or 3;

wherein at each occurrence, alkyl and cycloalkyl are each optionally and independently substituted with up to 3 instances of OH, SH, CN, NO_2, CO_2H, halo, or COOC_{1-4} alkyl;

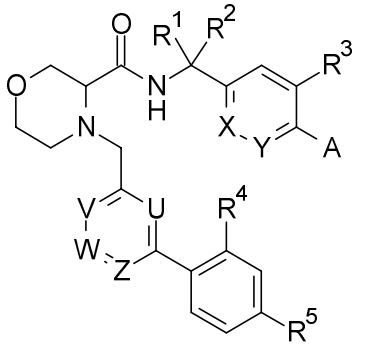
wherein heterocycloalkyl, aryl, and heteroaryl are each optionally and independently substituted with up to 3 instances of OR', SR', CN, NO_2, CO_2R', halo, C_{1-4} alkyl, or oxo.

2. The compound according to claim 1, wherein Ring B is a 6 membered aryl or a 5-6 membered heteroaryl, each optionally and independently substituted with up to 3 instances of OR', SR', CN, NO_2, CO_2R', halo, C_{1-4} alkyl, or oxo.

3. The compound according to claim 1, wherein Ring B is phenyl, which is optionally substituted with up to three instances of OH, or a 6 membered heteroaryl comprising one or two nitrogen atoms, wherein each nitrogen atom is optionally oxidized.

4. The compound according to any one of claims 1-3, wherein n is 0, 1 or 2, preferably wherein n is 0 or 1.

5. The compound according to any one of claims 1-4, which is a compound of Formula (1):

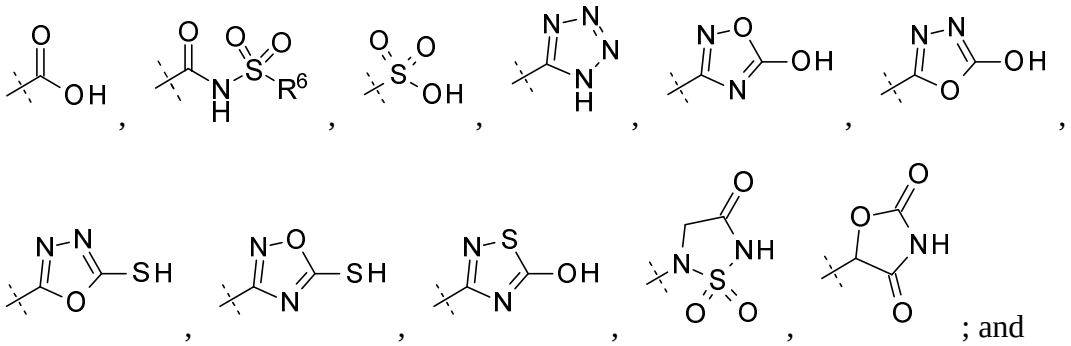


(1)

or pharmaceutically acceptable salt, solvate, hydrate, tautomer or optical isomer thereof, wherein;

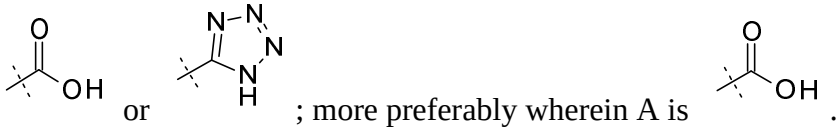
U, V, W, and Z are each independently selected from the group consisting of CH, COH, N or N^+-O^-, wherein at least three of U, V, W and Z are CH.

