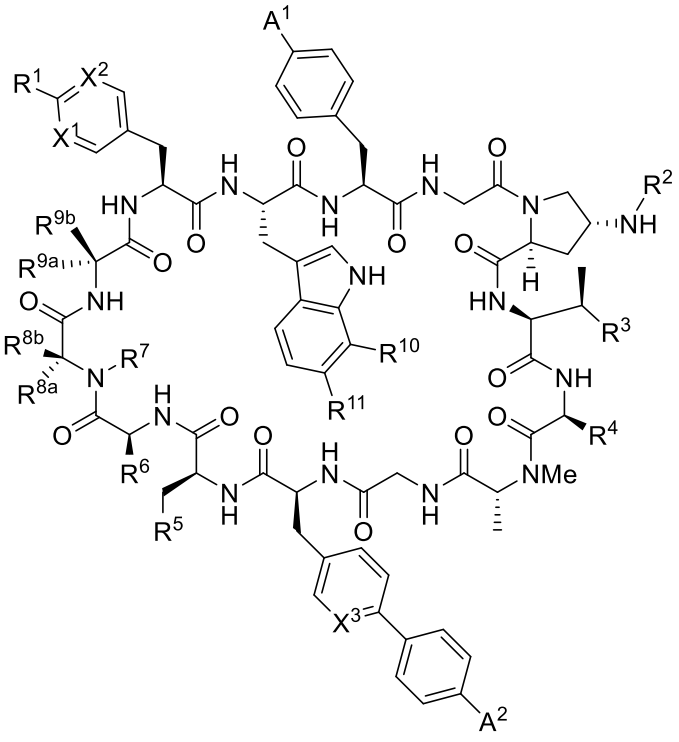
While cholesterol-lowering medications have served as an important standard of care for slowing the progression of atherosclerosis, clinical data support an additional critical role for inflammation in the progression of ASCVD that has remained untreated. Biomarkers of inflammation such as CRP are associated with increased risk of cardiovascular events, independent of cholesterol levels. The Canakinumab Anti-inflammatory Thrombosis Outcomes Study (CANTOS) was the first clinical trial to show that reducing vascular inflammation in the absence of concomitant lipid lowering reduces the rates of cardiovascular events. *N Engl J Med* 2017; 377:1119-1131. Canakinumab is an anti-interleukin-1 beta (IL-1β) human monoclonal antibody approved for clinical use in rheumatologic disorders. IL-1β is a proinflammatory cytokine that induces IL-6 and thereby elevates the downstream inflammatory biomarker high sensitivity CRP (hsCRP). Therefore, CANTOS provides proof of concept that therapies targeting IL-1β could reduce rates of MACE in certain patients in a manner that is complimentary and potentially additive to the LDL-lowering standard of care.

There is a need for additional, non-surgical therapeutic approaches beyond the standard of care cholesterol-lowering medications for slowing the progression of atherosclerosis and decreasing the risk of MACE. In addition, patients suffering from inflammatory disorders would benefit from orally administered agents which block the same cytokine, IL-1β, as canakinumab.

SUMMARY OF THE DISCLOSURE

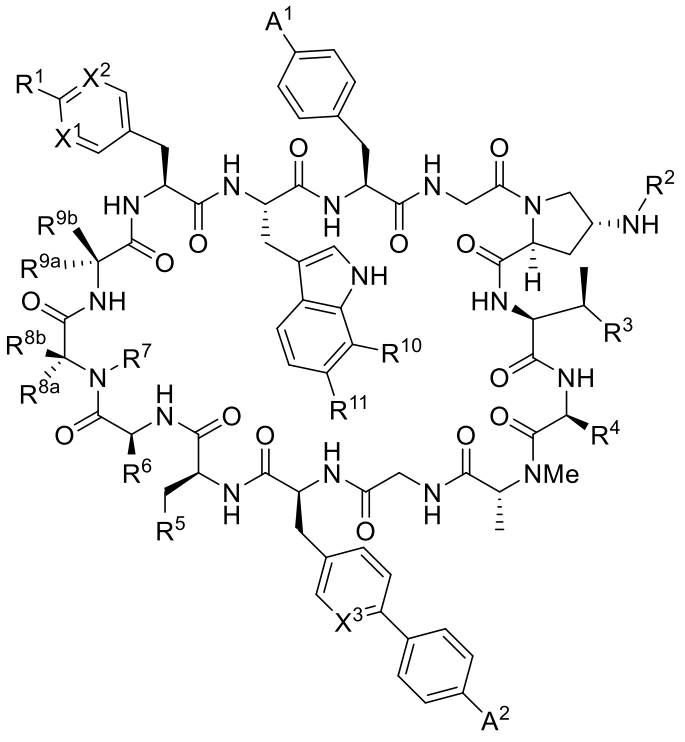
The present disclosure provides certain cyclic peptides that reduce inflammation by binding to the IL-1β cytokine and prevent engagement with the IL-1 receptor, resulting in inhibition of downstream pro-inflammatory signaling. These cyclic peptides can be valuable pharmaceutically active compounds for the treatment of cardiovascular diseases and inflammatory disorders. The present disclosure provides compounds of Formula (I)



(I),

and their pharmaceutically acceptable salts.

