plasma membrane, is instead retained in the endoplasmic reticulum and targeted for degradation by the ubiquitin-proteasome system.

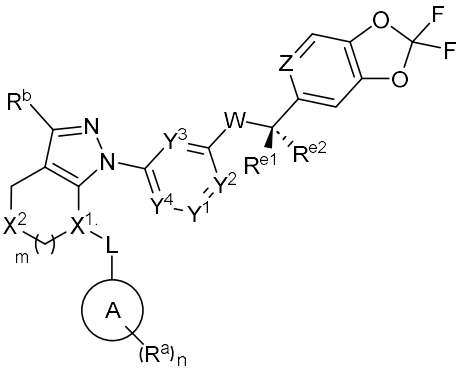
[005] The loss of a functional CFTR channel at the plasma membrane disrupts ionic homeostasis and airway surface hydration leading to reduced lung function. Reduced periciliary liquid volume and increased mucus viscosity impede mucociliary clearance resulting in chronic infection and inflammation. In the lung, the loss of CFTR-function leads to numerous physiological effects downstream of altered anion conductance that result in the dysfunction of additional organs such as the pancreas, intestine and gall bladder.

[006] By studying the mechanistic aspects of CFTR misfolding and corrections, small molecules have been identified as CF modulators, that can act as stabilizers.

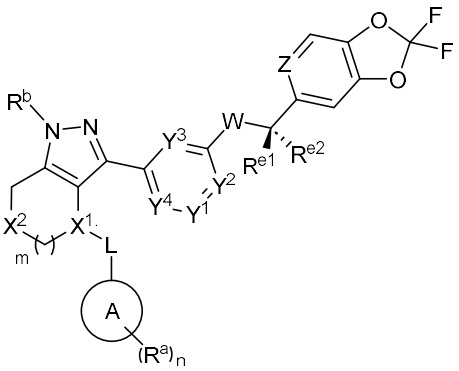
[007] Despite the identification of compounds that modulate CFTR, there is no cure for this fatal disease and identification of new compounds and new methods of therapy are needed as well as new methods for treating or lessening the severity of cystic fibrosis and other CFTR mediated conditions and diseases in a patient.

Summary

[008] The present disclosure includes a compound of Formula (I) or (II)



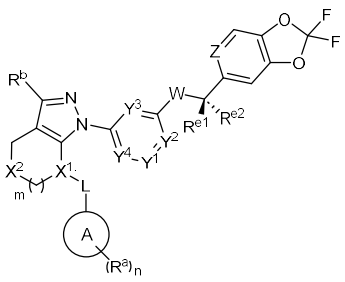
(I)



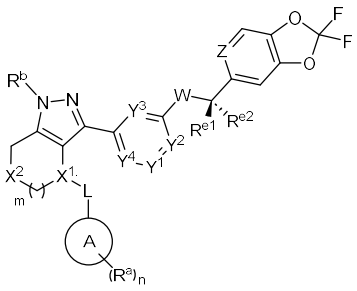
(II),

[009] or a pharmaceutically acceptable salt thereof Additionally, the present disclosure includes, among other things, pharmaceutical compositions, methods of using and methods of making a compound of Formula (I) or (II).

[009a] In one aspect, the present disclosure refers to a compound represented by Formula (I) or Formula (II):



(I)



(II),

or a pharmaceutically acceptable salt thereof

A is selected from the group consisting of optionally substituted 3-10 membered carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted phenyl, and optionally substituted 5-10 membered heteroaryl;

L is selected from the group consisting of a bond, -O-, -S-, -$S(O)_2$-, -CH_2-, -C(O)-, -N(H)-, and -N(H)C(O)-;

W is selected from the group consisting of -O-, -S-, -S(O)-, -$S(O)_2$-, -N(H)-, and optionally substituted 3-6 membered heterocyclylene;

X^1 is N or C(H);

X^2 is selected from the group consisting of -CH_2-, -N(H)-, and -N(C_{1-3} alkyl)-;

Y^1 is selected from the group consisting of -C(H)=, -C(F)=, and -N=;

Y^2 is selected from the group consisting of -C(H)=, -C(F)=, and -N=;

Y^3 is selected from the group consisting of -C(H)=, -C(F)=, and -N=;

Y^4 is selected from the group consisting of -C(H)=, -C(F)=, and -N=;

Z is selected from the group consisting of -C(H)=, -C(F)=, and -N=;

each R^a is independently selected from the group consisting of halogen, optionally substituted C_1-C_3 aliphatic, optionally substituted 5-7 membered heterocyclyl, optionally substituted 5-6 membered heteroaryl, and -COOH;

R^b is selected from the group consisting of -CN, optionally substituted C_1-C_6 aliphatic, optionally substituted C_1-C_6 haloaliphatic, and optionally substituted 3-7 membered heterocyclyl;

R^{e1} is selected from the group consisting of hydrogen, C_1-C_5-alkyl, and C_3-C_5-cycloalkyl;

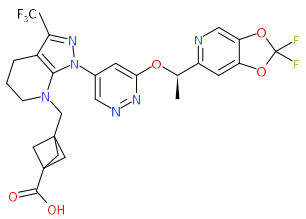
R^{e2} is selected from the group consisting of hydrogen, C_1-C_5-alkyl, and C_3-C_5-cycloalkyl;

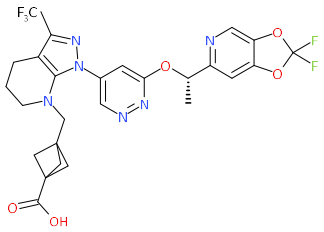
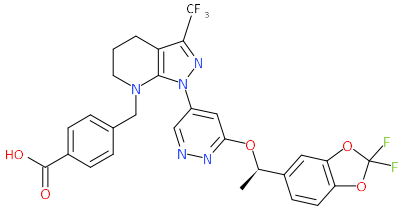
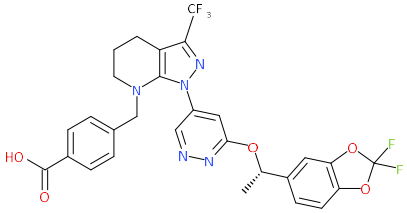
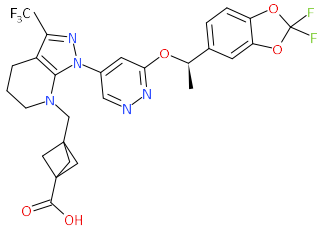
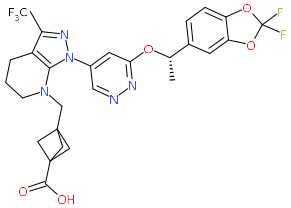
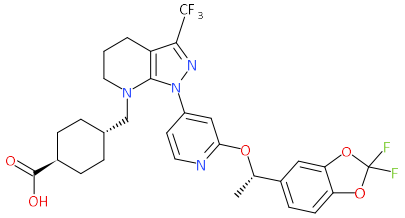
wherein R^{e1} and R^{e2}, together with the atom on which they are attached, are optionally taken together to form an optionally substituted 3-6 membered carbocyclyl ring;

