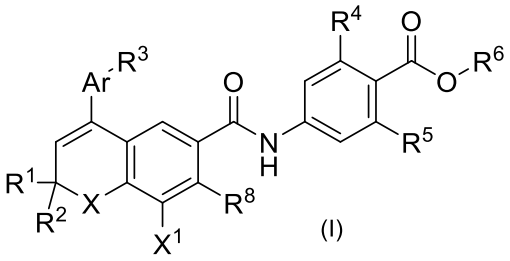
the same treatment session). In still other embodiments, the multiple RAR/RXR active agents are formulated together as a single, common medicament.

[0004a] In one aspect, there is provided a use of at least one retinoid active agent and/or rexinoid active agent (RAR/RXR active agent) in the preparation of a medicament for the treatment of cancer; wherein said medicament to be administered with chimeric antigen receptor (CAR)-modified immune cells, wherein the RAR/RXR active agent comprises a Retinoid X Receptor (RXR) active agent and wherein the RAR active agent is a RARα antagonist selected from

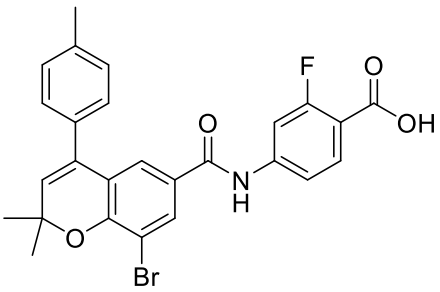
(a) a compound of general formula (I)



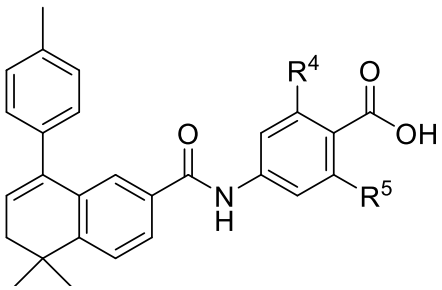
(I)

,

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

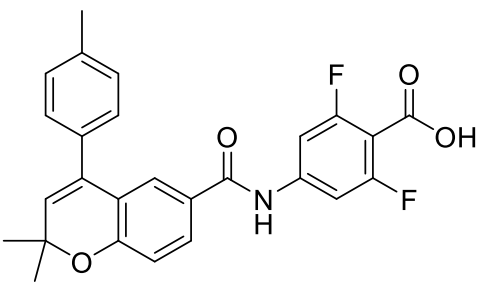


(b) AGN 194301



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

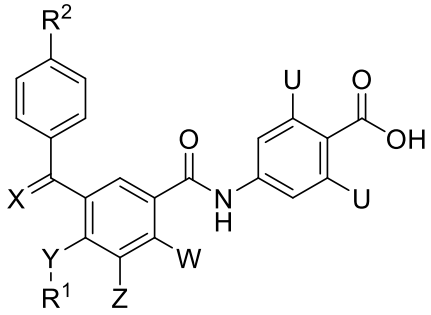
, or



AGN 194574

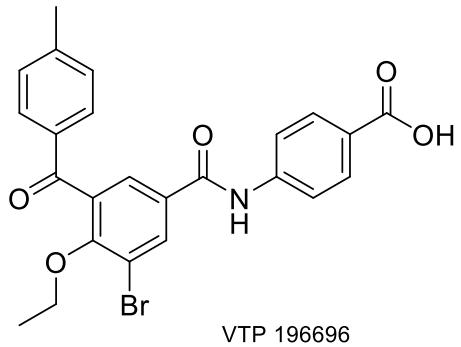
;

(c) a compound of general formula (II)



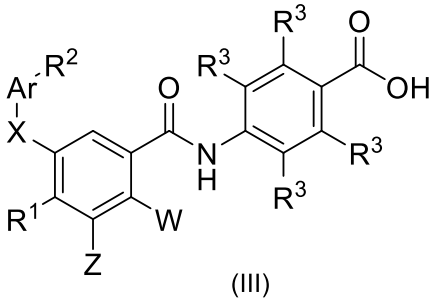
(II)