In one aspect, the present disclosure provides a compound of Formula (I)



(I),

wherein:

R^1 is $CH_3C(O)NH\text{-}CH_2CH_2\text{-}O\text{-}$ or C^1;

C^1 is:

(i) a 5- to 6-membered monocyclic aryl or heteroaryl, wherein said heteroaryl contains 1 to 2 heteroatoms selected from the group consisting of N, O, and S; or

(ii) a 5- to 6-membered mono- or bicyclic, saturated cycloalkyl or heterocycloalkyl containing 1 to 2 heteroatoms selected from the group consisting of N, O, and S; or

(iii) a 5- to 6-membered mono- or bicyclic cycloalkyl;

wherein C^1 is unsubstituted or substituted by 1 to 3 R^{C1} substituents independently selected from the group consisting of halo, C_1-C_3 alkyl, C_1-C_3 fluoroalkyl, carboxy, C_1-C_3 alkoxy, and C_2-C_3 acyl;

R^2 is H, C_1-C_3 alkyl, benzyl, or phenyl-CH_2CH_2-;

R^3 is a 9- to 10-membered bicyclic aryl or heteroaryl, wherein said heteroaryl contains 1 to 2 heteroatoms selected from the group consisting of N, O, and S;

wherein R^3 is unsubstituted or substituted by 1 to 3 R^{3a} substituents independently selected from the group consisting of halo, C_1-C_3 alkyl, C_1-C_3 fluoroalkyl, hydroxy and C_1-C_3 alkoxy;

R^4 is C_1-C_3 alkyl, HO_2C-$(CH_2)_m$-, $H_2NC(O)$-$(CH_2)_m$-, $(CH_3)_2NC(O)$-$(CH_2)_m$-, or tetrazolyl-$(CH_2)_m$-;

R^5 is amino, $H_2N(CH_2)_n$-, $H_2NC(O)$-$(CH_2)_n$-, $CH_3C(O)NH$-, $CH_3C(O)NH(CH_2)_n$-, C^5, or C^5-CH_2-,

C^5 is:

(ii) a 5- to 6-membered monocyclic aryl or heteroaryl, wherein said heteroaryl contains 1 to 2 heteroatoms selected from the group consisting of N, O, and S;

(ii) a 9- to 10-membered bicyclic aryl or heteroaryl, wherein said bicyclic heteroaryl contains 1 to 3 heteroatoms selected from the group consisting of N, O, and S;

(iii) a 5- to 6-memberered monocyclic or 9-to 10-membered heterocycloalkyl, wherein said heterocycloalkyl is saturated or partially unsaturated, and contains 1 to 2 heteroatoms selected from the group consisting of N, O, and S;

(iv) a 5- to 6-membered monocyclic cycloalkyl;

(v) 2,3-dihydroindolyl;

wherein C^5 is unsubstituted or substituted by 1 to 3 R^{C5} substituents independently selected from the group consisting of halo, amino, hydroxy, C_1-C_3 alkyl, C_1-C_3

fluoroalkyl, C_1-C_3 alkoxy, H_2N-$(CH_2)_k$-, $H_2NC(O)$-$(CH_2)_k$-, H_2C=CH-CH_2O-, and phenyl;

R^6 is H, C_1-C_5 alkyl, $H_2N(CH_2)_p$-, $HOCH_2$-, $(CH_3)_2NCH_2$-, H_3CO-$(CH_2)_q$-, or C^6-CH_2-;

C^6 is 5- or 6-membered monocyclic, saturated heterocycloalkyl containing 1 to 2 heteroatoms selected from the group consisting of N, O, and S; and wherein C^6 is unsubstituted or substituted by 1 to 3 R^{C6} substituents independently selected from the group consisting of halo, C_1-C_3 alkyl, C_1-C_3 fluoroalkyl, hydroxy and C_1-C_3 alkoxy;

R^7 is H or C_1-C_3 alkyl;

R^{8a} is H, C_1-C_5 alkyl, $HOCH_2$-, $H_2N(CH_2)_r$-, $(CH_3)_3N^+(CH_2)_r$-,or $CH_3C(O)NH(CH_2)_r$-;

R^{8b} is H or C_1-C_3 alkyl;

R^{9a} is H or C_1-C_3 alkyl;