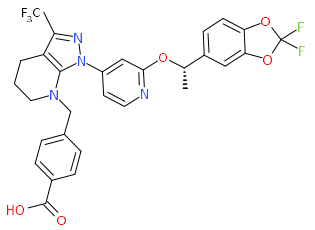
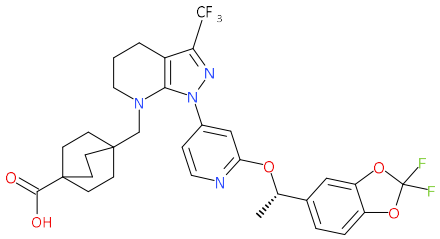
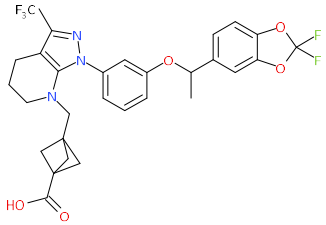
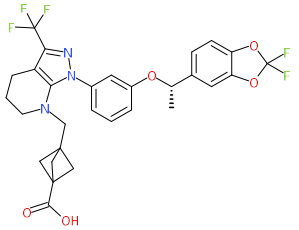
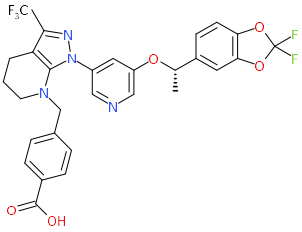
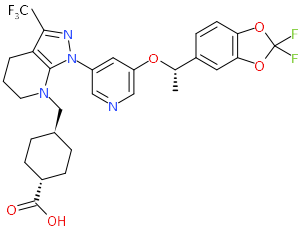
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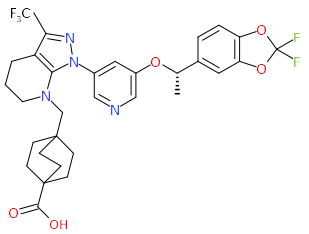
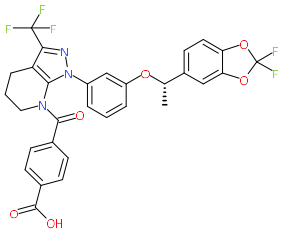
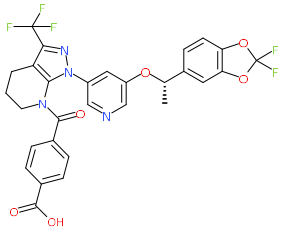
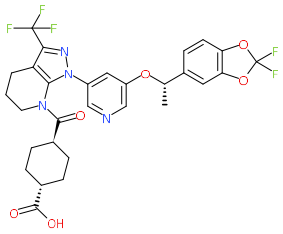
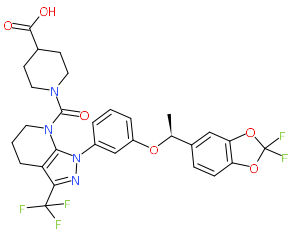
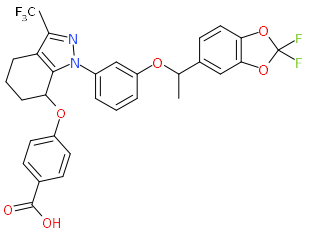
n is 0-5.

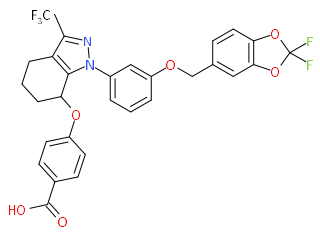
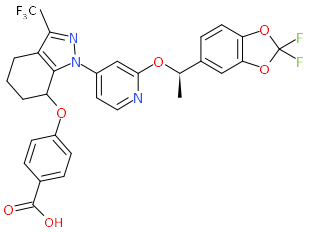
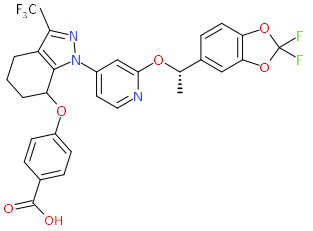
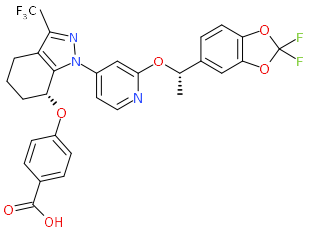
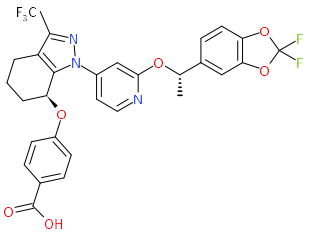
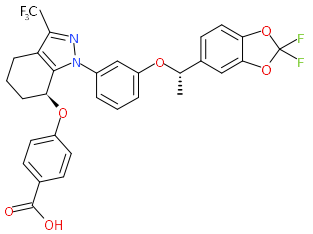
[009b] In one aspect, the present disclosure refers to a compound selected from the group consisting of

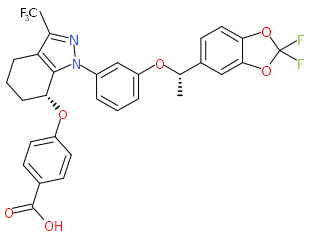
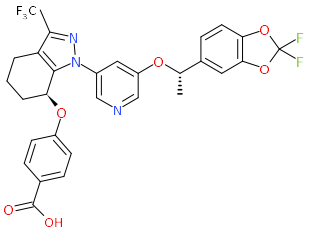
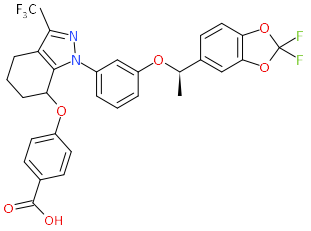
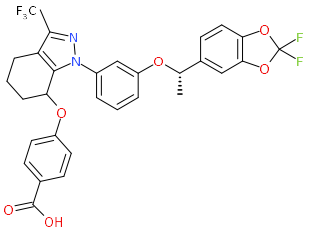
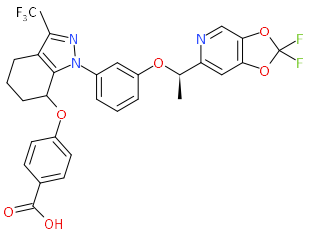
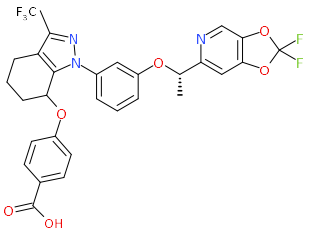
Ex. No.	Structure	IUPAC name
1		3-[[1-[6-[(1R)-1-(2,2-difluoro-[1,3]dioxolo[4,5-c]pyridin-6-yl)ethoxy]pyridazin-4-yl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridin-7-yl]methyl]bicyclo[1.1.1]pentane-1-carboxylic acid

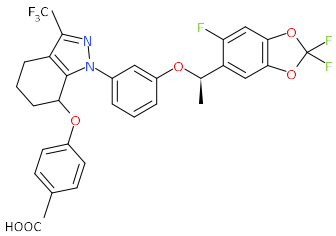
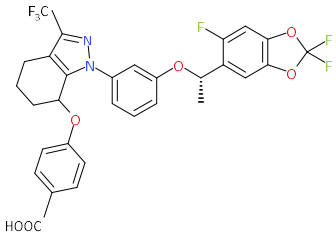
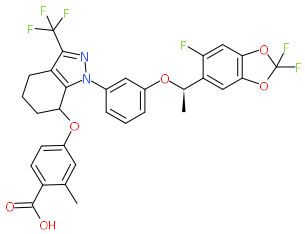
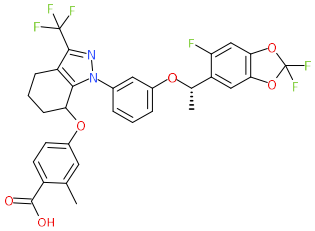
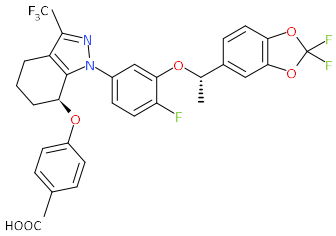
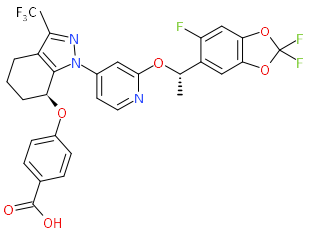
2		3-[[1-[6-[(1S)-1-(2,2-difluoro-[1,3]dioxolo[4,5-c]pyridin-6-yl)ethoxy]pyridazin-4-yl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridin-7-yl]methyl]bicyclo[1.1.1]pentane-1-carboxylic acid
3		4-[[1-[6-[(1R)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]pyridazin-4-yl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridin-7-yl]methyl]benzoic acid
4		4-[[1-[6-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]pyridazin-4-yl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridin-7-yl]methyl]benzoic acid
5		3-[[1-[6-[(1R)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]pyridazin-4-yl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridin-7-yl]methyl]bicyclo[1.1.1]pentane-1-carboxylic acid
6		3-[[1-[6-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]pyridazin-4-yl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridin-7-yl]methyl]bicyclo[1.1.1]pentane-1-carboxylic acid
7		Trans-4-[[1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridine-7-yl]methyl]cyclohexanecarboxylic acid

