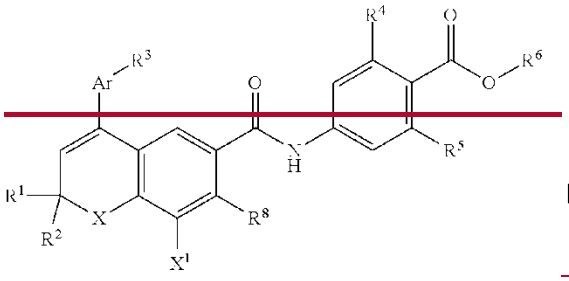
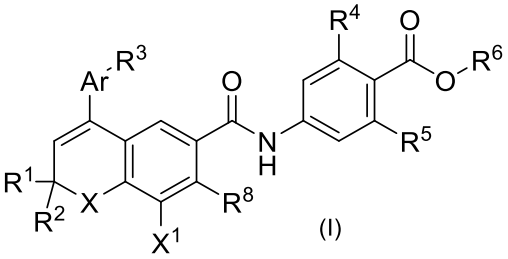
a) a RARα antagonist, wherein the RARα antagonist is:

i) a compound of general formula (I)

(I)

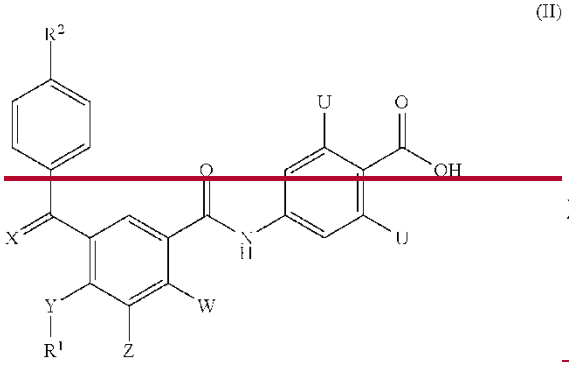


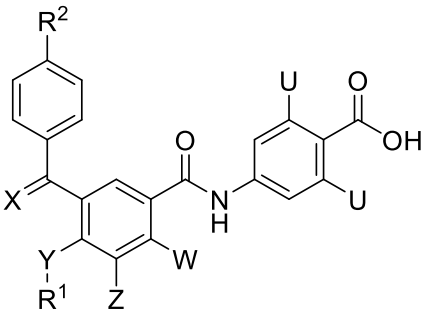


wherein R^1, R^2, R^3, and R^6 are independently H or C_{1-6} alkyl; R^4 and R^5 are independently H or F; Ar is phenyl, pyridyl, thienyl, furyl, or naphthyl; X is $C(CH_3)_2$, O, S, or NR^7, wherein R^7 is H or C_{1-6} alkyl; X^1 is H or halogen such as F, Cl or Br; and R^8 is H or OH; or

ii) a compound of general formula (II)

(II)

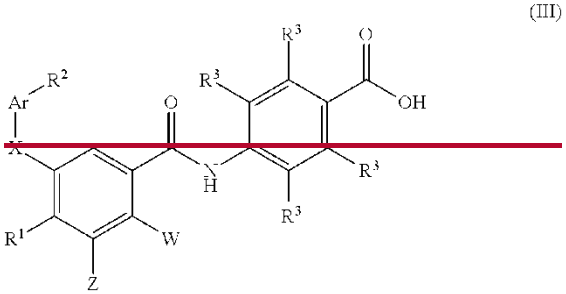


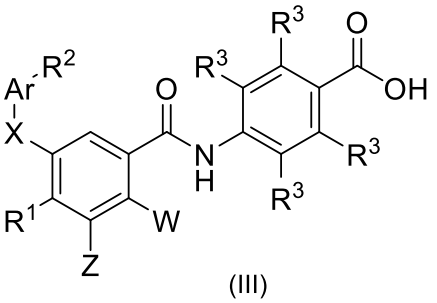


wherein R^1 and R^2 are independently C_{1-6} alkyl; X is O, S, or CH_2; Y is O, S, CH_2, or NR^3, wherein R^3 is C_{1-6}; Z is Cl or Br; W is H or OH; and U is independently H or F; or

iii) a compound of general formula (III):

(III)





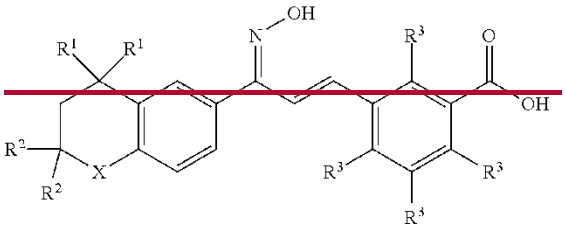
wherein R^1 and R^2 are independently H or C_{1-6} alkyl; R^3 is H or F; Ar is phenyl, pyridyl, thienyl, furyl, or naphthyl; X is O, S, N, or CH_2; W is H or OH; and Z is Cl or Br; or

iv) BMS185411, BMS614, Ro41-5253, Ro46-5471, or AGN 194777; or

b) a RARγ selective agonist, wherein the RARγ selective agonist is:

~~i) a compound of general formula (IV):~~

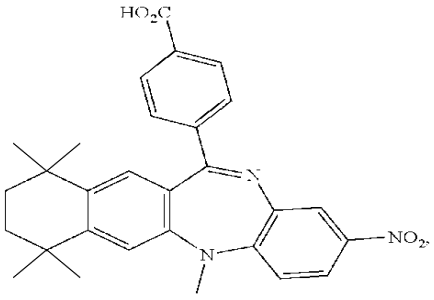
(IV)



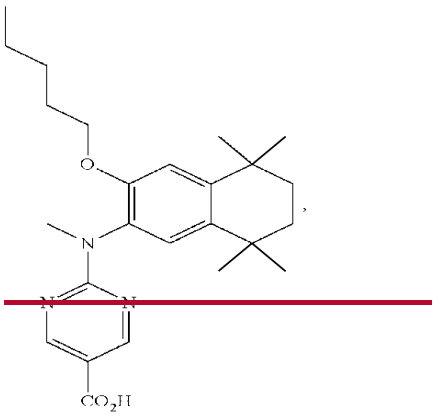
~~wherein R^1 and R^2 are independently H or C_{1-6} alkyl; R^3 is H or F; and X is O, S, CH_2, $C(R^4)_2$, or NR^5, wherein R^4 and R^5 are independently H or C_{1-6} alkyl; or~~

~~ii)~~ CD437, CD2325, CD666, or BMS961; or

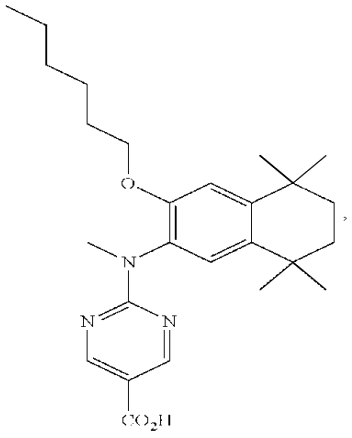
c) a RXR antagonist, wherein the RXR antagonist is: AGN195393, LGN100849,