R^{9b} is H, C_1-C_5 alkyl, C^9-CH_2-, or C^9-CH_2CH_2-;

C^9 is:

(i) a 5- to 6-membered monocyclic aryl or heteroaryl, wherein said heteroaryl contains 1 to 2 heteroatoms selected from the group consisting of N, O, and S; or

(ii) a 5- to 6-membered monocyclic, saturated cycloalkyl or heterocycloalkyl, wherein the heterocycloalkyl contains 1 to 2 heteroatoms selected from the group consisting of N, O, and S;

wherein C^9 is unsubstituted or substituted by 1 to 3 R^{C9} substituents independently selected from the group consisting of halo, amino, hydroxy, cyano, C_1-C_3 alkyl, C_1-C_3 fluoroalkyl, C_1-C_3 alkoxy, H_2N-$(CH_2)_k$-, $H_2NC(O)$-$(CH_2)_k$-, $H_2NCH_2CH_2O$-, $CH_3C(O)NH$-CH_2CH_2O-, and morpholinyl-CH_2CH_2O-;

R^{10} is H, halo, or C_1-C_3 alkyl;

R^{11} is H, halo, or C_1-C_3 alkyl;

each occurrence of subscript k is independently 1 or 2;

subscript m is 1 or 2;

subscript n is 1, 2, 3, or 4;

subscript p is 1, 2, 3, or 4;

subscript q is 1 or 2;

subscript r is 1, 2, 3, or 4;

X^1, X^2, and X^3 are independently C(H) or N; and

A^1 and A^2 are independently selected from the group consisting of HO_2C-, $H_2NC(O)$-, $CH_3C(O)N(H)$-, $H_2NS(O)_2$-, $CH_3S(O)_2N(H)$-, tetrazolyl, and 5-oxo oxadiazolyl; or

a pharmaceutically acceptable salt thereof.

In another aspect, the present disclosure provides a pharmaceutical composition comprising the compound as defined herein or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

The compounds can trap IL-1β and thereby affect the downstream pro-inflammatory signaling pathway which may be associated with cardiovascular disorders. Accordingly, the present disclosure also provides a method for treating cardiovascular disorder (*e.g.*, atherosclerosis, vascular inflammation) comprising administering a therapeutically effective amount of the compound of the disclosure to a subject in need thereof. In another aspect, the present disclosure provides a compound as defined herein or a pharmaceutically acceptable salt thereof for use in therapy. In another aspect, the present disclosure provides use of a compound as defined herein or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating atherosclerosis. In another aspect, the present disclosure provides use of a compound as defined herein or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating vascular inflammation. In another aspect, the present disclosure provides use of a compound as defined herein or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating an inflammatory disorder. In some examples, the administration comprises an oral administration of the compound.

The disclosure furthermore provides processes for preparing compounds of the disclosure and pharmaceutical compositions which comprise compounds of the disclosure and a pharmaceutically acceptable carrier.

DETAILED DESCRIPTION OF THE INVENTION

Compounds of the Disclosure

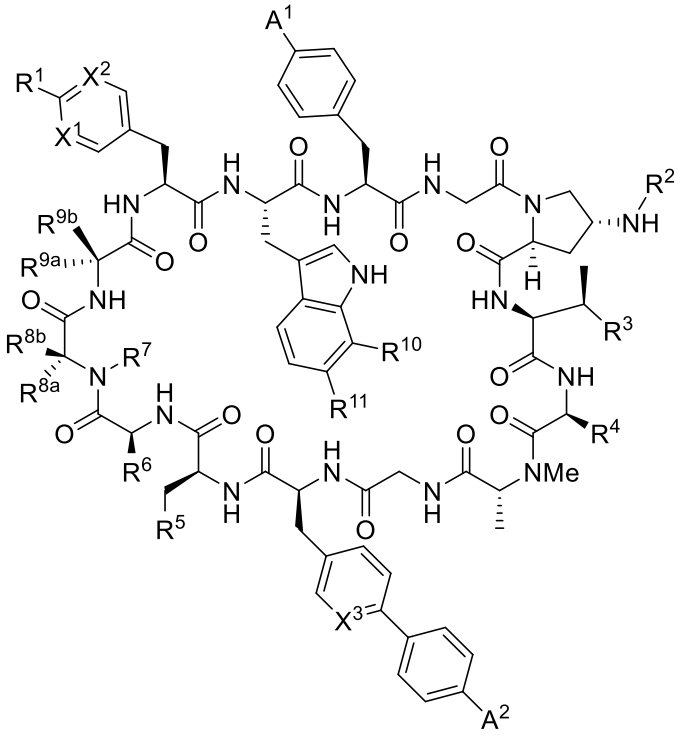
In one embodiment, the present disclosure provides a compound having structural Formula (I) as shown above wherein:

R^1 is $CH_3C(O)NH$-CH_2CH_2-O- or C^1;

C^1 is:

WHAT IS CLAIMED IS:

1. A compound of Formula (I)



(I),

wherein:

R^1 is $CH_3C(O)NH\text{-}CH_2CH_2\text{-}O\text{-}$ or C^1;

C^1 is:

(i) a 5- to 6-membered monocyclic aryl or heteroaryl, wherein said heteroaryl contains 1 to 2 heteroatoms selected from the group consisting of N, O, and S; or

(ii) a 5- to 6-membered mono- or bicyclic, saturated cycloalkyl or heterocycloalkyl containing 1 to 2 heteroatoms selected from the group consisting of N, O, and S; or

(iii) a 5- to 6-membered mono- or bicyclic cycloalkyl;

wherein C^1 is unsubstituted or substituted by 1 to 3 R^{C1} substituents independently selected from the group consisting of halo, C_1-C_3 alkyl, C_1-C_3 fluoroalkyl, carboxy, C_1-C_3 alkoxy, and C_2-C_3 acyl;

R^2 is H, C_1-C_3 alkyl, benzyl, or phenyl-CH_2CH_2-;

R^3 is a 9- to 10-membered bicyclic aryl or heteroaryl, wherein said heteroaryl contains 1 to 2 heteroatoms selected from the group consisting of N, O, and S;

wherein R^3 is unsubstituted or substituted by 1 to 3 R^{3a} substituents independently selected from the group consisting of halo, C_1-C_3 alkyl, C_1-C_3 fluoroalkyl, hydroxy and C_1-C_3 alkoxy;

R^4 is C_1-C_3 alkyl, HO_2C-$(CH_2)_m$-, $H_2NC(O)$-$(CH_2)_m$-, $(CH_3)_2NC(O)$-$(CH_2)_m$-, or tetrazolyl-$(CH_2)_m$-;

R^5 is amino, $H_2N(CH_2)_n$-, $H_2NC(O)$-$(CH_2)_n$-, $CH_3C(O)NH$-, $CH_3C(O)NH(CH_2)_n$-, C^5, or C^5-CH_2-,

C^5 is:

(ii) a 5- to 6-membered monocyclic aryl or heteroaryl, wherein said heteroaryl contains 1 to 2 heteroatoms selected from the group consisting of N, O, and S;

(ii) a 9- to 10-membered bicyclic aryl or heteroaryl, wherein said bicyclic heteroaryl contains 1 to 3 heteroatoms selected from the group consisting of N, O, and S;

(iii) a 5- to 6-memberered monocyclic or 9-to 10-membered heterocycloalkyl, wherein said heterocycloalkyl is saturated or partially unsaturated, and contains 1 to 2 heteroatoms selected from the group consisting of N, O, and S;

(iv) a 5- to 6-membered monocyclic cycloalkyl;

(v) 2,3-dihydroindolyl;

wherein C^5 is unsubstituted or substituted by 1 to 3 R^{C5} substituents independently selected from the group consisting of halo, amino, hydroxy, C_1-C_3 alkyl, C_1-C_3 fluoroalkyl, C_1-C_3 alkoxy, H_2N-$(CH_2)_k$-, $H_2NC(O)$-$(CH_2)_k$-, H_2C=CH-CH_2O-, and phenyl;

R^6 is H, C_1-C_5 alkyl, $H_2N(CH_2)_p$-, $HOCH_2$-, $(CH_3)_2NCH_2$-, H_3CO-$(CH_2)_q$-, or C^6-CH_2-;

C^6 is 5- or 6-membered monocyclic, saturated heterocycloalkyl containing 1 to 2 heteroatoms selected from the group consisting of N, O, and S; and wherein C^6 is unsubstituted or substituted by 1 to 3 R^{C6} substituents independently selected from the group consisting of halo, C_1-C_3 alkyl, C_1-C_3 fluoroalkyl, hydroxy and C_1-C_3 alkoxy;

R^7 is H or C_1-C_3 alkyl;

R^{8a} is H, C_1-C_5 alkyl, $HOCH_2$-, $H_2N(CH_2)_r$-, $(CH_3)_3N^+(CH_2)_r$-,or $CH_3C(O)NH(CH_2)_r$-;

R^{8b} is H or C_1-C_3 alkyl;

R^{9a} is H or C_1-C_3 alkyl;

R^{9b} is H, C_1-C_5 alkyl, C^9-CH_2-, or C^9-CH_2CH_2-;

C^9 is:

(i) a 5- to 6-membered monocyclic aryl or heteroaryl, wherein said heteroaryl contains 1 to 2 heteroatoms selected from the group consisting of N, O, and S; or