6. The compound according to any one of claims 1-5, wherein A is selected from the group consisting of:



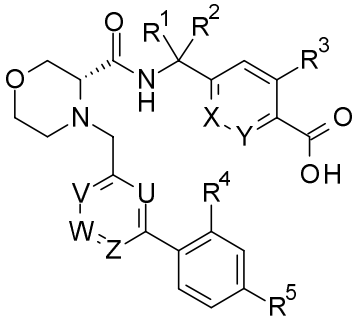
; and

R^6 is C_{1-3} alkyl or a C_{3-6} cycloalkyl ring; preferably wherein A is:

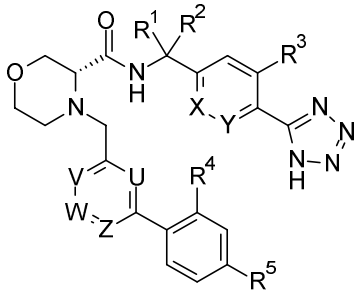


; more preferably wherein A is .

7. The compound according to claim 5, which is a compound of Formula (2a) or (2b):



(2a)



(2b)

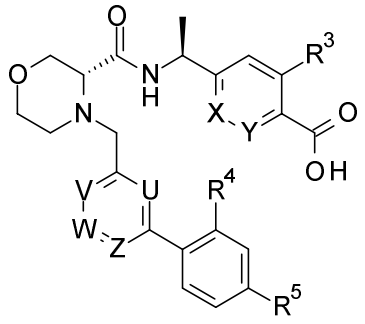
or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or optical isomer thereof, wherein U, V, W, X, Y, Z, R^1, R^2, R^3, R^4, and R^5 are the same as defined in claim 5.

8. The compound according to any one of claims 1-7, wherein R^1 and R^2 are each independently selected from the group consisting of H and C_{1-3} alkyl optionally substituted with 1-3 fluorine atoms.

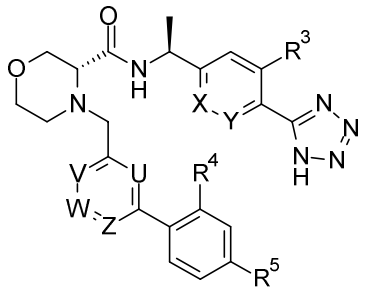
9. The compound according to any one of claims 1-7, wherein R^1 is H or methyl or R^1 is joined to R^2 to form a cyclopropane-1,1-diyl ring; preferably wherein R^1 is methyl.

10. The compound according to any one of claims 1-9, wherein R^2 is H.

11. The compound according to claim 5, which is a compound of Formula (3a) or (3b):



(3a)



(3b)

or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or optical isomer thereof, wherein U, V, W, X, Y, Z, R^3, R^4, and R^5 are the same as defined in claim 5.

12. The compound according to any one of claims 1-11, wherein R^3 is selected from the group consisting of H, OH or F; preferably R^3 is H or F; more preferably R^3 is H.

13. The compound according to any one of claims 1-12, wherein R^4 is selected from the group consisting of H, OH, CN, halo, C_{1-3} alkoxy optionally substituted with 1-3 fluorine atoms or C_{1-3} alkyl optionally substituted with 1-3 fluorine atoms; preferably wherein R^4 is H, OH or methyl; more preferably wherein R^4 is methyl.

14. The compound according to any one of claims 1-13, wherein R^5 is selected from the group consisting of OH, CO_2H, $CONH_2$, SO_2NH_2 or OSO_2NH_2; preferably wherein R^5 is OH, $CONH_2$, SO_2NH_2 or OSO_2NH_2; more preferably wherein R^5 is $CONH_2$ or SO_2NH_2.

15. The compound according to any one of claims 1-14, wherein X and Y are each independently selected from the group consisting of CH, CF, COH or N; preferably wherein X is CH or N and Y is selected from the group consisting of CH, CF, COH or N; more preferably wherein X and Y are both CH.