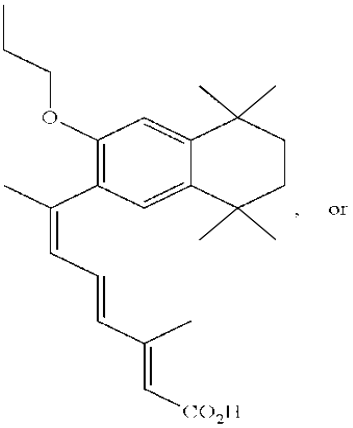
HX 531



PA 451

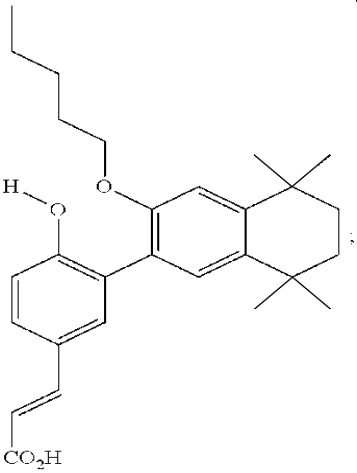


PA 452

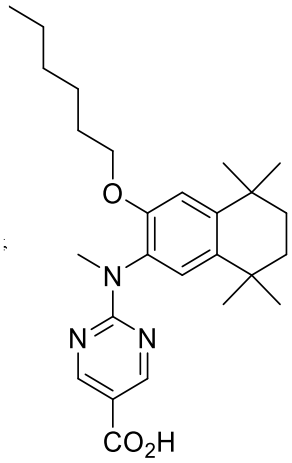


, or

LG 100754

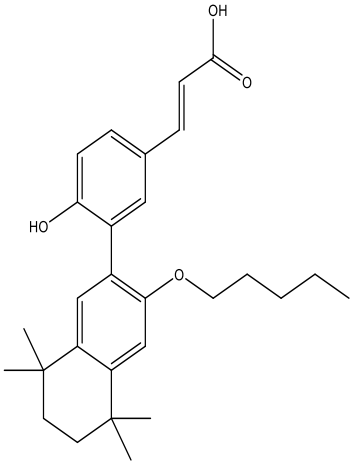


UVI 3003



PA 452

, or

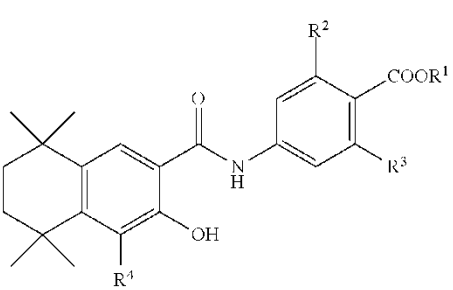


UVI 3003

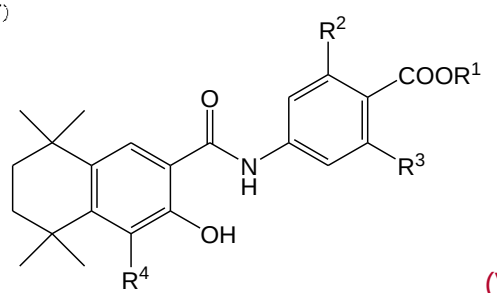
or

d) a combination thereof; and

wherein the differentiating RAR active agent is a CYP26-resistant RARα agonist, wherein the RARα agonist is a compound of general formula (V):



(V)



(V)

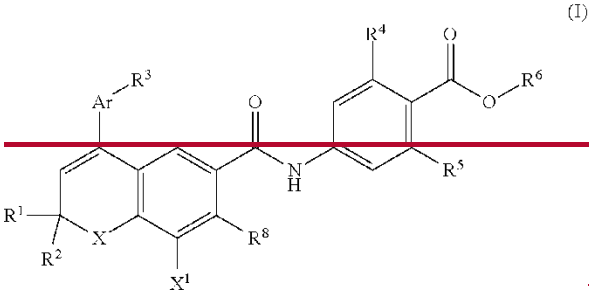
wherein R^1 is H or C_{1-6} alkyl, R^2 and R^3 are independently H or F, and R^4 is a halogen.

~~**[0010b]** In another aspect, provided herein is a use of an immunomodulatory retinoid active agent and/or rexinoid active agent (RAR/RXR active agent) in the manufacture of a medicament for potentiating chimeric antigen receptor-modified immune cells (CAR-MIC) cancer immunotherapy, wherein the RAR/RXR active agent is to be administered to a cancer patient who is receiving, has received, or is scheduled to receive, CAR-MIC, and wherein the RAR/RXR active agent is to be administered with a differentiating RAR active agent, wherein the RAR/RXR active agent and differentiating RAR active agent are not to be administered at the same time, wherein the immunomodulatory RAR/RXR active agent is:~~

~~a) a RARα antagonist, wherein the RARα antagonist is:~~

~~i) a compound of general formula (I)~~

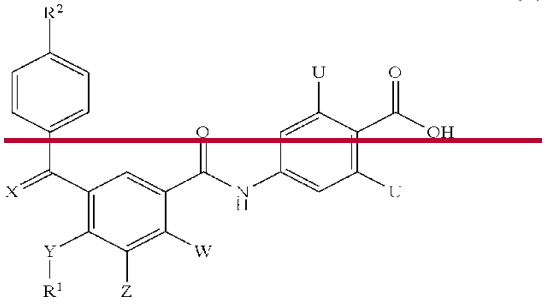
~~(I)~~



~~wherein R^1, R^2, R^3, and R^6 are independently H or C_{1-6} alkyl; R^4 and R^5 are independently H or F; Ar is phenyl, pyridyl, thienyl, furyl, or naphthyl; X is $C(CH_3)_2$, O, S, or NR^7, wherein R^7 is H or C_{1-6} alkyl; X^1 is H or halogen such as F, Cl or Br; and R^8 is H or OH; or~~

~~ii) a compound of general formula (II)~~

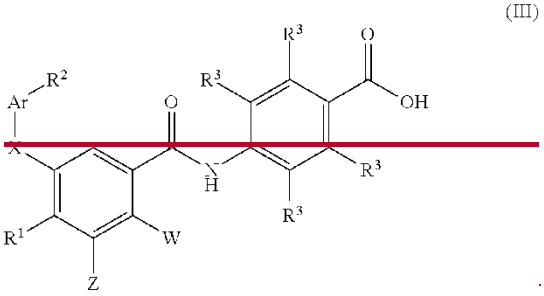
~~(II)~~



wherein R^1 and R^2 are independently C_{1-6} alkyl; X is O, S, or CH_2; Y is O, S, CH_2, or NR^3, wherein R^3 is C_{1-6} alkyl; Z is Cl or Br; W is H or OH; and U is independently H or F; or

iii) a compound of general formula (III):

(III)



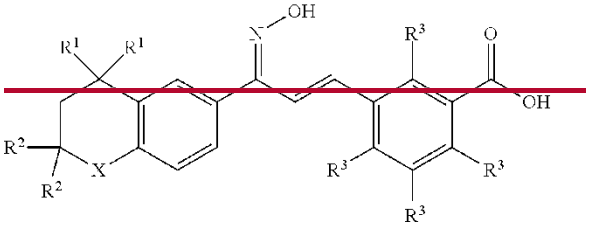
wherein R^1 and R^2 are independently H or C_{1-6} alkyl; R^3 is H or F; Ar is phenyl, pyridyl, thienyl, furyl, or naphthyl; X is O, S, N, or CH_2; W is H or OH; and Z is Cl or Br; or

iv) BMS185411, BMS614, Ro41-5253, Ro46-5471, or AGN 194777; or

b) a RARγ selective agonist, wherein the RARγ selective agonist is:

i) a compound of general formula (IV):