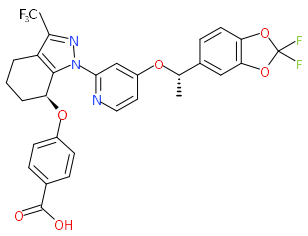
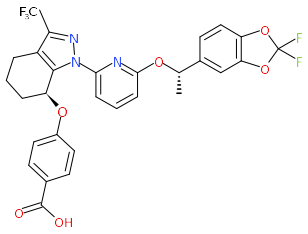
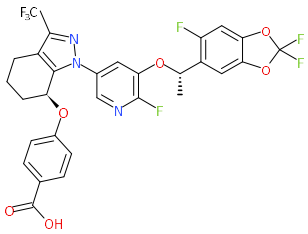
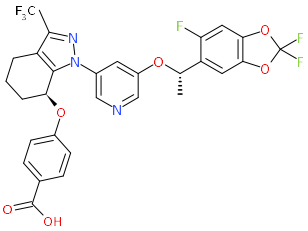
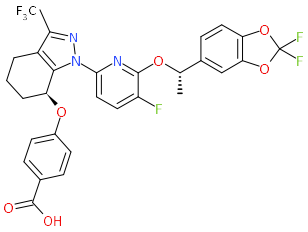
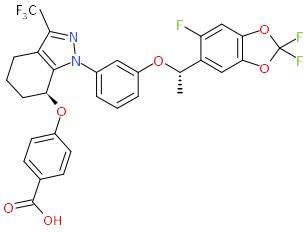
8		4-[[1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridine-7-yl]methyl]benzoic acid
9		4-[[1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridine-7-yl]methyl]bicyclo[2.2.2]octane-1-carboxylic acid
10		3-[[1-[3-[1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridine-7-yl]methyl]bicyclo[1.1.1]pentane-1-carboxylic acid
11		3-[[1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridine-7-yl]methyl]bicyclo[1.1.1]pentane-1-carboxylic acid
12		4-[[1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridine-7-yl]methyl]benzoic acid
13		Trans-4-[[1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridine-7-yl]methyl]cyclohexanecarboxylic acid

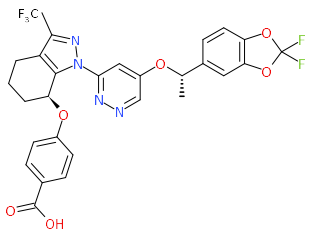
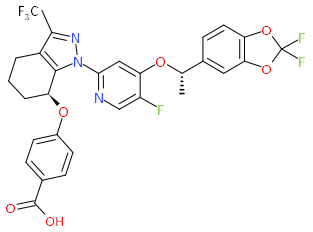
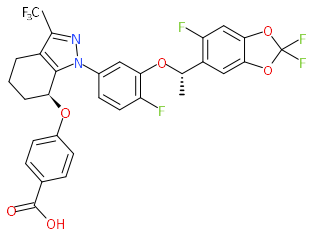
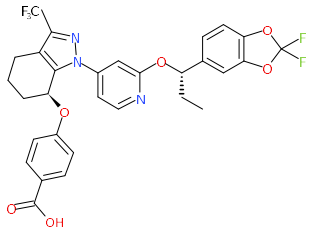
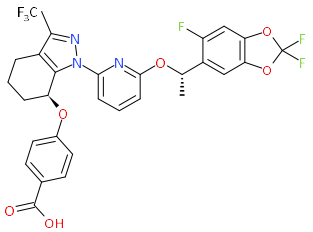
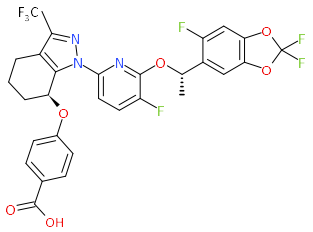
14		4-[[1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridine-7-yl]methyl]bicyclo[2.2.2]octane-1-carboxylic acid
15		4-[1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridine-7-carbonyl]benzoic acid
16		4-[1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridine-7-carbonyl]benzoic acid
17		Trans-4-[1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridine-7-carbonyl]cyclohexanecarboxylic acid
18		1-[1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-5,6-dihydro-4H-pyrazolo[3,4-b]pyridine-7-carbonyl]piperidine-4-carboxylic acid
19		4-[[1-[3-[1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid

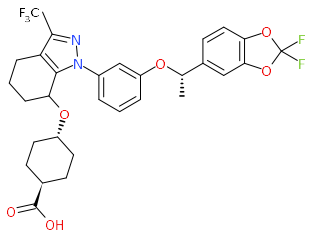
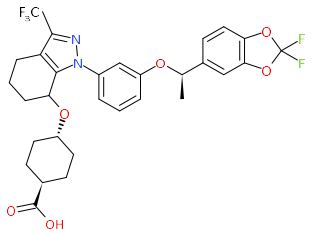
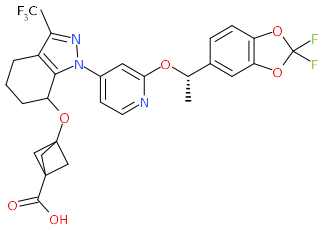
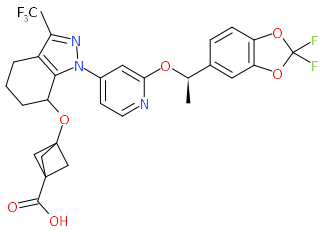
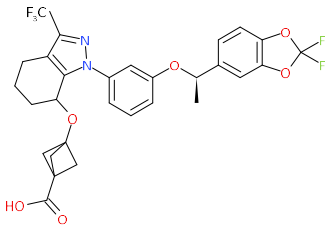
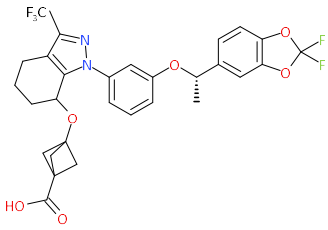
20		4-[[1-[3-[(2,2-difluoro-1,3-benzodioxol-5-yl)methoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
21		4-[[1-[2-[(1R)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
22		4-[[1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
23		4-[[(7R)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
24		4-[[(7S)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
25		4-[[(7S)-1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid

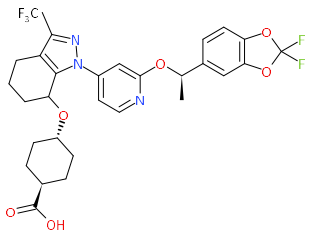
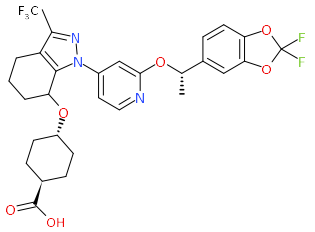
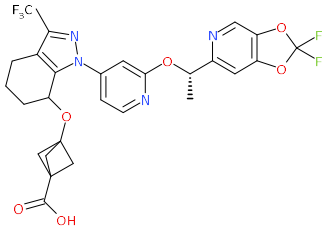
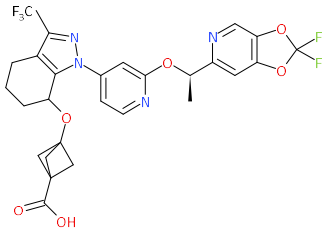
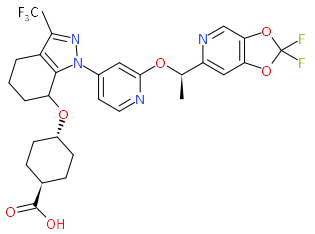
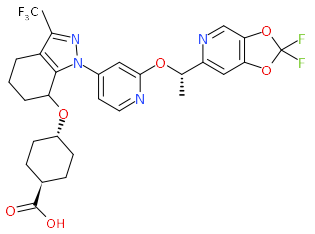
26		4-[[(7R)-1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
27		4-[[(7S)-1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
28		4-[[1-[3-[(1R)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
29		4-[[1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
30		4-[[1-[3-[(1R)-1-(2,2-difluoro-[1,3]dioxolo[4,5-c]pyridine-6-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
31		4-[[1-[3-[(1S)-1-(2,2-difluoro-[1,3]dioxolo[4,5-c]pyridine-6-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid

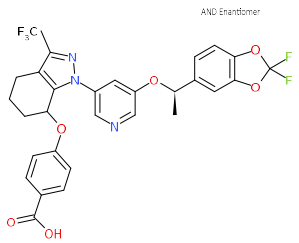
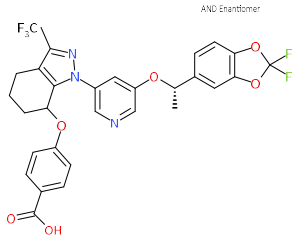
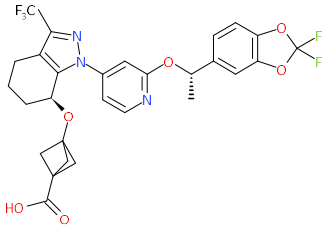
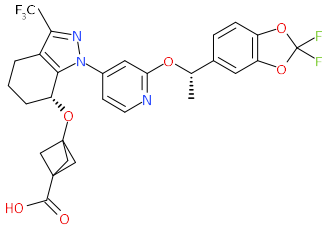
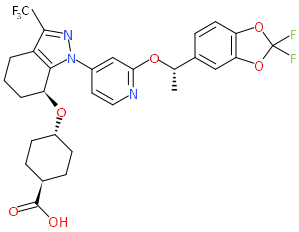
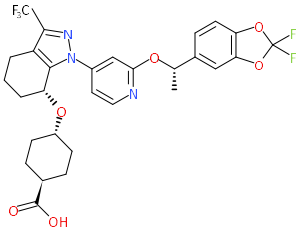
32		4-[[1-[3-[(1R)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
33		4-[[1-[3-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
34		2-methyl-4-[[1-[3-[(1R)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
35		2-methyl-4-[[1-[3-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
36		4-[[(7S)-1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-fluoro-phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
36a		4-[[(7S)-1-[2-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid

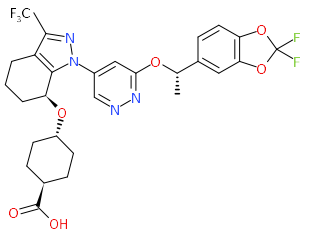
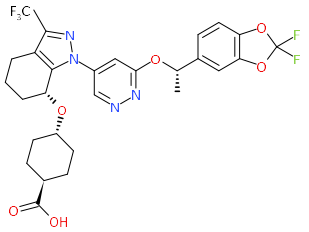
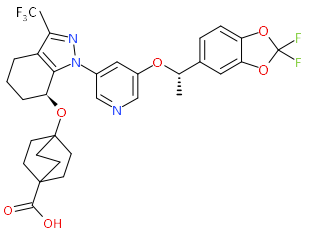
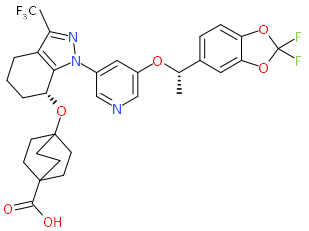
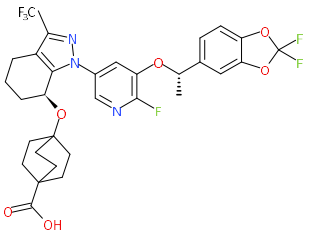
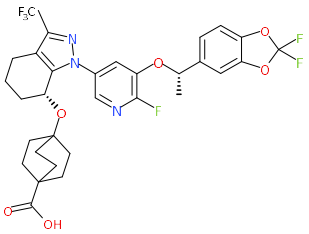
36b		4-[[(7S)-1-[4-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
36c		4-[[(7S)-1-[6-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
36d		4-[[(7S)-1-[6-fluoro-5-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
36e		4-[[(7S)-1-[5-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
36f		4-[[(7S)-1-[6-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-5-fluoro-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
36g		4-[[(7S)-1-[3-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid

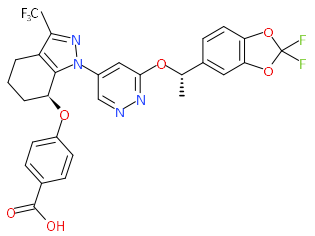
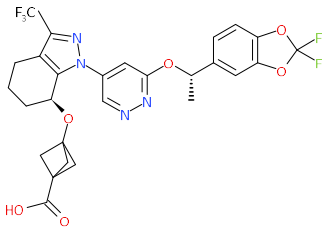
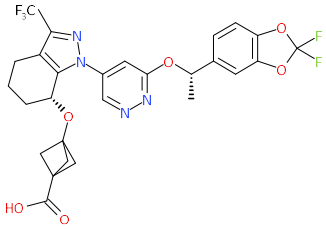
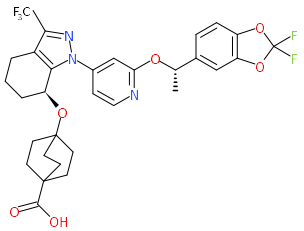
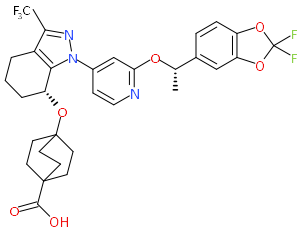
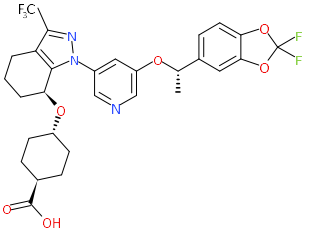
36h		4-[[(7S)-1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]pyridazin-3-yl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
36i		4-[[(7S)-1-[4-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-5-fluoro-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
36j		4-[[(7S)-1-[4-fluoro-3-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
36k		4-[[(7S)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)propoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
36l		4-[[(7S)-1-[6-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
36m		4-[[(7S)-1-[5-fluoro-6-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid

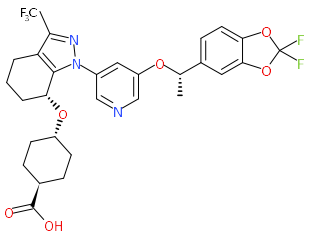
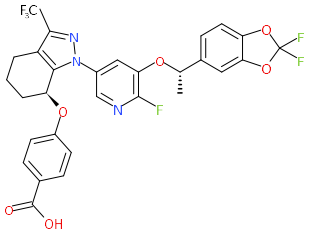
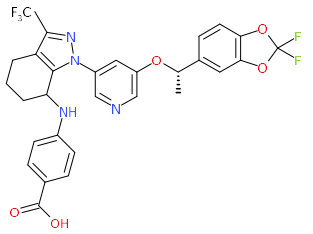
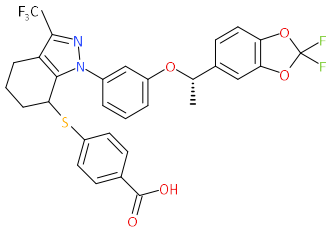
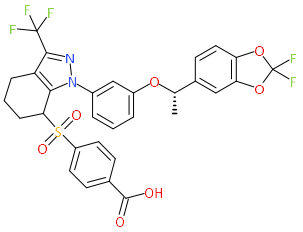
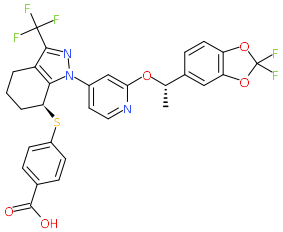
37		4-[[1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclohexanecarboxylic acid
38		4-[[1-[3-[(1R)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclohexanecarboxylic acid
39		3-[[1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
40		3-[[1-[2-[(1R)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
41		3-[[1-[3-[(1R)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
42		3-[[1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid

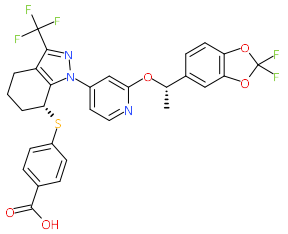
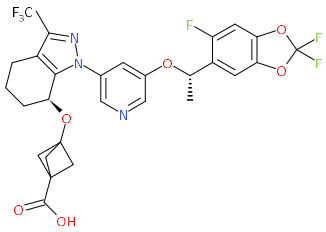
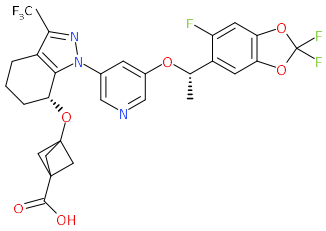
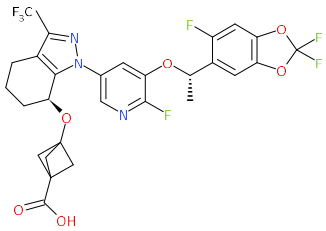
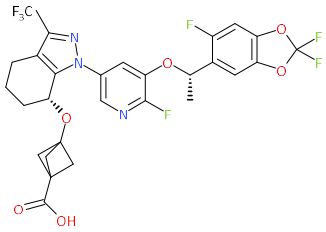
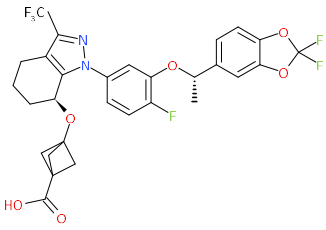
43		Trans-4-[[1-[2-[(1R)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclohexanecarboxylic acid
44		Trans-4-[[1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclohexanecarboxylic acid
45		3-[[1-[2-[(1S)-1-(2,2-difluoro-[1,3]dioxolo[4,5-c]pyridin-6-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
46		3-[[1-[2-[(1R)-1-(2,2-difluoro-[1,3]dioxolo[4,5-c]pyridin-6-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
47		Trans-4-[[1-[2-[(1R)-1-(2,2-difluoro-[1,3]dioxolo[4,5-c]pyridin-6-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclohexanecarboxylic acid
48		Trans-4-[[1-[2-[(1S)-1-(2,2-difluoro-[1,3]dioxolo[4,5-c]pyridin-6-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclohexanecarboxylic acid