16. The compound according to any one of claims 5-15, wherein

(i) U is CH or N; and/or

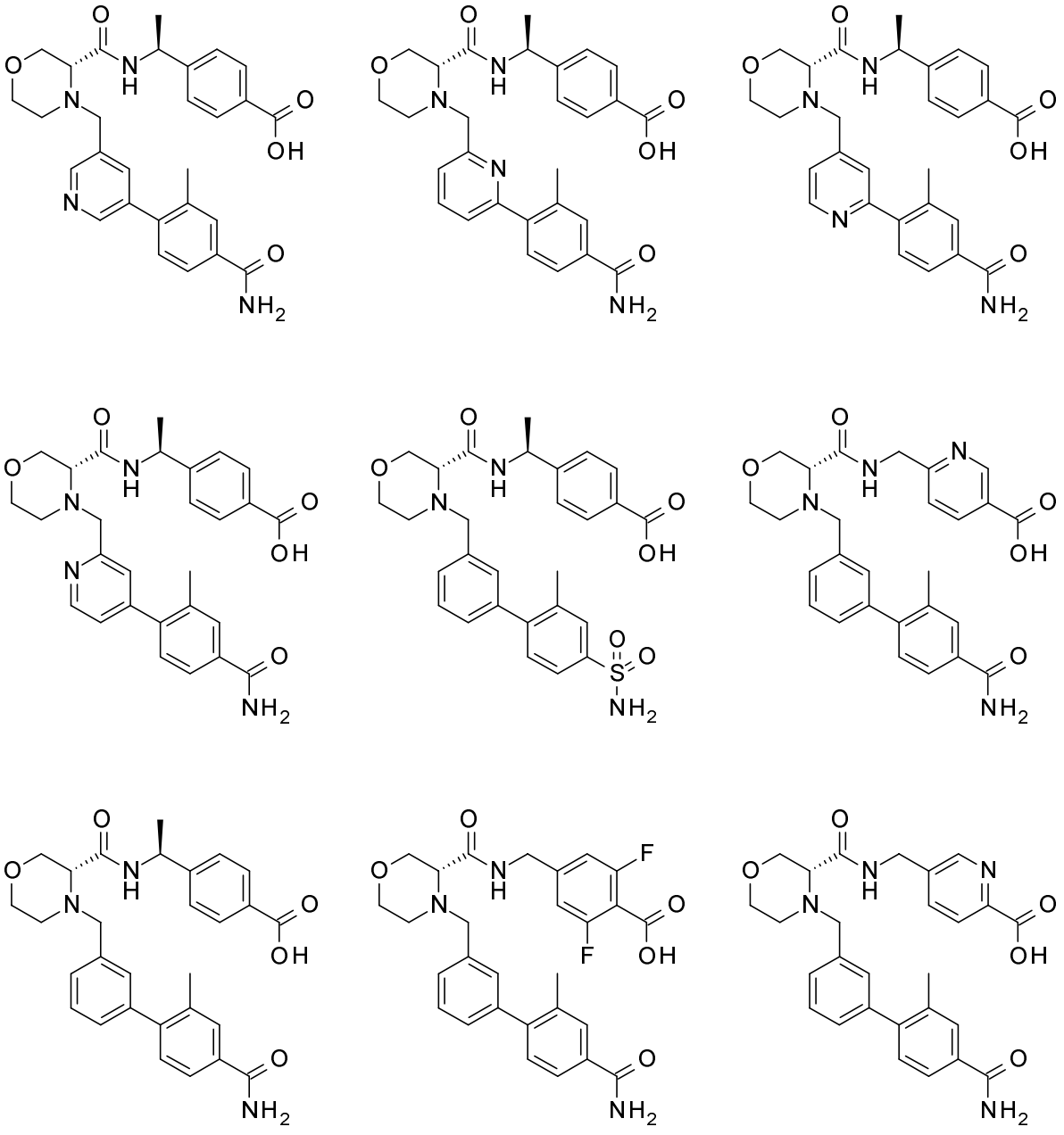
(ii) V is CH or N; and/or

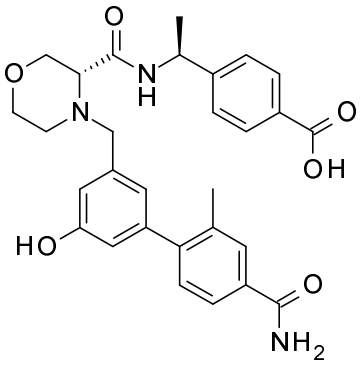
(iii) W is selected from the group consisting of CH, COH, N or N^+-O^-; and/or