(IV)

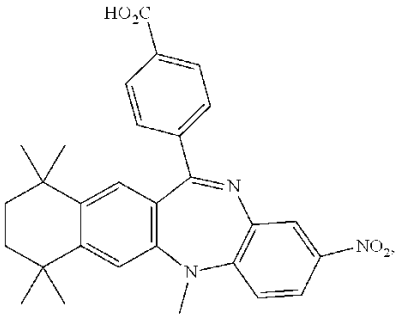


wherein R^1 and R^2 are independently H or C_{1-6} alkyl; R^3 is H or F; and X is O, S, CH_2, $C(R^4)_2$, or NR^5, wherein R^4 and R^5 are independently H or C_{1-6} alkyl; or

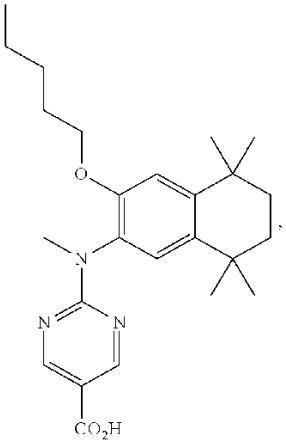
ii) CD437, CD2325, CD666, or BMS961; or

c) a RXR antagonist, wherein the RXR antagonist is:

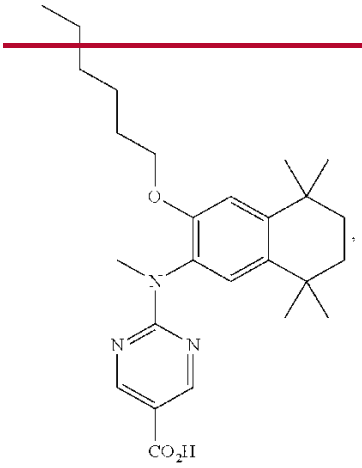
AGN195393, LGN100849,



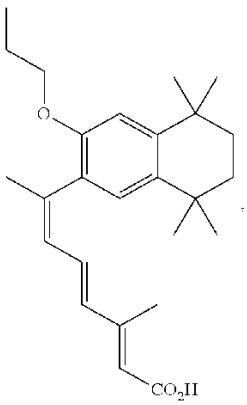
HX 531



PA 451

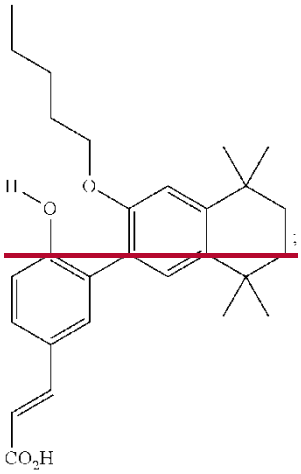


PA 452



or

LG 100754



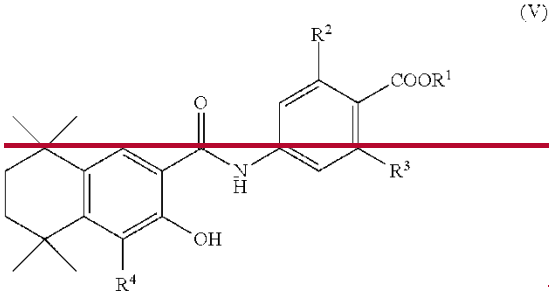
UVI 3003

or

d) a combination thereof; and

wherein the differentiating RAR active agent is a CYP26-resistant RARα agonist, wherein the RARα agonist is a compound of general formula (V):

(V)



wherein R^1 is H or C_{1-6} alky, R^2 and R^3 are independently H or F, and R^4 is a halogen.

[0011] In some embodiments, the retinoid active agent is a RARα antagonist. In some embodiments, the RARα antagonist is a compound of general formula (I):

What is claimed is:

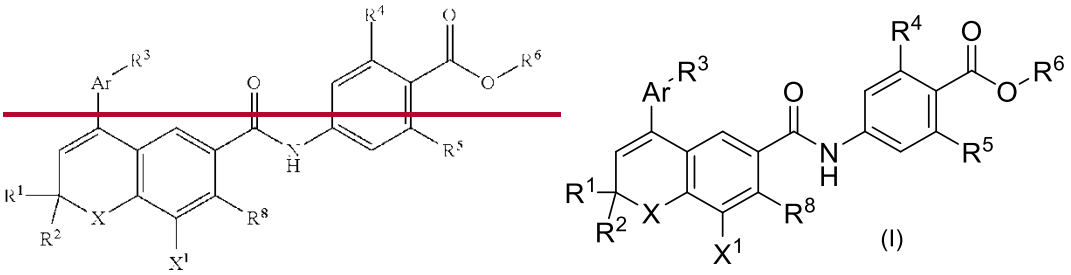
1. Use of an immunomodulatory retinoid active agent and/or rexinoid active agent (RAR/RXR active agent) in the manufacture of a medicament for cancer immunotherapy, wherein the RAR/RXR active agent is to be administered to a subject in need thereof, and wherein the RAR/RXR active agent is to be administered with chimeric antigen receptor-modified immune cells (CAR-MIC) and a differentiating RAR active agent, wherein the RAR/RXR active agent and differentiating RAR active agent are not to be administered at the same time,

wherein the immunomodulatory RAR/RXR active agent is:

a) a RARα antagonist, wherein the RARα antagonist is:

i) a compound of general formula (I)

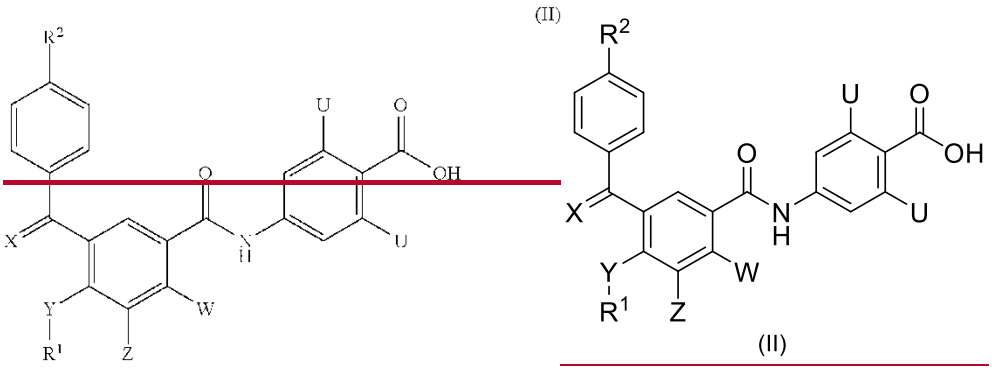
(I)



wherein R^1, R^2, R^3, and R^6 are independently H or $C_{1\text{-}6}$ alkyl; R^4 and R^5 are independently H or F; Ar is phenyl, pyridyl, thienyl, furyl, or naphthyl; X is $C(CH_3)_2$, O, S, or NR^7, wherein R^7 is H or $C_{1\text{-}6}$ alkyl; X^1 is H or halogen such as F, Cl or Br; and R^8 is H or OH; or