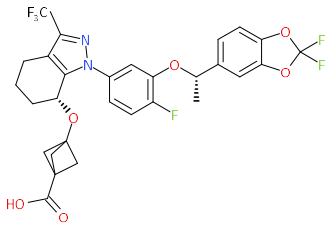
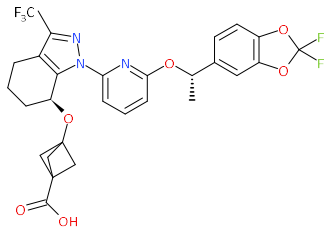
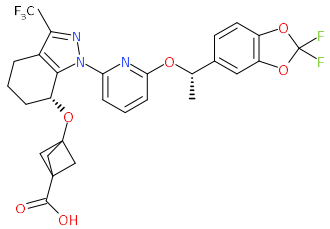
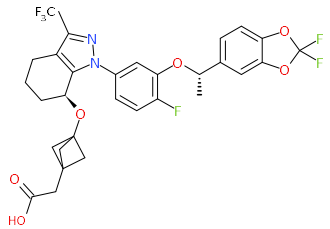
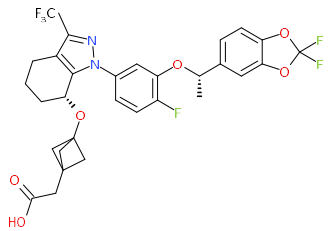
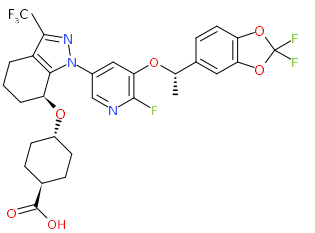
49		4-[[1-[5-[rac-(1R)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
50		4-[[1-[5-[rac-(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
51		3-[[(7S)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
52		3-[[(7R)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
53		Trans-4-[[(7S)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclohexanecarboxylic acid
54		Trans-4-[[(7R)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclohexanecarboxylic acid

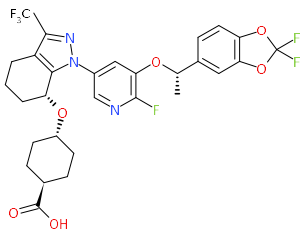
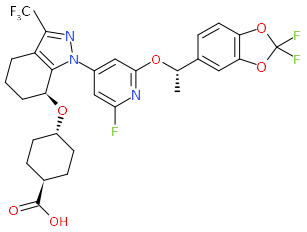
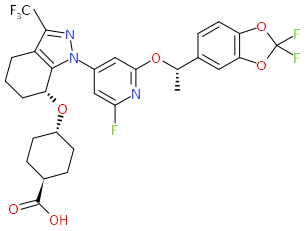
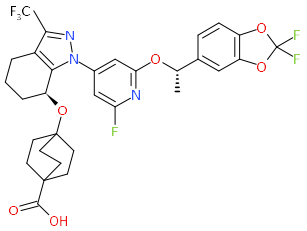
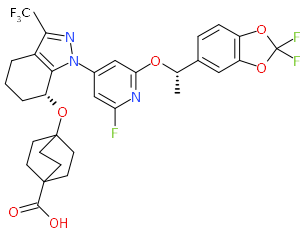
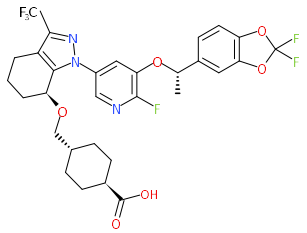
55		Trans-4-[[(7S)-1-[6-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]pyridazin-4-yl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclohexanecarboxylic acid
56		Trans-4-[[(7R)-1-[6-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]pyridazin-4-yl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclohexanecarboxylic acid
57		4-[[(7S)-1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[2.2.2]octane-1-carboxylic acid
58		4-[[(7R)-1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[2.2.2]octane-1-carboxylic acid
59		4-[[(7S)-1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-6-fluoro-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[2.2.2]octane-1-carboxylic acid
60		4-[[(7R)-1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-6-fluoro-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[2.2.2]octane-1-carboxylic acid

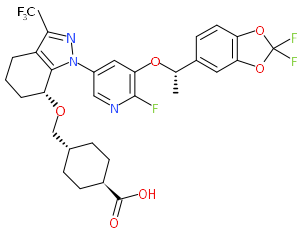
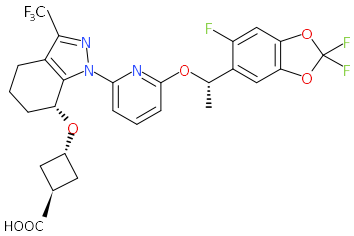
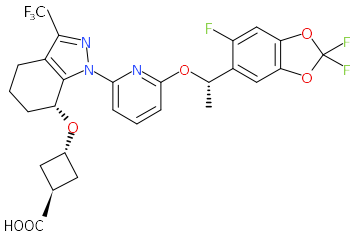
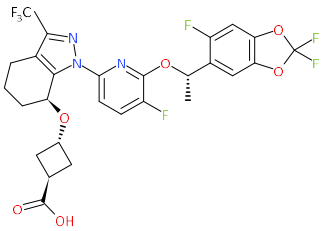
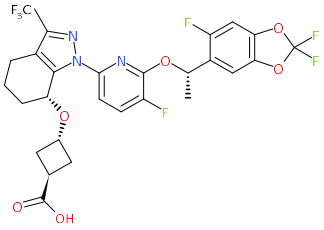
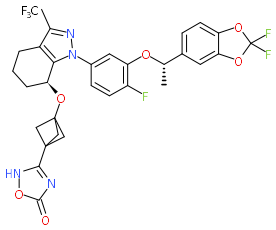
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62		3-[[(7S)-1-[6-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]pyridazin-4-yl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
63		3-[[(7R)-1-[6-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]pyridazin-4-yl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
64		4-[[(7S)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[2.2.2]octane-1-carboxylic acid
65		4-[[(7R)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[2.2.2]octane-1-carboxylic acid
66		Trans-4-[[(7S)-1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclohexanecarboxylic acid

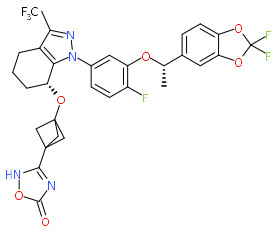
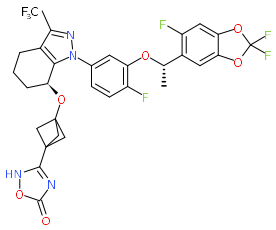
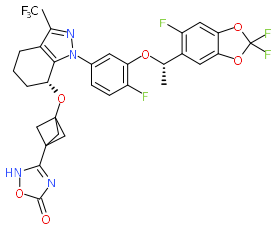
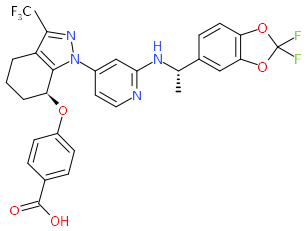
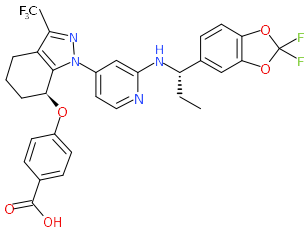
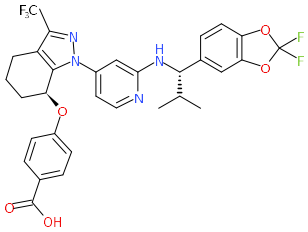
67		Trans-4-[[(7R)-1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclohexanecarboxylic acid
68		4-[[(7S)-1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-6-fluoro-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
69		4-[[1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]amino]benzoic acid
70		4-[[1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]sulfanyl]benzoic acid
71		4-[[1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]sulfonyl]benzoic acid
72		4-[[(7S)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]sulfanyl]benzoic acid