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;

(d) 

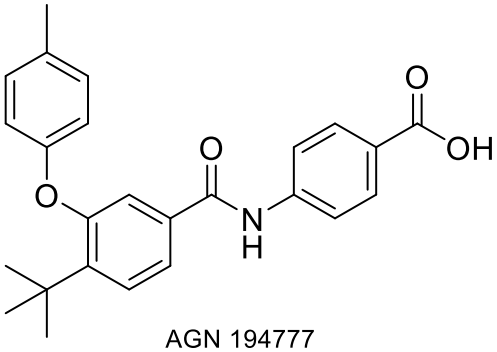
VTP 196696 ;

(e) a compound of general formula (III):



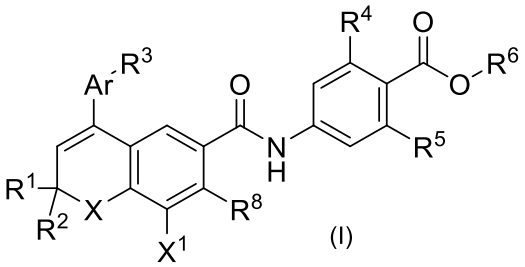
(III) ,

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; and

(f)  AGN 194777 , BMS185411, BMS614, Ro41-5253, or Ro46-5471.

[0005] In some embodiments, the CAR-modified immune cells are, or comprise, CAR-modified T cells. In some embodiments, the CAR-modified immune cells are, or comprise, CAR-modified NK cells. In some embodiments, the CAR-modified immune cells are, or comprise, CAR-modified NKT cells. In some embodiments, the CAR-modified immune cells are, or comprise, CAR-modified macrophages. Further embodiments can comprise mixtures of these cell types. Most typically such cellular preparations are administered by infusion, for example intravenous infusion. In contrast, the RAR/RXR active agents are small molecules that can be administered orally, for example as pills or capsules and the like. Thus the RAR/RXR active agents and the CAR-modified immune cells may be administered on independent schedules.

[0006] In some embodiments, the retinoid active agent is a RARα antagonist. In some embodiments, the RARα antagonist is a compound of general formula (I):

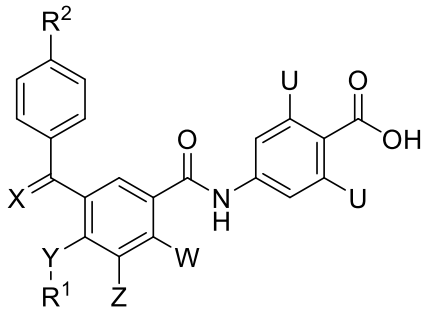

(I)

,

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.

[0007] In some embodiments, the RARα antagonist is AGN194301, AGN193491, AGN193618, AGN194202, or AGN194574.

[0008] In some embodiments, the RARα antagonist is a compound of general formula (II):

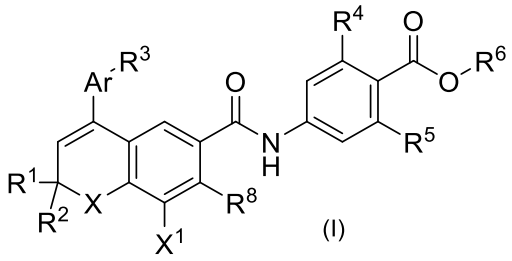


(II)

What is claimed is:

1. Use of at least one retinoid active agent and/or rexinoid active agent (RAR/RXR active agent) in the preparation of a medicament for the treatment of cancer; wherein said medicament is to be administered with chimeric antigen receptor (CAR)-modified immune cells, wherein the RAR/RXR active agent comprises a Retinoid X Receptor (RXR) active agent and wherein the RAR active agent is a RARα antagonist selected from:

(a) a compound of general formula (I)