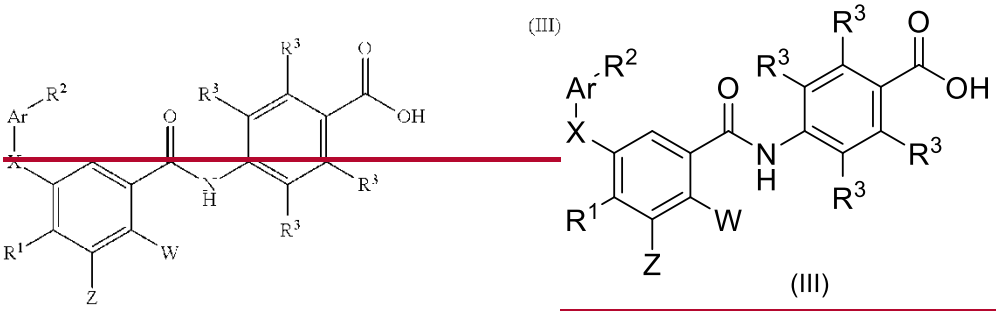
ii) a compound of general formula (II)

(II)



wherein R^1 and R^2 are independently $C_{1\text{-}6}$ alkyl; X is O, S, or CH_2; Y is O, S, CH_2, or NR^3, wherein R^3 is $C_{1\text{-}6}$; Z is Cl or Br; W is H or OH; and U is independently H or F; or

iii) a compound of general formula (III):



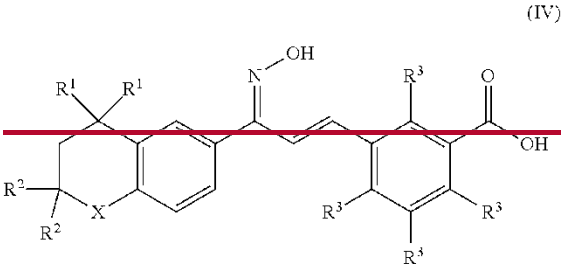
(III)

wherein R^1 and R^2 are independently H or C_{1-6} alkyl; R^3 is H or F; Ar is phenyl, pyridyl, thienyl, furyl, or naphthyl; X is O, S, N, or CH_2; W is H or OH; and Z is Cl or Br; or

iv) BMS185411, BMS614, Ro41-5253, Ro46-5471, or AGN 194777; or

b) a RARγ selective agonist, wherein the RARγ selective agonist is:

~~i) a compound of general formula (IV):~~

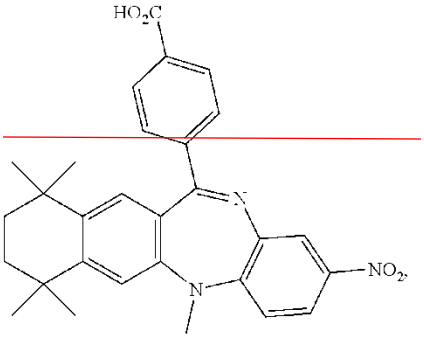


(IV)

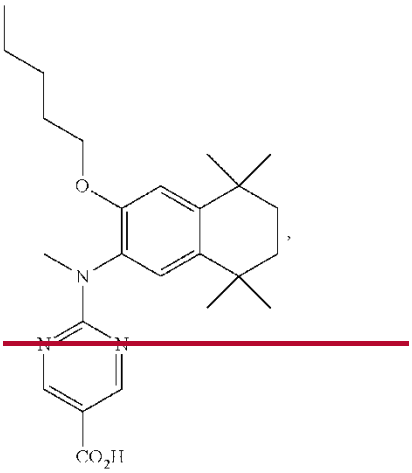
~~wherein R^1 and R^2 are independently H or C_{1-6} alkyl; R^3 is H or F; and X is O, S, CH_2, $C(R^4)_2$, or NR^5, wherein R^4 and R^5 are independently H or C_{1-6} alkyl; or~~

~~ii)~~ CD437, CD2325, CD666, or BMS961; or

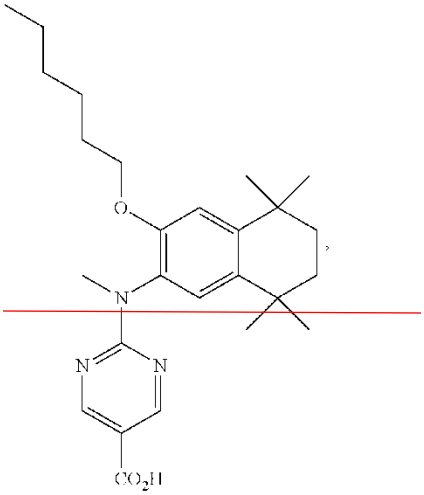
c) a RXR antagonist, wherein the RXR antagonist is: AGN195393, LGN100849,



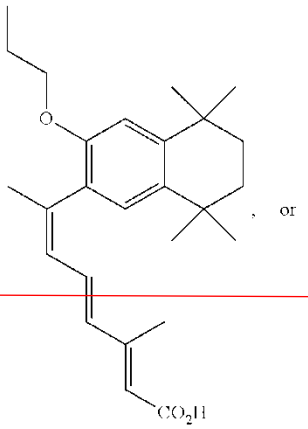
HX 531



PA 451

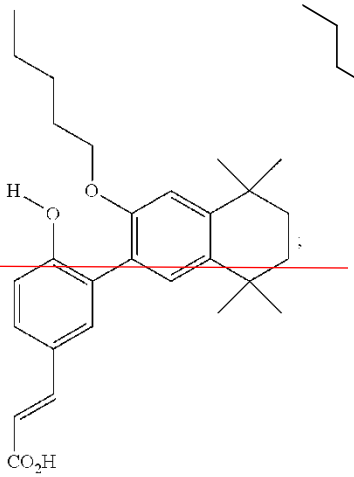


PA 452

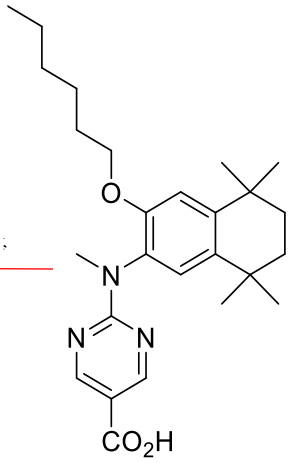


, or

LG 100754

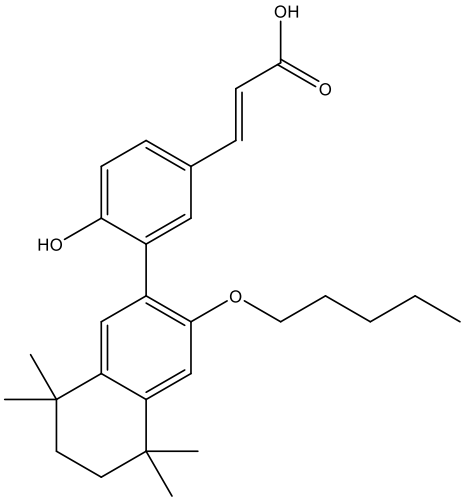


UVI 3003



PA 452

, or

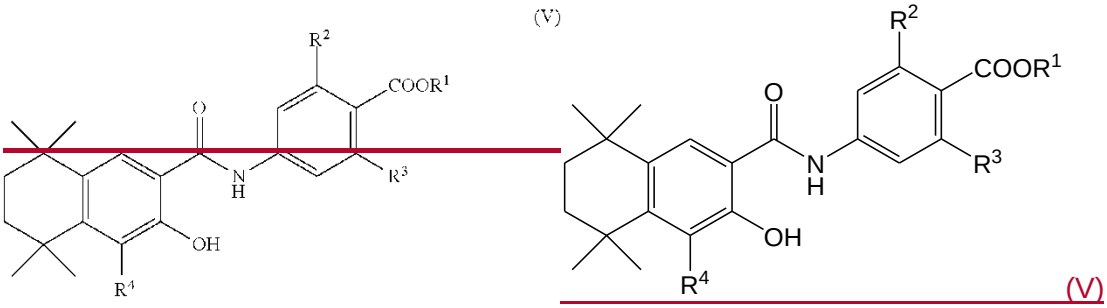


UVI 3003

or

d) a combination thereof; and

wherein the differentiating RAR active agent is a CYP26-resistant RARα agonist, wherein the RARα agonist is a compound of general formula (V):