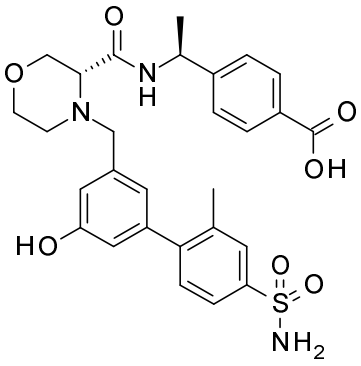
(iv) Z is selected from the group consisting of CH, COH or N.

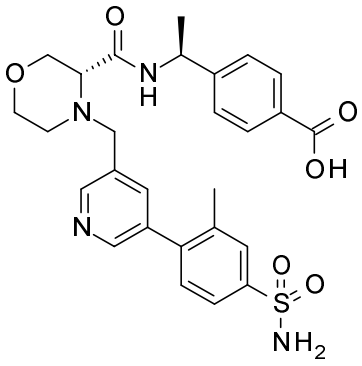
17. The compound according to any one of claims 5-16, wherein U, V, W and Z are CH, or wherein U, V and Z are CH and W is COH.

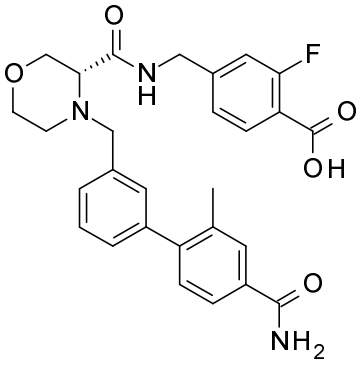
18. The compound according to claim 1, which is selected from:

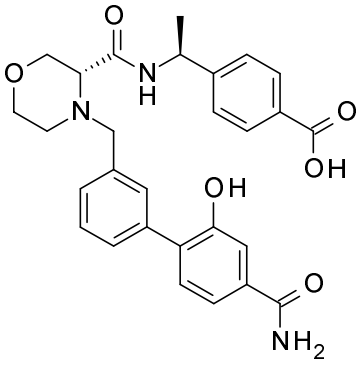


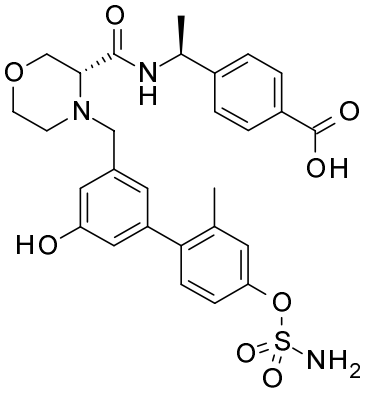


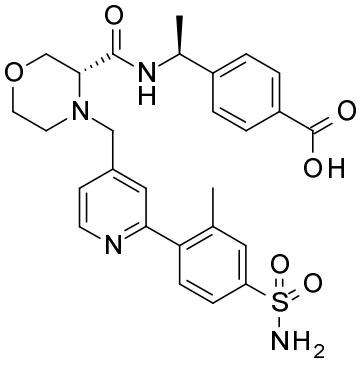


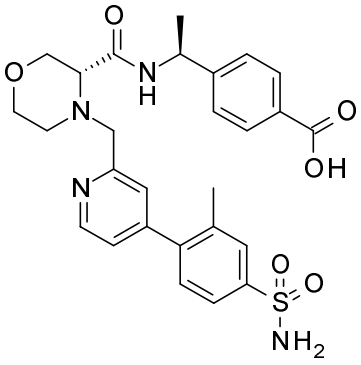


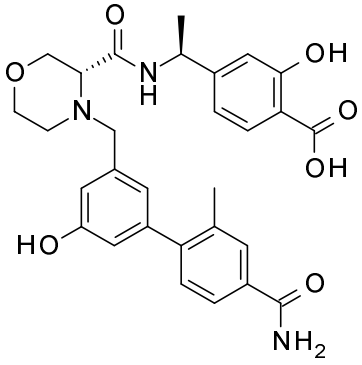


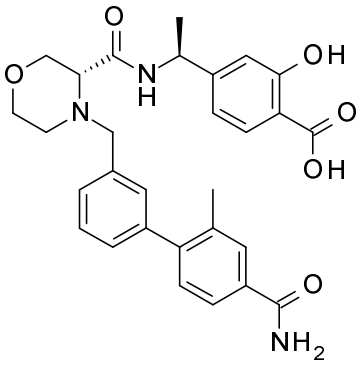


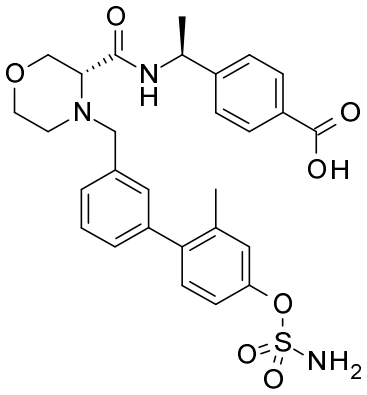


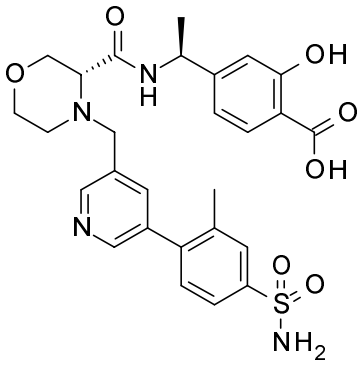


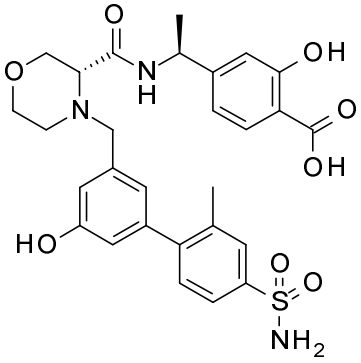


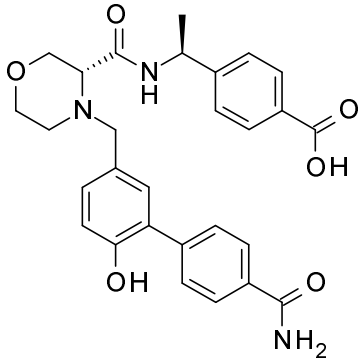


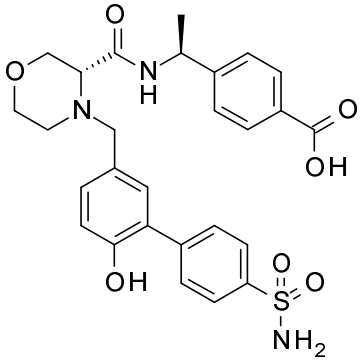


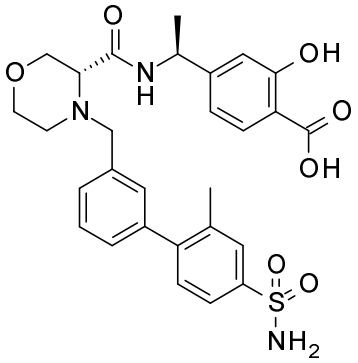


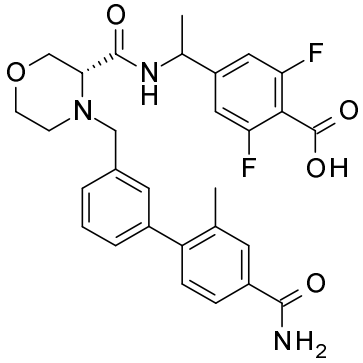


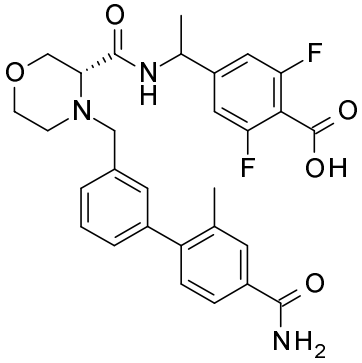


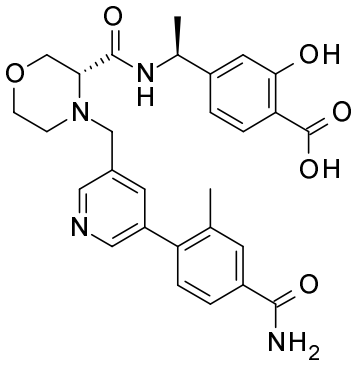


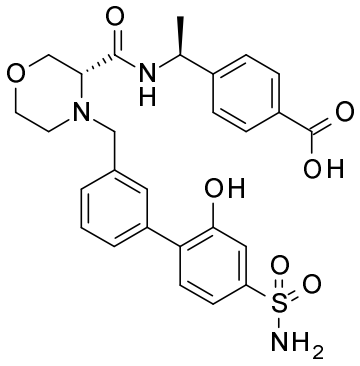


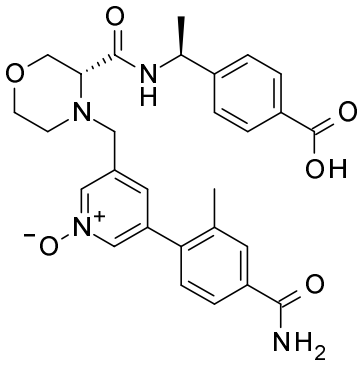


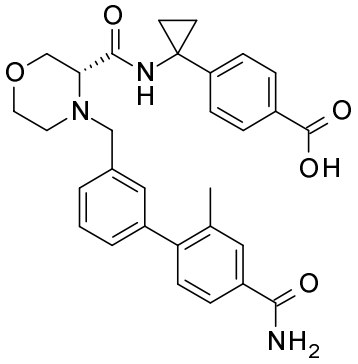


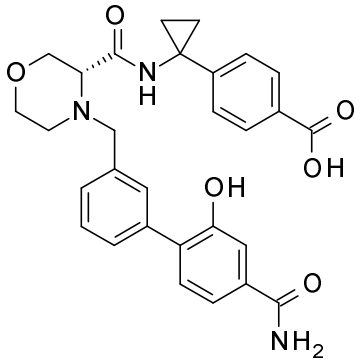


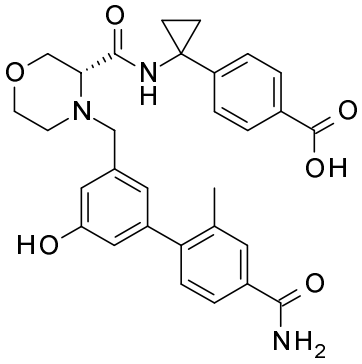


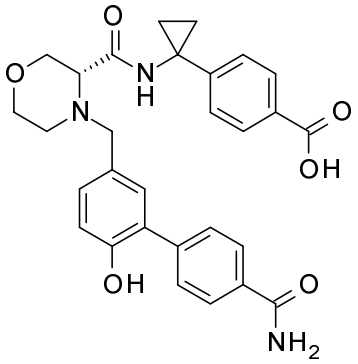


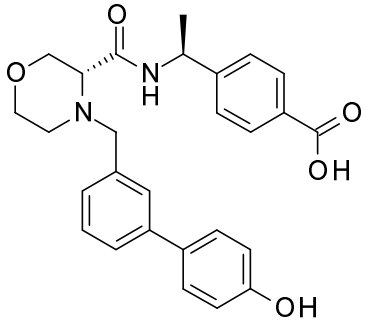


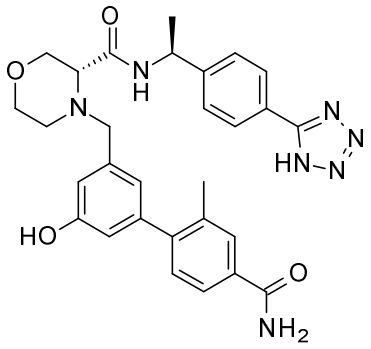


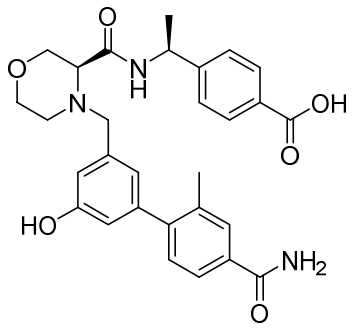
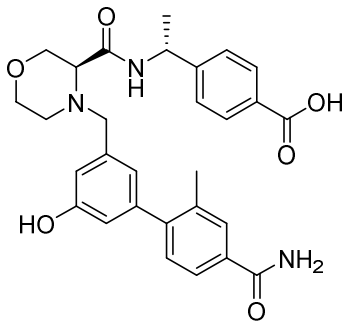
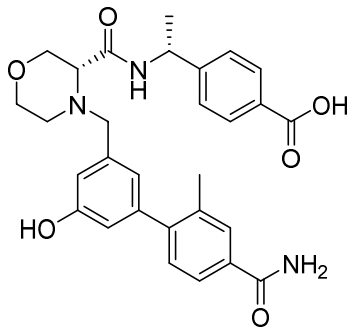










or a pharmaceutically acceptable salt, solvate, hydrate or tautomer thereof.