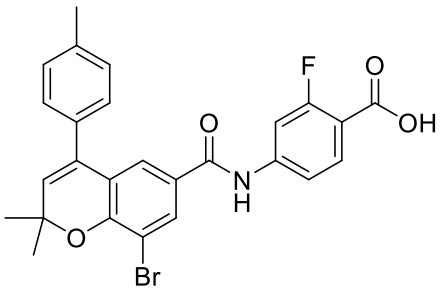


(I)

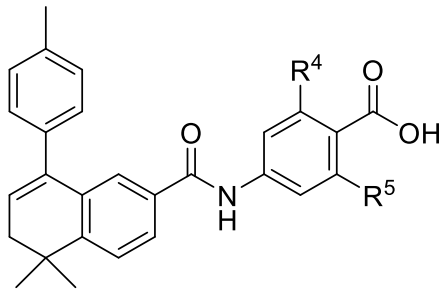
,

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;

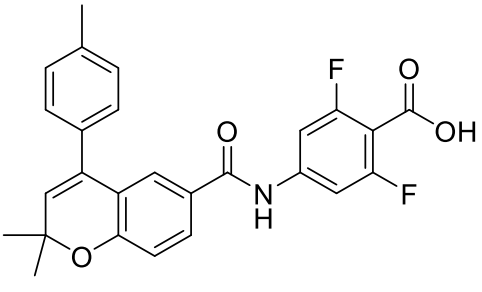
b)



AGN 194301



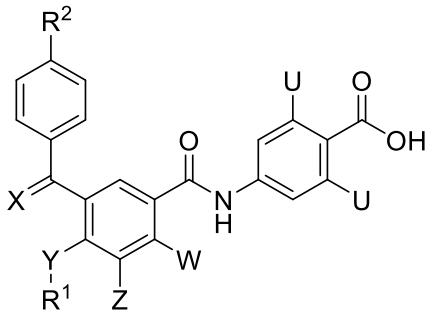
$R^4 = R^5$ = H; AGN 193491



AGN 194574

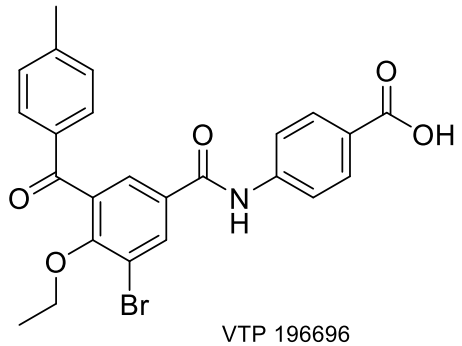
R^4 and R^5 both H; AGN193491
R^4 = F, R^5 = H; AGN193618 , or ;
R^4 and R^5 both F; AGN194202

(c) a compound of general formula (II)



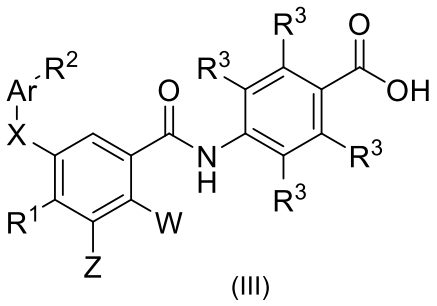
(II)

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;

(d) 

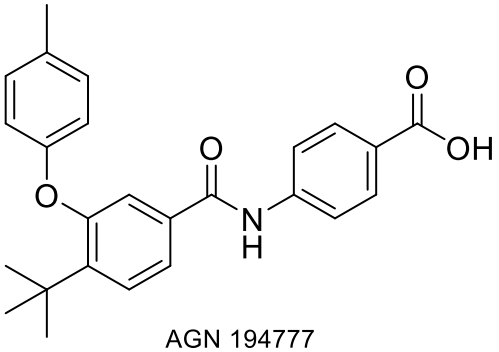
VTP 196696 ;

(e) a compound of general formula (III):