(ii) a 5- to 6-membered monocyclic, saturated cycloalkyl or heterocycloalkyl, wherein the heterocycloalkyl contains 1 to 2 heteroatoms selected from the group consisting of N, O, and S;

wherein C^9 is unsubstituted or substituted by 1 to 3 R^{C9} substituents independently selected from the group consisting of halo, amino, hydroxy, cyano, C_1-C_3 alkyl, C_1-C_3 fluoroalkyl, C_1-C_3 alkoxy, H_2N-$(CH_2)_k$-, $H_2NC(O)$-$(CH_2)_k$-, $H_2NCH_2CH_2O$-, $CH_3C(O)NH$-CH_2CH_2O-, and morpholinyl-CH_2CH_2O-;

R^{10} is H, halo, or C_1-C_3 alkyl;

R^{11} is H, halo, or C_1-C_3 alkyl;

each occurrence of subscript k is independently 1 or 2;

subscript m is 1 or 2;

subscript n is 1, 2, 3, or 4;

subscript p is 1, 2, 3, or 4;

subscript q is 1 or 2;

subscript r is 1, 2, 3, or 4;

X^1, X^2, and X^3 are independently C(H) or N; and

A^1 and A^2 are independently selected from the group consisting of HO_2C-, $H_2NC(O)$-, $CH_3C(O)N(H)$-, $H_2NS(O)_2$-, $CH_3S(O)_2N(H)$-, tetrazolyl, and 5-oxo oxadiazolyl; or

a pharmaceutically acceptable salt thereof.

2. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein:

R^5 is amino, $H_2N(CH_2)_n$-, $H_2NC(O)$-$(CH_2)_n$-, C^5, or C^5-CH_2-,

C^5 is:

(i) a 5- to 6-membered monocyclic aryl or heteroaryl, wherein said heteroaryl contains 1 to 2 heteroatoms selected from the group consisting of N, O, and S:

(ii) a 9- to 10-membered bicyclic aryl or heteroaryl, wherein said bicyclic heteroaryl contains 1 to 3 heteroatoms selected from the group consisting of N, O, and S;

(iii) a 5- to 6-memberered monocyclic or 9-to 10-membered heterocycloalkyl, wherein said heterocycloalkyl is saturated or partially unsaturated, and contains 1 to 2 heteroatoms selected from the group consisting of N, O, and S; or

(iv) 2,3-dihydroindolyl;

wherein C^5 is unsubstituted or substituted by 1 to 3 R^{C5} substituents independently selected from the group consisting of halo, amino, hydroxy, C_1-C_3 alkyl, C_1-C_3 fluoroalkyl, C_1-C_3 alkoxy, H_2N-$(CH_2)_k$-, $H_2NC(O)$-$(CH_2)_k$-, H_2C=CH-CH_2O-, and phenyl;

R^6 is H, C_2-C_5 alkyl, $H_2N(CH_2)_p$-, $HOCH_2$-, $(CH_3)_2NCH_2$-, H_3CO-$(CH_2)_q$-, or C^6-CH_2-;

R^{8a} is H, C_1-C_3 alkyl, $HOCH_2$-, or $H_2N(CH_2)_r$-;

R^{9a} is H;

R^{9b} is H, C_1-C_3 alkyl, C^9-CH_2-, or C^9-CH_2CH_2-;

R^{10} is H;

R^{11} is H;

subscript p is 1, 2, or 3; and

subscript r is 2, 3, or 4.

3. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein:

C1 is phenyl, pyrimidyl, or piperazinyl, wherein C^1 is unsubstituted or substituted by 1 to 2 R^{C1} substituents;

R^3 is naphthyl or indolyl, wherein R^3 is unsubstituted or substituted by 1 to 2 R^{3a} substituents;

C^5 is phenyl, pyridyl, pyrimidyl, naphthyl, indolyl, 7-azaindolyl, indazolyl, 2,3-dihydroindolyl, piperidinyl, tetrahydropyranyl, or cyclohexyl, wherein C^5 is unsubstituted or substituted by 1 to 2 R^{C5};

C^6 is tetrahydropyranyl or morpholinyl; wherein C^6 is unsubstituted or substituted by 1 to 2 R^{C6}; and

C^{9a} is H or methyl;

C^{9b} is phenyl, pyridyl, cyclohexyl, morpholinyl, or piperidinyl, wherein C^9 is unsubstituted or substituted by 1 to 2 R^{C9}.

4. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein X1 and X2 are C(H); and R1 is phenyl substituted by carboxy.

5. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein X1 and X2 are C(H); and R1 is CH3C(O)NH-CH2CH2-O-.

6. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^2 is H.

7. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^3 is indolyl substituted by one halo.

8. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^3 is naphthyl.

9. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^4 is $HO_2C-(CH_2)_m-$.

10. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein X^3 is C(H).

11. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^5 is $H_2N(CH_2)_n-$, indole, 7-azaindole, naphthyl or pyridyl.

12. The compound of claim 5 or a pharmaceutically acceptable salt thereof, wherein R^5 is $H_2N(CH_2)_n-$, indole, naphthyl or pyridyl.

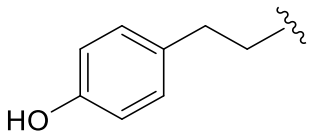
13. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^6 is H, $HOCH_2-$, C_2-C_5 alkyl or $H_2N(CH_2)_p-$.

14. The compound of claim 13 or a pharmaceutically acceptable salt thereof, wherein R^6 is C_2-C_5 alkyl or $H_2N(CH_2)_p-$.

15. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^7 is H.

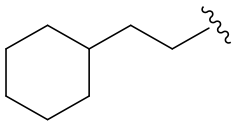
16. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein: R^{8a} is methyl or $H_2NCH_2CH_2$-; and R^{8b} is H.

17. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^{9b} is



.

18. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^{9b} is



.

19. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^{10} is H; and R^{11} is H, F or Cl.

20. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein A^1 and A^2 are both HO_2C-.

21. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein:

R^1 is 4-$CH_3C(O)$-piperazin-1-yl, $CH_3C(O)NH$-CH_2CH_2-O-, 5-CO_2H-pyrimidin-2-yl, or 4-CO_2H-phenyl;

R^2 is H, ethyl, benzyl, or phenyl-CH_2CH_2-;

R^3 is naphth-1-yl, 4-fluoroindol-3-yl, or 4-chloroindol-3-yl;

R^4 is methyl, HO_2C-$(CH_2)_m$-, or $H_2NC(O)$-$(CH_2)_m$-;

R^5 is amino, $H_2N(CH_2)_n$-, naphth-1-yl, indol-3-yl, 7-aza-indol-3-yl, indazol-1-yl, 2,3-dihydroindol-1-yl, pyrid-3-yl, pyrid-4-yl, piperidin-4-yl, 3-aminomethylphenyl, 4-aminomethylphenyl, 3-aminophenyl, 4-aminophenyl, phenyl, pyrid-4-yl-CH_2-, pyrimidin-5-yl, tetrahydropyran-4-yl-, $H_2NC(O)$-$(CH_2)_2$-, 3-biphenyl, 3-CH_2=CH-CH_2O-phenyl, $CH_3C(O)NH$-, $CH_3C(O)NH(CH_2)_3$-, or cyclohexyl;

R^6 is H, $(CH_3)_2CHCH_2$-, $(CH_3)_3CCH_2$-, $H_2N(CH_2)_p$-, $HOCH_2$-, $H_3CCH_2CH_2$-, morpholin-4-yl-CH_2-, tetrahydropyran-4-yl-CH_2-, $(CH_3)_2NCH_2$-, or H_3CO-$(CH_2)_q$-;

R^7 is H or methyl;

R^{8a} is H, methyl, $HOCH_2$-, $H_2N(CH_2)_r$-, $(CH_3)_3NCH_2CH_2$-, or $CH_3C(O)NH(CH_2)_4$-;

R^{8b} is H or methyl;

R^{9a} is H or methyl;

R^{9b} is H, methyl, $H_3CCH_2CH_2CH_2$-, 4-HO-phenyl-CH_2CH_2-, phenyl-CH_2CH_2-, cyclohexyl-CH_2CH_2-, 5-NC-pyrid-3-yl-CH_2CH_2-, 4-F_3C-phenyl-CH_2-, 3-F_3C-phenyl-CH_2-, 2-F_3C-phenyl-CH_2-, morpholin-4-yl-CH_2CH_2O-phenyl-CH_2-, 4-aminophenyl-CH_2-, 4,4-difluorocyclohexyl-CH_2-, 4-$H_2NCH_2CH_2O$-phenyl-CH_2-, 4-$H_2NCH_2CH_2O$-pyrid-3-yl-CH_2-, piperidin-4-yl-CH_2-, or 4-$CH_3C(O)NH$-CH_2CH_2O-phenyl-CH_2-;

R^{10} is H, fluoro, or methyl;