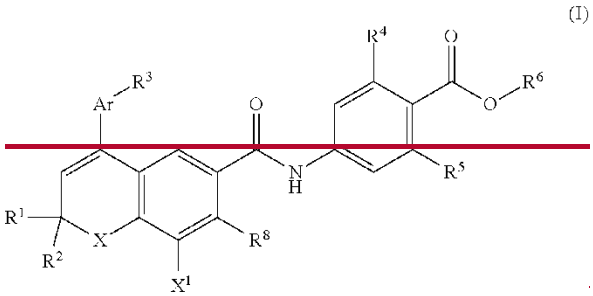
(V)

wherein R^1 is H or C_{1-6} alkyl, R^2 and R^3 are independently H or F, and R^4 is a halogen.

2. Use of an immunomodulatory retinoid active agent and/or rexinoid active agent (RAR/RXR active agent) in the manufacture of a medicament for potentiating chimeric antigen receptor-modified immune cells (CAR-MIC) cancer immunotherapy, wherein the RAR/RXR active agent is to be administered to a cancer patient who is receiving, has received, or is scheduled to receive, CAR-MIC, and wherein the RAR/RXR active agent is to be administered with a differentiating RAR active agent, wherein the RAR/RXR active agent and differentiating RAR active agent are not to be administered at the same time, wherein the immunomodulatory RAR/RXR active agent is:

a) a RARα antagonist, wherein the RARα antagonist is:

i) a compound of general formula (I)

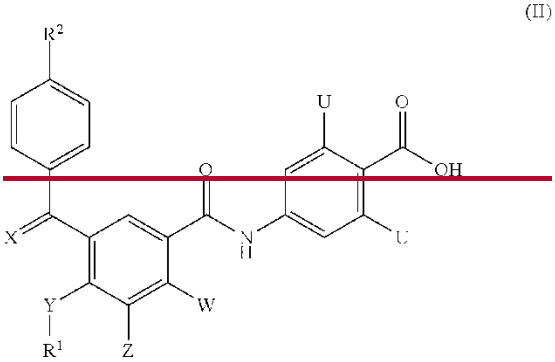


(I)

wherein R^1, R^2, R^3, and R^6 are independently H or C_{1-6} alkyl; R^4 and R^5 are independently H or F; Ar is phenyl, pyridyl, thienyl, furyl, or naphthyl; X is $C(CH_3)_2$, O, S, or NR^7, wherein R^7 is H or C_{1-6} alkyl; X^1 is H or halogen such as F, Cl or Br; and R^8 is H or OH; or

ii) a compound of general formula (II)

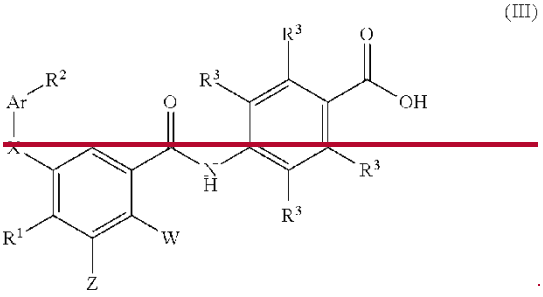
(II)



wherein R^1 and R^2 are independently C_{1-6} alkyl; X is O, S, or CH_2; Y is O, S, CH_2, or NR^3, wherein R^3 is C_{1-6} alkyl; Z is Cl or Br; W is H or OH; and U is independently H or F; or

iii) a compound of general formula (III):

(III)



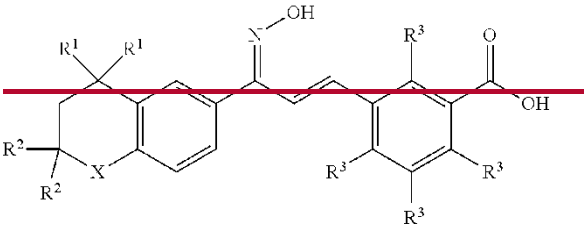
wherein R^1 and R^2 are independently H or C_{1-6} alkyl; R^3 is H or F; Ar is phenyl, pyridyl, thienyl, furyl, or naphthyl; X is O, S, N, or CH_2; W is H or OH; and Z is Cl or Br; or

iv) BMS185411, BMS614, Ro41-5253, Ro46-5471, or AGN 194777; or

b) a RARγ selective agonist, wherein the RARγ selective agonist is:

i) a compound of general formula (IV):

(IV)

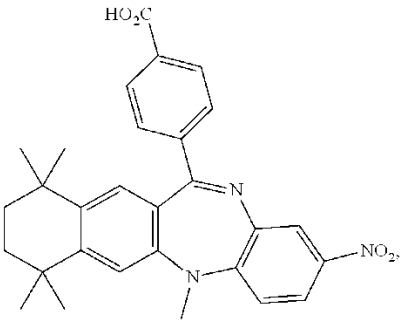


wherein R^1 and R^2 are independently H or C_{1-6} alkyl; R^3 is H or F; and X is O, S, CH_2, $C(R^4)_2$, or NR^5, wherein R^4 and R^5 are independently H or C_{1-6} alkyl; or

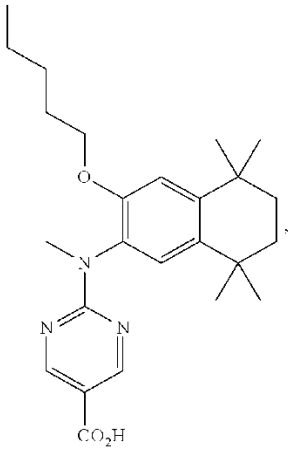
ii) CD437, CD2325, CD666, or BMS961; or

c) a RXR antagonist, wherein the RXR antagonist is:

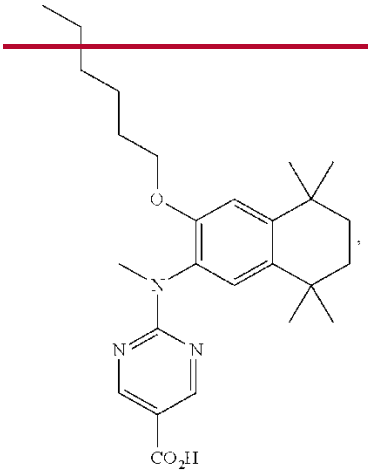
AGN195393, LGN100849,



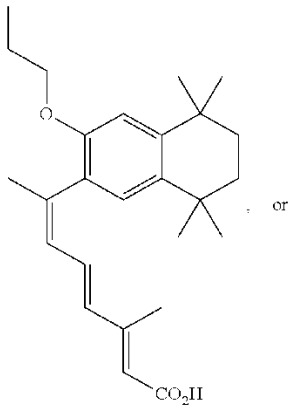
HX 531



PA 451

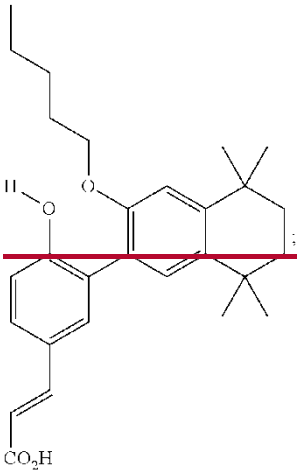


PA 452



or

LG 100754

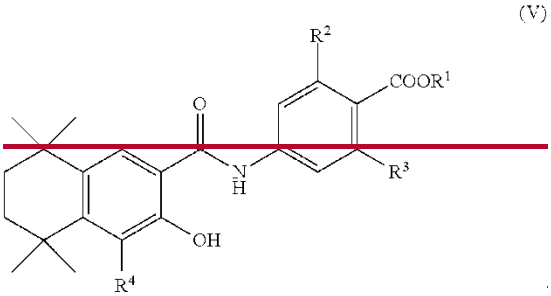


UVI 3003

or

d) a combination thereof; and

wherein the differentiating RAR active agent is a CYP26-resistant RARα agonist, wherein the RARα agonist is a compound of general formula (V):



(V)

wherein R^1 is H or C_{1-6} alky, R^2 and R^3 are independently H or F, and R^4 is a halogen.

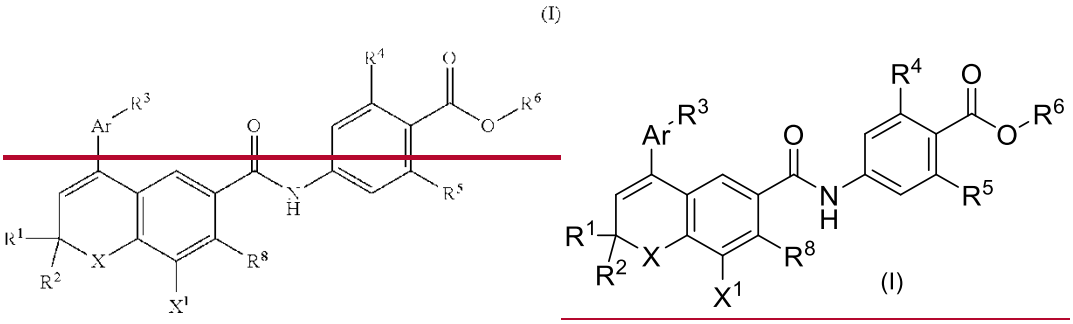
23. The use of claim 1 or 2, wherein the CAR-MIC are cultured in a culture medium comprising an immunomodulatory RAR/RXR active agent prior to administration to the subject or cancer patient.

34. The use of claim 1 or 2, wherein an immune checkpoint inhibitor that is an inhibitor of at least one of CTLA-4, PD-1, TIM-3, LAG-3, PD-L1 ligand, B7-H3, B7-H4, BTLA, or is an ICOS, or OX40 agonist is to be further administered, wherein the immune checkpoint inhibitor is an antibody.

45. The use of claim 1 or 2, wherein the immunomodulatory RAR/RXR active agent comprises at least two RAR active agents.

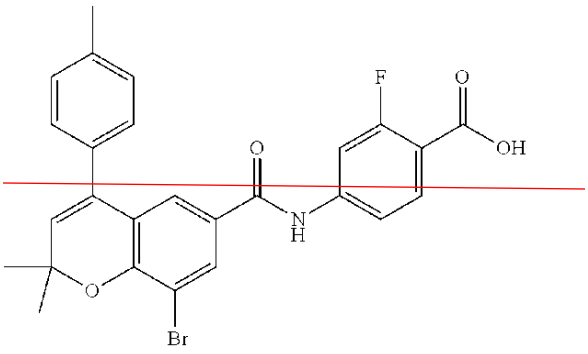
56. The use of claim 45, wherein a first RAR active agent is a RARα antagonist, and a second RAR active agent is a RARγ selective agonist, or wherein a first RAR active agent is a RARα selective antagonist, and a second RAR active agent is a RARγ agonist.

67. The use of claim 1 or 2, wherein the RARα antagonist is a compound of general formula (I)

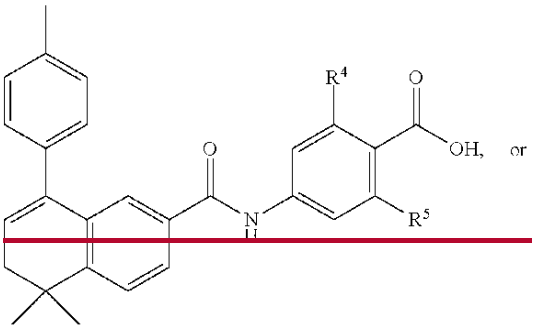


wherein R^1, R^2, R^3, and R^6 are independently H or C_{1-6} alkyl; R^4 and R^5 are independently H or F; Ar is phenyl, pyridyl, thienyl, furyl, or naphthyl; X is $C(CH_3)_2$, O, S, or NR^7, wherein R^7 is H or C_{1-6} alkyl; X^1 is H or halogen such as F, Cl or Br; and R^8 is H or OH.

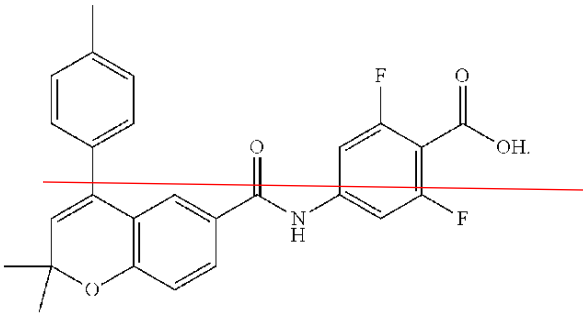
78. The method of claim 76, wherein the RARα antagonist is:



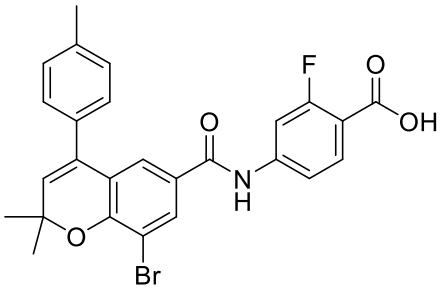
AGN 194301



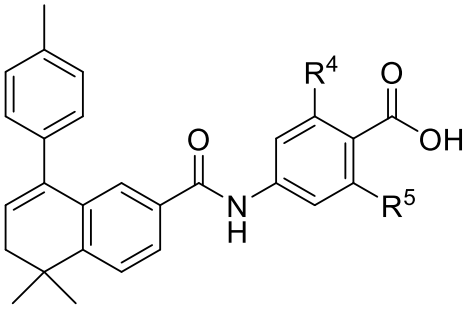
R^4 and R^5 both H; AGN193491
R^4 – F, R^5 – H; AGN193618
R^4 and R^5 both F; AGN194202