(III) ,

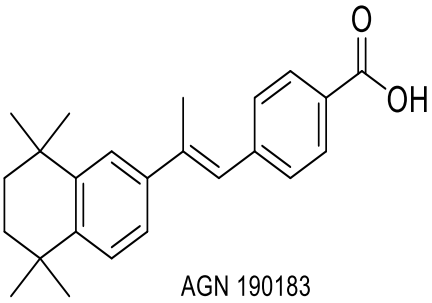
wherein R^1 and R^2 are independently H or C_{1-6} alkyl; R^3 is H or F; Ar is phenyl, pyridyl, thienyl, furyl, or naphthyl; X is O, S, N, or CH_2; W is H or OH; and Z is Cl or Br; and

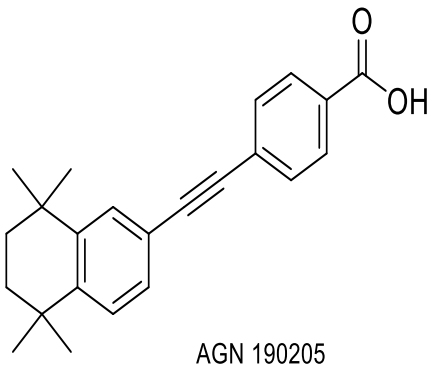
(f)  AGN 194777 , BMS185411, BMS614, Ro41-5253, or Ro46-5471.

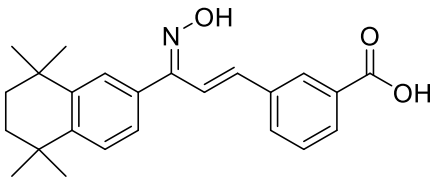
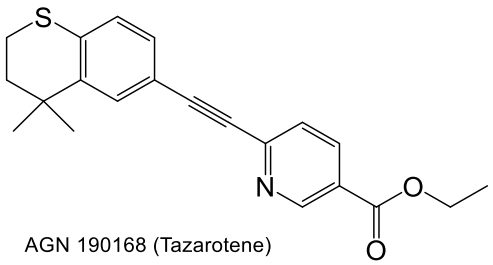
2. The use of claim 1, wherein two RAR active agents are to be administered.

3. The use of claim 2, wherein the second RAR active agent is a RARɣ agonist.

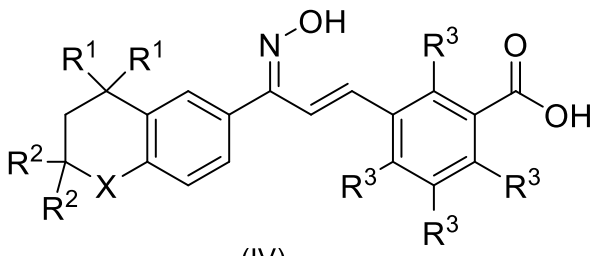
4. The use of claim 3, wherein the RARɣ agonist is:


AGN 190183

, 
AGN 190205 ,


, or 
AGN 190168 (Tazarotene) .

5. The use of claim 3, wherein the RAR agonist is a RARɣ selective 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.

6. The use of claim 3, wherein the RAR agonist is a RARɣ selective agonist selected from CD437, CD2325, CD666, and BMS961.

7. The use of claim 1, wherein the medicament is to be administered with at least one cancer chemotherapy agent.

8. The use of claim 1, wherein the medicament is to be administered with at least one immune checkpoint inhibitor.

9. The use of claim 1, wherein the immune checkpoint inhibitor 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.

10. The use of claim 1, wherein the immune checkpoint inhibitor is an antibody specific for at least one of CTLA-4, PD-1, TIM-3, LAG-3, PD-L1 ligand, B7-H3, B7-H4, BTLA, ICOS, or OX40.

11. The use of claim 1, wherein the medicament prolongs the disease-free survival of a cancer patient.

12. The use of claim 1, wherein the medicament decreases the toxicity of CAR modified immune cells, such that as a result of the combination, a lower dose of CAR-modified immune cells are administered than if the CAR-modified immune cells were administered alone.

13. The use of claim 1, further comprising administration of at least one immune checkpoint inhibitor .

14. The use of claim 1, wherein the medicament is to be administered prior to, simultaneously with, or after the CAR-modified immune cells.