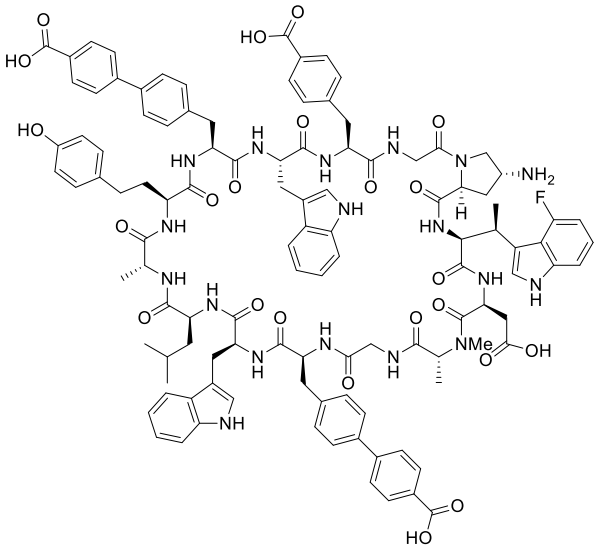
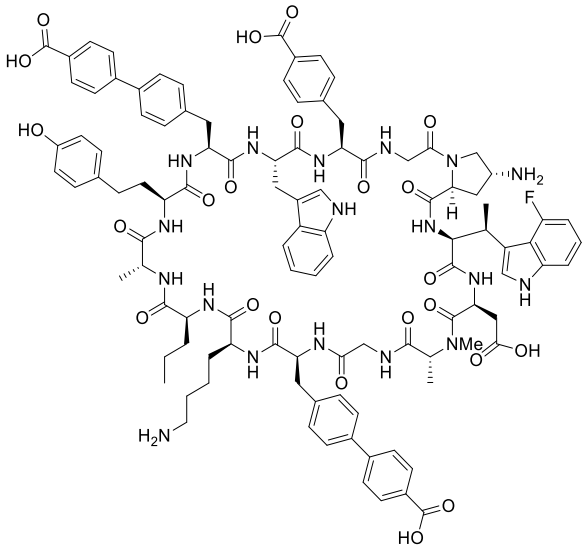
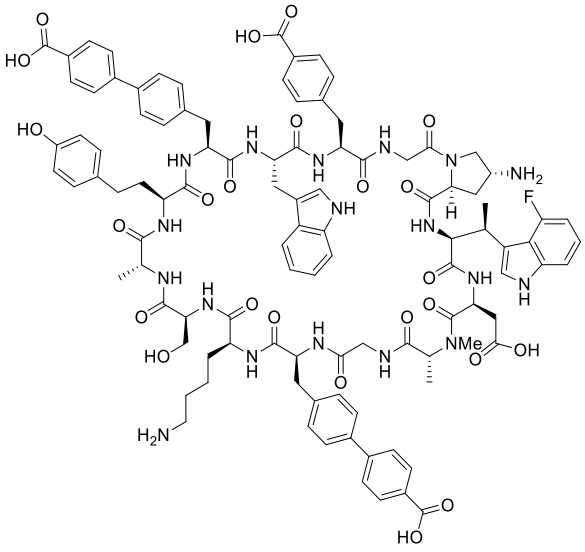
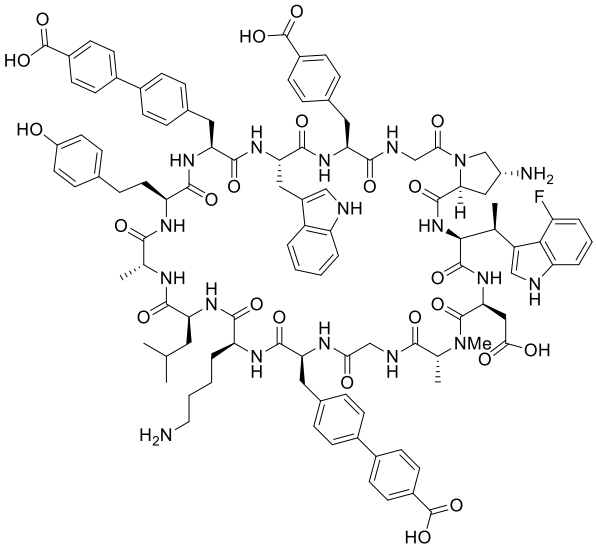
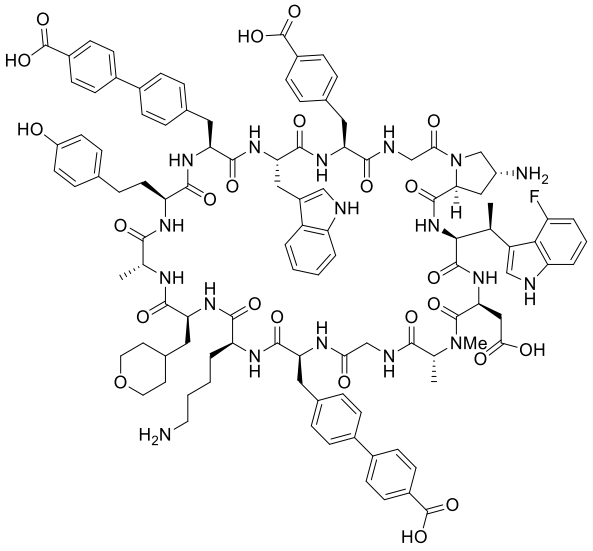
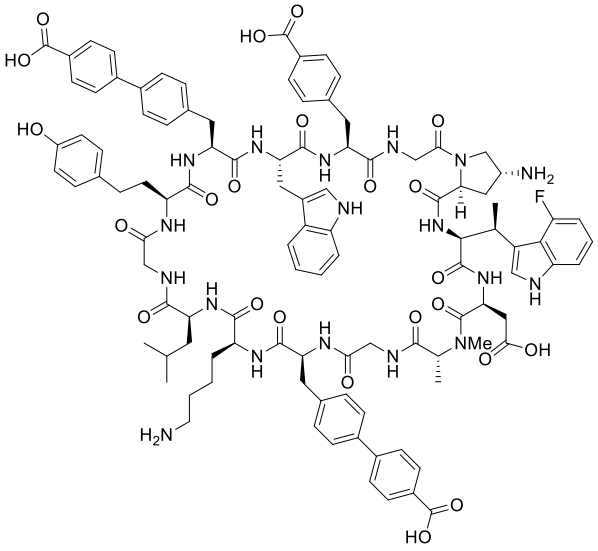
R^{11} is H, fluoro, or chloro;