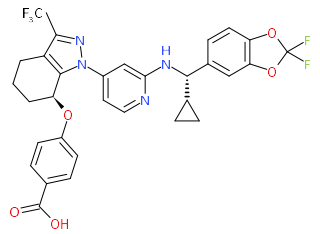
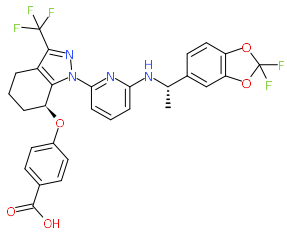
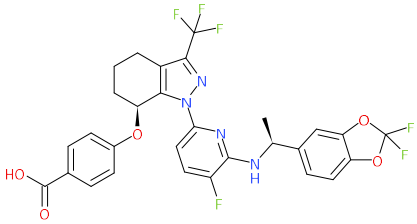
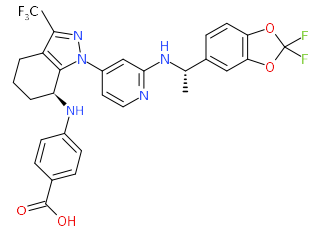
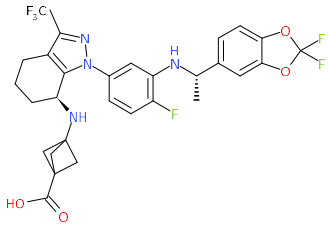
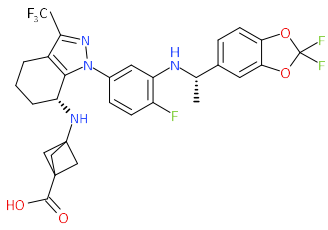
73		4-[[(7R)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]sulfanyl]benzoic acid
74 (P1)		3-[[(7S)-1-[5-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
74 (P2)		3-[[(7R)-1-[5-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
75 (P1)		3-[[(7S)-1-[6-fluoro-5-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
75 (P2)		3-[[(7R)-1-[6-fluoro-5-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
76 (P1)		3-[[(7S)-1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-fluoro-phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid

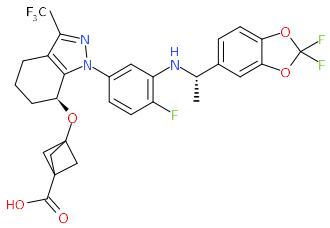
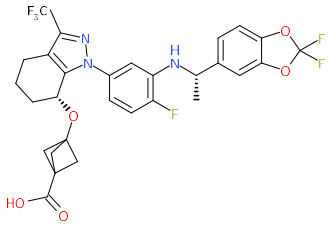
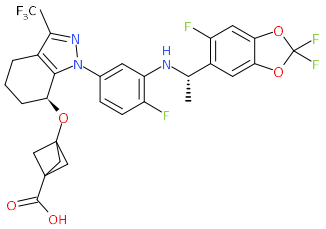
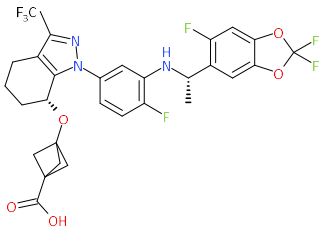
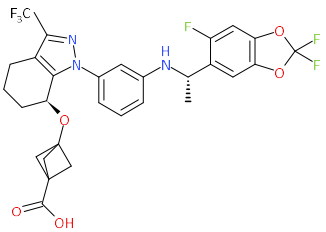
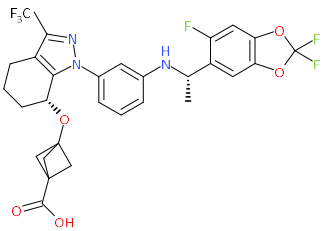
76 (P2)		3-[[(7R)-1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-fluoro-phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
77 (P1)		3-[[(7S)-1-[6-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
77 (P2)		3-[[(7R)-1-[6-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
78 (P1)		2-[3-[[(7S)-1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-fluoro-phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]-1-bicyclo[1.1.1]pentanyl]acetic acid
78 (P2)		2-[3-[[(7R)-1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-fluoro-phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]-1-bicyclo[1.1.1]pentanyl]acetic acid
79 (P1)		Trans-4-[[(7S)-1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-6-fluoro-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclohexanecarboxylic acid

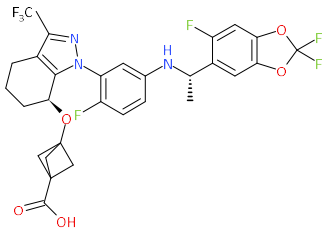
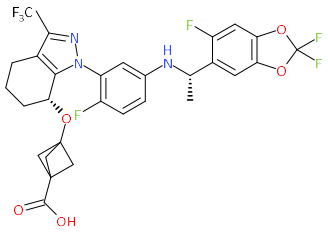
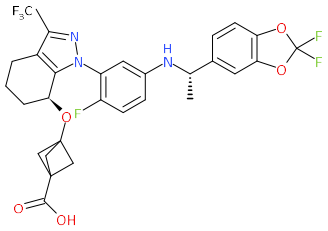
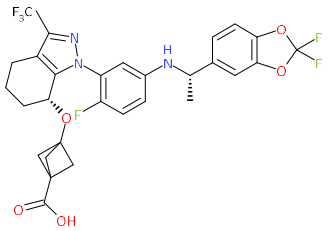
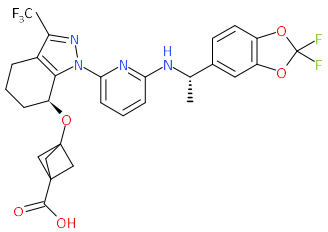
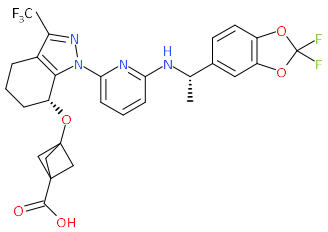
79 (P2)		Trans-4-[[(7R)-1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-6-fluoro-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclohexanecarboxylic acid
80 (P1)		Trans-4-[[(7S)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-6-fluoro-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclohexanecarboxylic acid
80 (P2)		Trans-4-[[(7R)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-6-fluoro-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclohexanecarboxylic acid
81 (P1)		4-[[(7S)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-6-fluoro-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[2.2.2]octane-1-carboxylic acid
81 (P2)		4-[[(7R)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-6-fluoro-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[2.2.2]octane-1-carboxylic acid
82 (P1)		Trans-4-[[(7S)-1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-6-fluoro-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxymethyl]cyclohexanecarboxylic acid

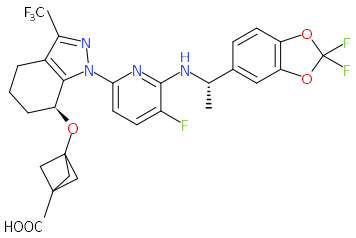
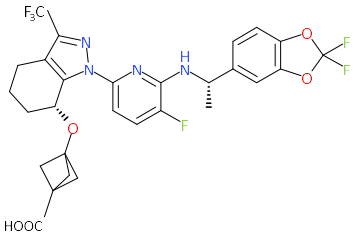
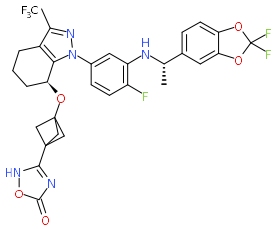
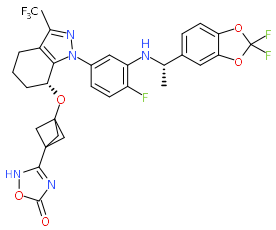
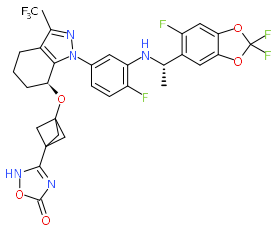
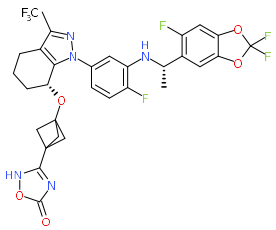
82 (P2)		Trans-4-[[(7R)-1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-6-fluoro-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxymethyl]cyclohexanecarboxylic acid
83 (P1)		Trans-3-[[(7S)-1-[6-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclobutanecarboxylic acid
83 (P2)		Trans-3-[[(7R)-1-[6-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclobutanecarboxylic acid
84 (P1)		Trans-3-[[(7S)-1-[5-fluoro-6-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclobutanecarboxylic acid
84 (P2)		Trans-3-[[(7R)-1-[5-fluoro-6-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]cyclobutanecarboxylic acid
85 (P1)		3-[3-[[(7S)-1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-fluoro-phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]-1-bicyclo[1.1.1]pentanyl]-2H-1,2,4-oxadiazol-5-one