AGN
194574

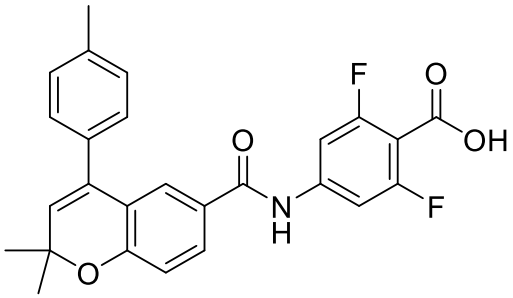


AGN 194301



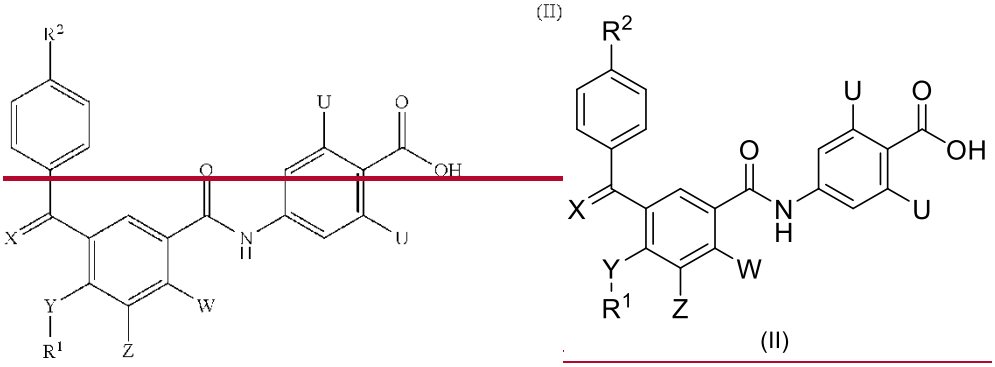
R^4 and R^5 both H; AGN193491
R^4 = F, R^5 = H; AGN193618
R^4 and R^5 both F; AGN194202

, or



AGN 194574

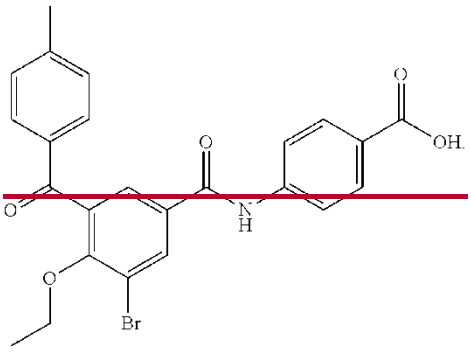
8~~9~~. The use of claim 1 ~~or 2~~, wherein the RARα antagonist is a compound of general formula (II)



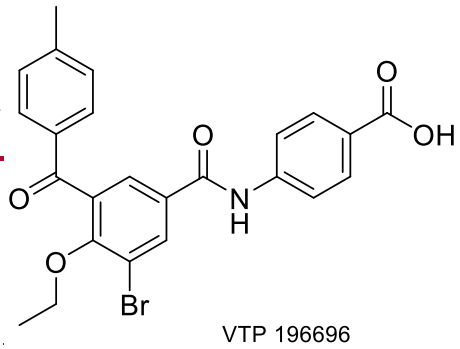
(II)

wherein R^1 and R^2 are independently C_{1-6} alkyl; X is O, S, or CH_2; Y is O, S, CH_2, or NR^3, wherein R^3 is C_{1-6}; Z is Cl or Br; W is H or OH; and U is independently H or F.

9~~10~~. The use of claim ~~98~~, wherein the RARα antagonist is:

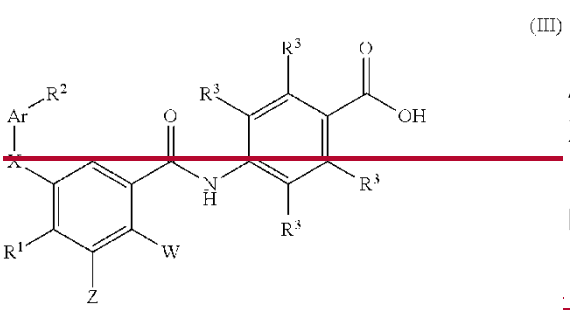


VTP 196696

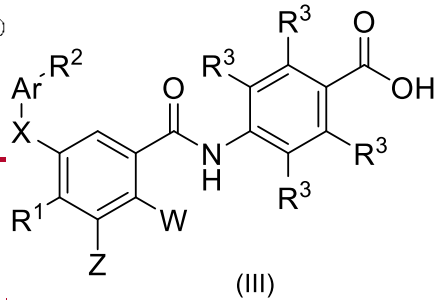


VTP 196696

10~~11~~. The use of ~~claim~~ claim 1, wherein the RARα antagonist is a compound of general formula (III):



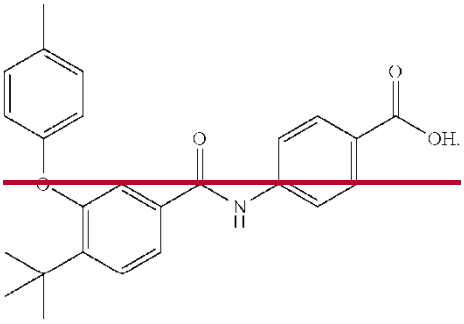
(III)



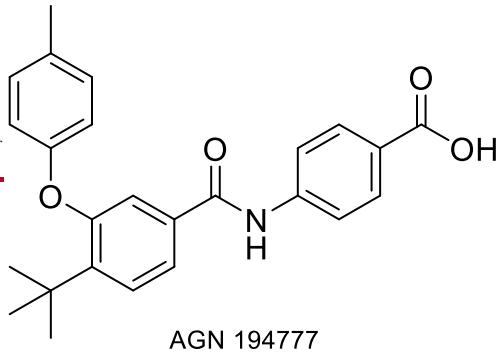
(III)

wherein R^1 and R^2 are independently H or $C_{1\text{-}6}$ alkyl; R^3 is H or F; Ar is phenyl, pyridyl, thienyl, furyl, or naphthyl; X is O, S, N, or CH_2; W is H or OH; and Z is Cl or Br.

1~~2~~1. The use of ~~claim~~ claim 1 ~~or 2~~, wherein the RARα antagonist is BMS185411, BMS614, Ro41-5253, Ro46-5471, or



AGN 194777

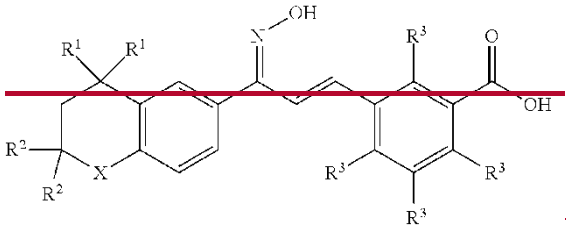


AGN 194777

1~~3~~2. The use of ~~claim~~ claim 1 ~~or 2~~, wherein the RARγ selective agonist is: selected from CD437, CD2325, CD666, and BMS961.