19. A pharmaceutical composition comprising a compound, pharmaceutically acceptable salt, solvate, hydrate, tautomer or optical isomer according to any one of claims 1-18 and a pharmaceutically acceptable excipient.

20. The pharmaceutical composition according to claim 19, wherein the composition further comprises at least one additional therapeutic agent selected from the group consisting of aminosalicylates, corticosteroids, immunomodulators and combinations thereof.

21. A kit comprising a compound, pharmaceutically acceptable salt, solvate, hydrate, tautomer or optical isomer according to any one of claims 1-18 and at least one additional therapeutic agent selected from the group consisting of aminosalicylates, corticosteroids, immunomodulators and combinations thereof.

22. A compound according to any one of claims 1-18, a composition according to claim 19 or 20, or a kit according to claim 21 for use as a medicament.

23. A compound according to any one of claims 1 to 18, a composition according to claim 19 or 20, or a kit according to claim 21, for use in the treatment of an EP4 receptor mediated disease.

24. The compound, composition or kit for use according to claim 23, wherein the EP4 receptor mediated disease is a gastrointestinal disorder.

25. The compound, composition or kit for use according to claim 24, wherein the gastrointestinal disorder is selected from the group consisting of constipation disorders, constipation-predominant irritable bowel syndrome, mixed type irritable bowel syndrome, chronic idiopathic constipation, gastrointestinal symptoms associated with Parkinson’s disease, gastrointestinal symptoms associated with cystic fibrosis, intestinal dysmotility, postoperative ileus, food allergy or food intolerance, celiac disease, gastrointestinal motility disorders, functional gastrointestinal disorders, drug induced enteropathy, NSAID induced gastric and intestinal injury, chemotherapy induced mucositis, gastroesophageal reflux disease (GERD), duodenogastric reflux, diarrhoeal diseases, immune mediated gastrointestinal diseases, Crohn's disease, ulcerative colitis, inflammatory bowel disease, and ischemic colitis.

26. The compound, composition or kit for use according to claim 23, wherein the EP4 receptor mediated disease is a pulmonary disease or condition.

27. The compound, composition or kit for use according to claim 26, wherein the pulmonary disease or condition is selected from chronic obstructive pulmonary diseases, asthma, chronic bronchitis, cystic fibrosis, emphysema, chronic idiopathic cough, hyperactive airway disorder, and idiopathic pulmonary fibrosis.