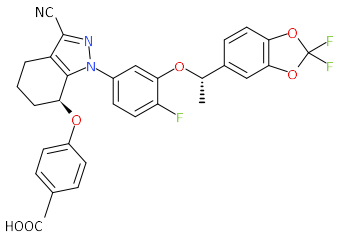
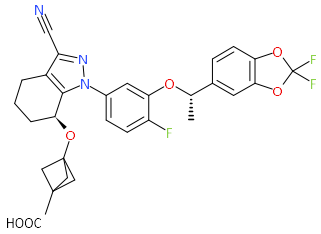
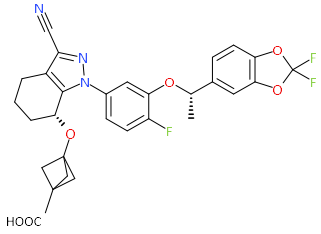
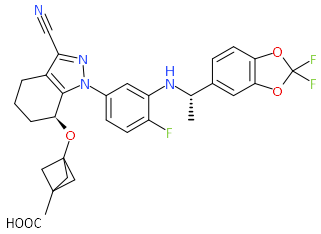
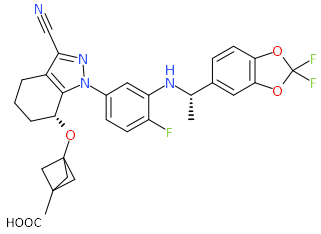
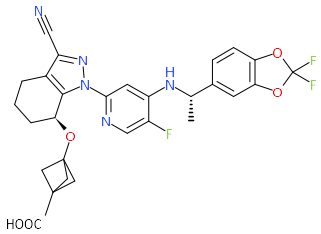
85 (P2)		3-[3-[[(7R)-1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-fluoro-phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]-1-bicyclo[1.1.1]pentanyl]-2H-1,2,4-oxadiazol-5-one
86 (P1)		3-[3-[[(7S)-1-[4-fluoro-3-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]-1-bicyclo[1.1.1]pentanyl]-2H-1,2,4-oxadiazol-5-one
86 (P2)		3-[3-[[(7R)-1-[4-fluoro-3-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]-1-bicyclo[1.1.1]pentanyl]-2H-1,2,4-oxadiazol-5-one
87		4-[[(7S)-1-[2-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
88		4-[[(7S)-1-[2-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)propyl]amino]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
89		4-[[(7S)-1-[2-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)-2-methyl-propyl]amino]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid

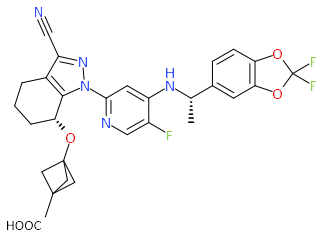
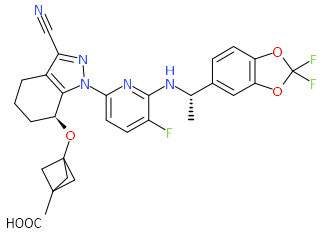
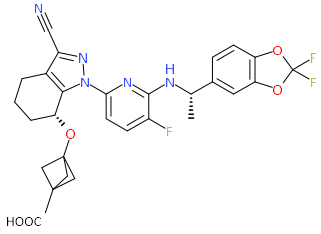
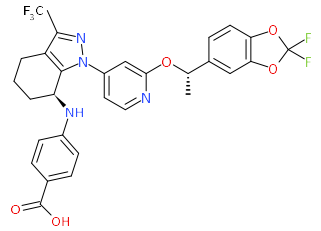
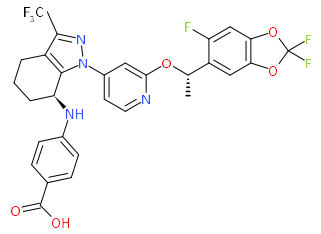
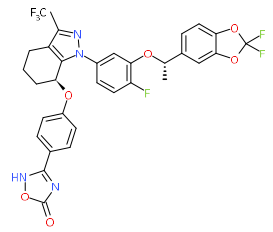
90		4-[[(7S)-1-[2-[[(S)-cyclopropyl-(2,2-difluoro-1,3-benzodioxol-5-yl)methyl]amino]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
91		4-[[(7S)-1-[6-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
92		4-[[(7S)-1-[6-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-5-fluoro-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
93		4-[[(7S)-1-[2-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]amino]benzoic acid
94 (P1)		3-[[(7S)-1-[3-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-4-fluoro-phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]amino]bicyclo[1.1.1]pentane-1-carboxylic acid
94 (P2)		3-[[(7R)-1-[3-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-4-fluoro-phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]amino]bicyclo[1.1.1]pentane-1-carboxylic acid

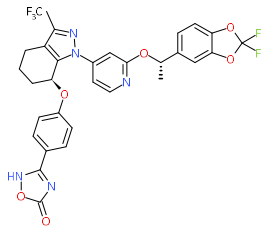
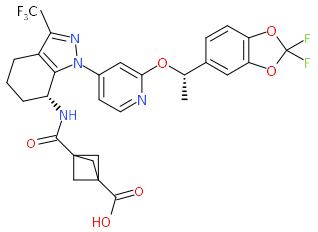
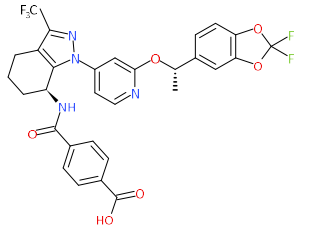
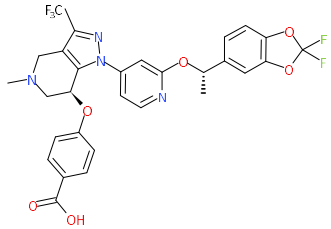
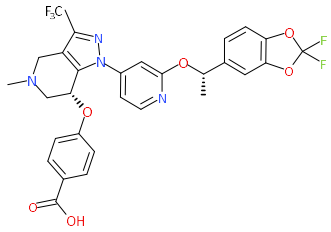
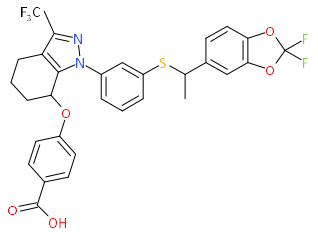
95 (P1)		3-[[(7S)-1-[3-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-4-fluoro-phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
95 (P2)		3-[[(7R)-1-[3-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-4-fluoro-phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
96 (P1)		3-[[(7S)-1-[4-fluoro-3-[[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethyl]amino]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
96 (P2)		3-[[(7R)-1-[4-fluoro-3-[[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethyl]amino]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
97 (P1)		3-[[(7S)-1-[3-[[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethyl]amino]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
97 (P2)		3-[[(7R)-1-[3-[[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethyl]amino]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid

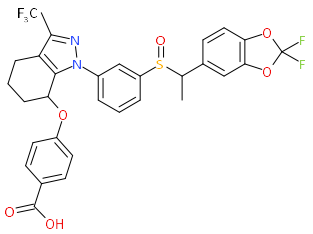
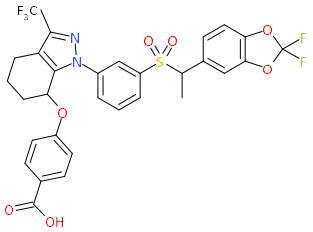
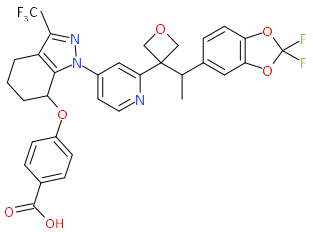
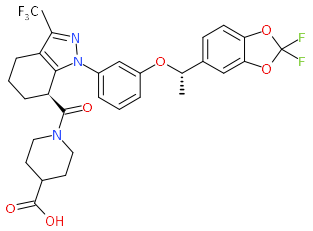
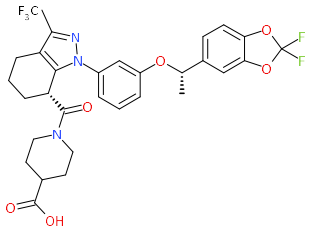
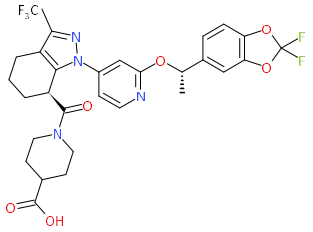
98 (P1)		3-[[(7S)-1-[2-fluoro-5-[[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethyl]amino]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
98 (P2)		3-[[(7R)-1-[2-fluoro-5-[[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethyl]amino]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
99 (P1)		3-[[(7S)-1-[5-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-2-fluoro-phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
99 (P2)		3-[[(7R)-1-[5-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-2-fluoro-phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
100 (P1)		3-[[(7S)-1-[6-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
100 (P2)		3-[[(7R)-1-[6-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid

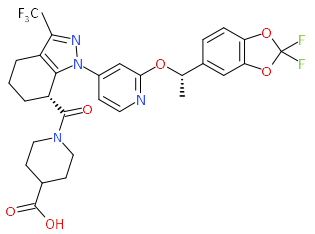
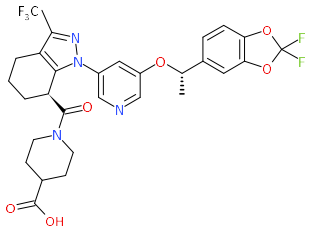
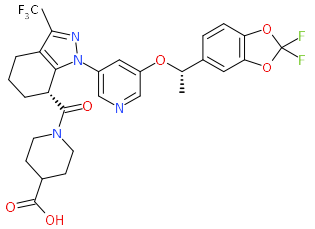
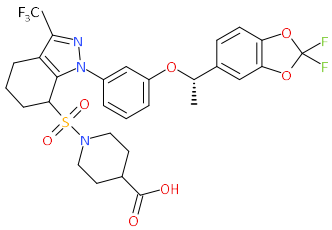
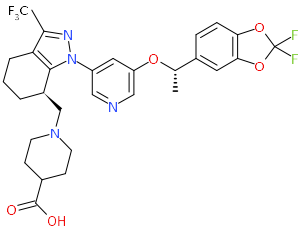
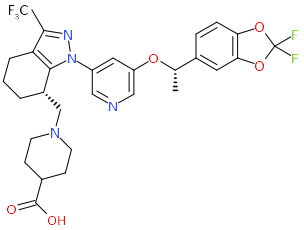
101 (P1)		3-[[(7S)-1-[6-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-5-fluoro-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
101 (P2)		3-[[(7R)-1-[6-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-5-fluoro-2-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
102 (P1)		3-[3-[[(7S)-1-[3-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-4-fluoro-phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]-1-bicyclo[1.1.1]pentanyl]-2H-1,2,4-oxadiazol-5-one
102 (P2)		3-[3-[[(7R)-1-[3-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-4-fluoro-phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]-1-bicyclo[1.1.1]pentanyl]-2H-1,2,4-oxadiazol-5-one
103 (P1)		3-[3-[[(7S)-1-[4-fluoro-3-[[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethyl]amino]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]-1-bicyclo[1.1.1]pentanyl]-2H-1,2,4-oxadiazol-5-one
103 (P2)		3-[3-[[(7R)-1-[4-fluoro-3-[[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethyl]amino]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]-1-bicyclo[1.1.1]pentanyl]-2H-1,2,4-oxadiazol-5-one

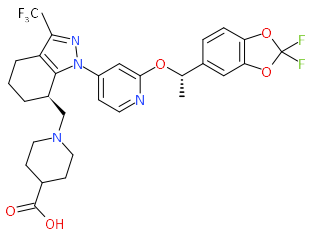
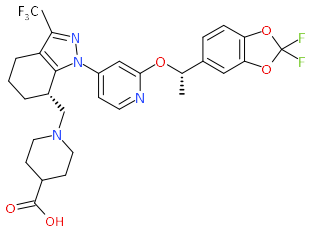
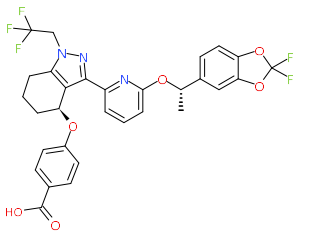
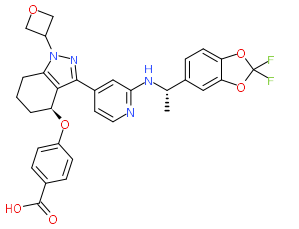
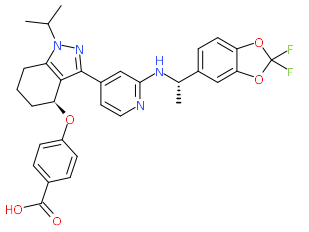
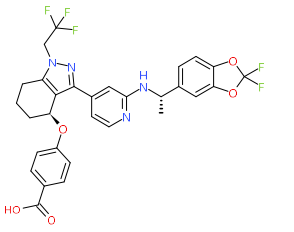
104		4-[[(7S)-3-cyano-1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-fluoro-phenyl]-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
105 (P1)		3-[[(7S)-3-cyano-1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-fluoro-phenyl]-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
105 (P2)		3-[[(7R)-3-cyano-1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-fluoro-phenyl]-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
106 (P1)		3-[[(7S)-3-cyano-1-[3-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-4-fluoro-phenyl]-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
106 (P2)		3-[[(7R)-3-cyano-1-[3-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-4-fluoro-phenyl]-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
107 (P1)		3-[[(7S)-3-cyano-1-[4-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-5-fluoro-2-pyridyl]-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid

107 (P2)		3-[[(7R)-3-cyano-1-[4-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-5-fluoro-2-pyridyl]-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
108 (P1)		3-[[(7S)-3-cyano-1-[6-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-5-fluoro-2-pyridyl]-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
108 (P2)		3-[[(7R)-3-cyano-1-[6-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-5-fluoro-2-pyridyl]-4,5,6,7-tetrahydroindazol-7-yl]oxy]bicyclo[1.1.1]pentane-1-carboxylic acid
109		4-[[(7S)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]amino]benzoic acid
110		4-[[(7S)-1-[2-[(1S)-1-(2,2,6-trifluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]amino]benzoic acid
111		3-[4-[[(7S)-1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-fluoro-phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]phenyl]-2H-1,2,4-oxadiazol-5-one

112		3-[4-[[(7S)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]phenyl]-2H-1,2,4-oxadiazol-5-one
113		3-[[(7R)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]carbamoyl]bicyclo[1.1.1]pentane-1-carboxylic acid
114		4-[[(7S)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]carbamoyl]benzoic acid
115 (P1)		4-[[(7S)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-5-methyl-3-(trifluoromethyl)-6,7-dihydro-4H-pyrazolo[4,3-c]pyridin-7-yl]oxy]benzoic acid
115 (P2)		4-[[(7R)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-5-methyl-3-(trifluoromethyl)-6,7-dihydro-4H-pyrazolo[4,3-c]pyridin-7-yl]oxy]benzoic acid
116		4-[[1-[3-[1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethylsulfanyl]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid

117		4-[[1-[3-[1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethylsulfinyl]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
118		4-[[1-[3-[1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethylsulfonyl]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
119		4-[[1-[2-[3-[1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]oxetan-3-yl]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]oxy]benzoic acid
120 (P1)		1-[(7S)-1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazole-7-carbonyl]piperidine-4-carboxylic acid
120 (P2)		1-[(7R)-1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazole-7-carbonyl]piperidine-4-carboxylic acid
121 (P1)		1-[(7S)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazole-7-carbonyl]piperidine-4-carboxylic acid

121 (P2)		1-[(7R)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazole-7-carbonyl]piperidine-4-carboxylic acid
122 (P1)		1-[(7S)-1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazole-7-carbonyl]piperidine-4-carboxylic acid
122 (P2)		1-[(7R)-1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazole-7-carbonyl]piperidine-4-carboxylic acid
123		1-[[1-[3-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]phenyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]sulfonyl]piperidine-4-carboxylic acid
124 (P1)		1-[[(7R)-1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]methyl]piperidine-4-carboxylic acid
124 (P2)		1-[[(7S)-1-[5-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-3-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]methyl]piperidine-4-carboxylic acid

125 (P1)		1-[[(7R)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]methyl]piperidine-4-carboxylic acid
125 (P2)		1-[[(7S)-1-[2-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-4-pyridyl]-3-(trifluoromethyl)-4,5,6,7-tetrahydroindazol-7-yl]methyl]piperidine-4-carboxylic acid
126		4-[[(4S)-3-[6-[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethoxy]-2-pyridyl]-1-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydroindazol-4-yl]oxy]benzoic acid
127		4-[[(4S)-3-[2-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-4-pyridyl]-1-(oxetan-3-yl)-4,5,6,7-tetrahydroindazol-4-yl]oxy]benzoic acid
128		4-[[(4S)-3-[2-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-4-pyridyl]-1-isopropyl-4,5,6,7-tetrahydroindazol-4-yl]oxy]benzoic acid
129		4-[[(4S)-3-[2-[[(1S)-1-(2,2-difluoro-1,3-benzodioxol-5-yl)ethyl]amino]-4-pyridyl]-1-(2,2,2-trifluoroethyl)-4,5,6,7-tetrahydroindazol-4-yl]oxy]benzoic acid

[009c] In one aspect, the present disclosure refers to a pharmaceutical composition comprising a compound disclosed herein and a pharmaceutically acceptable adjuvant.

[009d] In one aspect, the present disclosure refers to a method of treating a CFTR-mediated disease or disorder comprising administering a patient in need there of a compound disclosed herein or a pharmaceutical composition disclosed herein.

[009e] In one aspect, the present disclosure refers to a method of treating cystic fibrosis in a subject, comprising administering to the subject a therapeutically effective amount of a compound disclosed herein or a pharmaceutical composition disclosed herein.