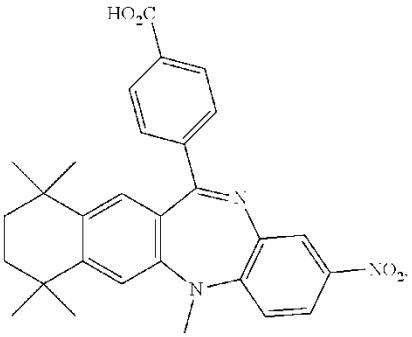
~~14. The use of claim 1 or 2, wherein the RARγ agonist is a RARγ agonist of general formula IV~~

~~(IV)~~

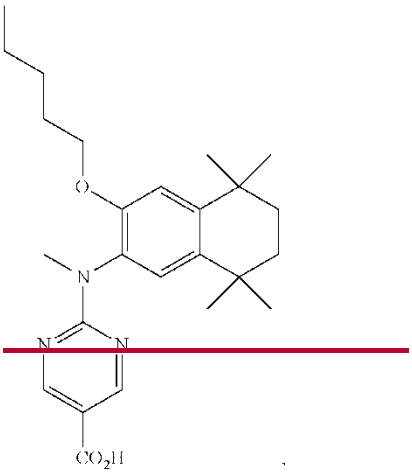


~~wherein R^1 and R^2 are independently H or C_{1-6} alkyl; R^3 is H or F; and X is O, S, CH_2, $C(R^4)_2$, or NR^5, wherein R^4 and R^5 are independently H or C_{1-6} alkyl.~~

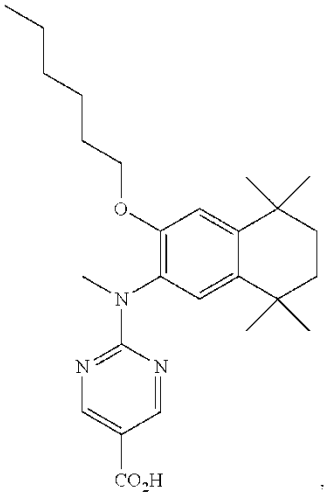
13~~15~~. The use of ~~-~~claim 1 ~~or 2~~, wherein the RXR antagonist is selected from AGN195393, LGN100849,



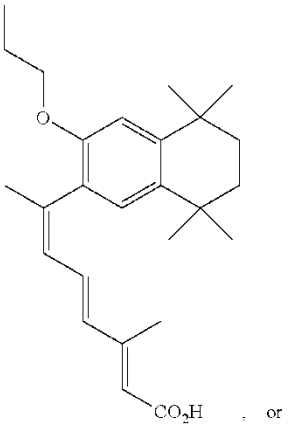
HX 531



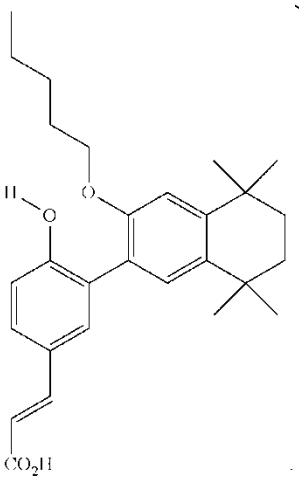
PA 451



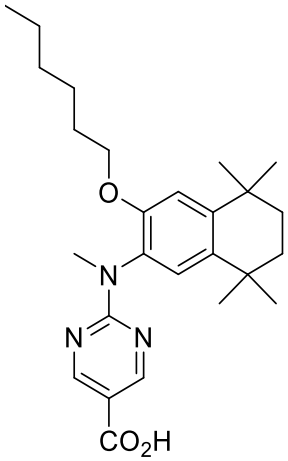
PA 452



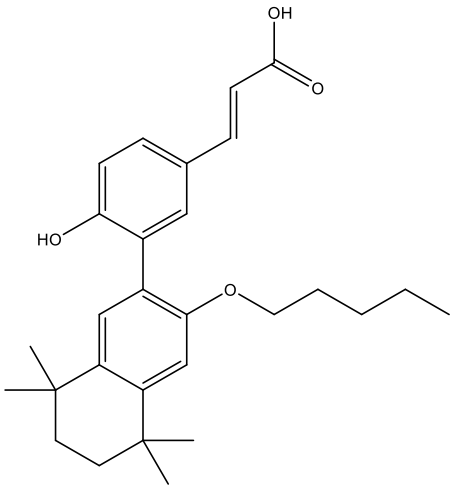
LG 100754 . or



UVI 3003

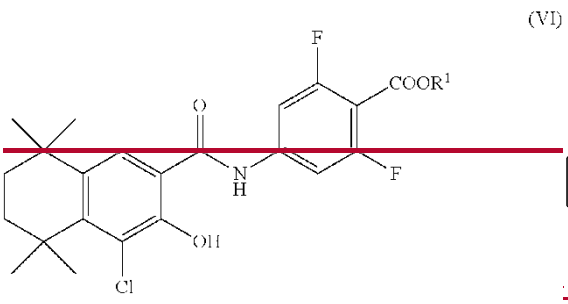


PA 452 , or

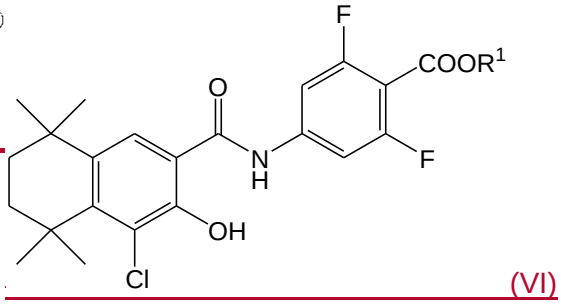


UVI 3003

1416. The use of claim 1 ~~or 2~~, wherein the RARα agonist is a compound of general formula (VI):



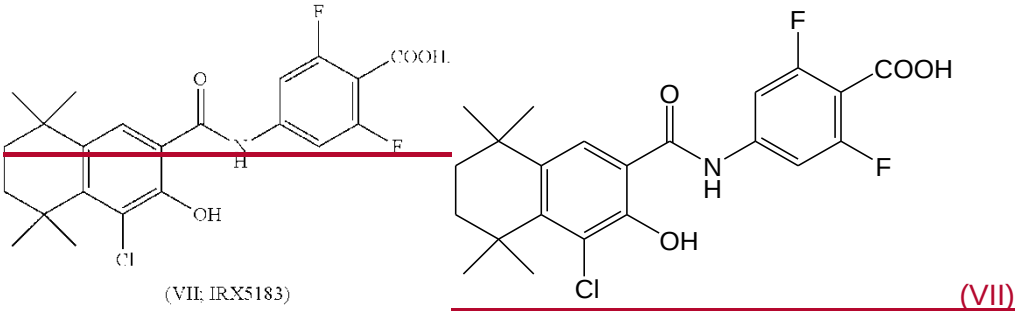
(VI)



(VI)

wherein R^1 is H or C_{1-6} alkyl.

1517. The use of claim 146, wherein the RARα agonist is a compound of formula (VII):



(VII)

1618. The use of claim 1 or 2, wherein the CAR-MIC is a CAR-T cell.

1719. The use of claim 1 or 2, wherein the differentiating RAR active agent is to be administered for a period of time of 1 to 4 weeks, and its administration is to be discontinued 2-10 days, before administration of CAR-MIC is scheduled to begin.

1820. The use of claim 1 or 2, wherein the immunomodulatory RAR/RXR active agent is to be administered for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days before administration of CAR-MIC is scheduled to begin.

1921. The use of claim 1 or 2, wherein the immunomodulatory RAR/RXR active agent is to be administered subsequent to administration of the CAR-MIC, wherein administration of the immunomodulatory RAR/RXR active agent is to be suspended for a period of 1 to 3 weeks during which time a differentiating RAR active agent is to be administered, and administration of the immunomodulatory RAR/RXR active agent is to be resumed thereafter.