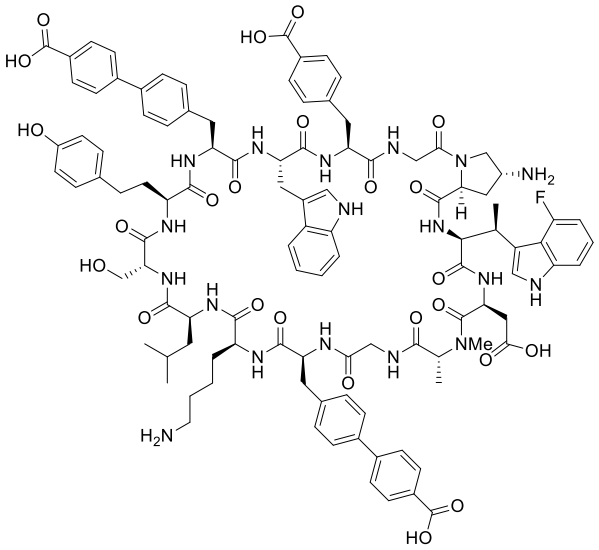
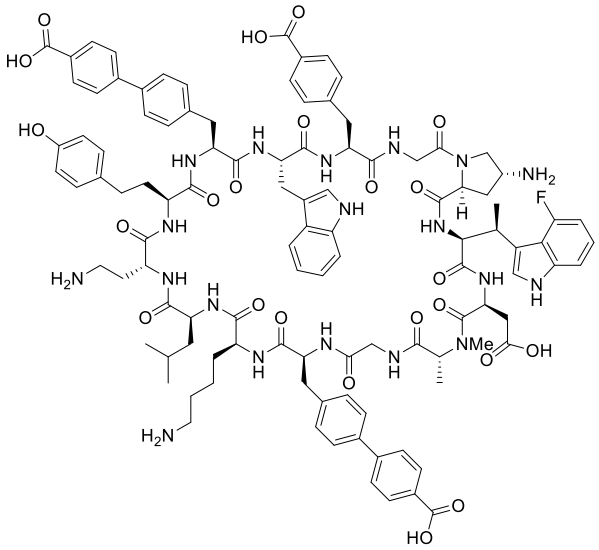
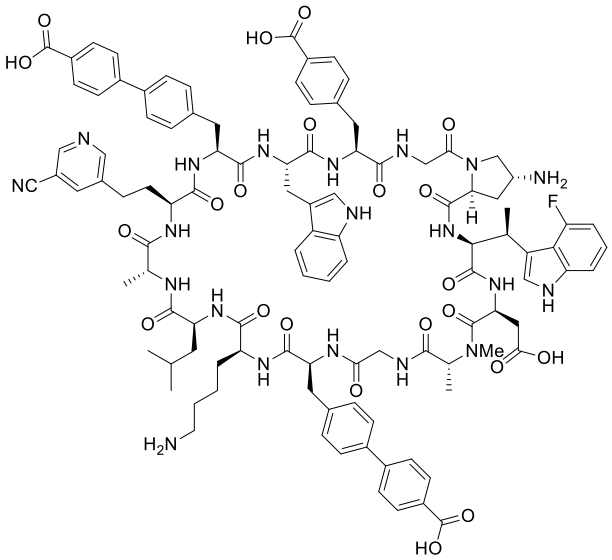
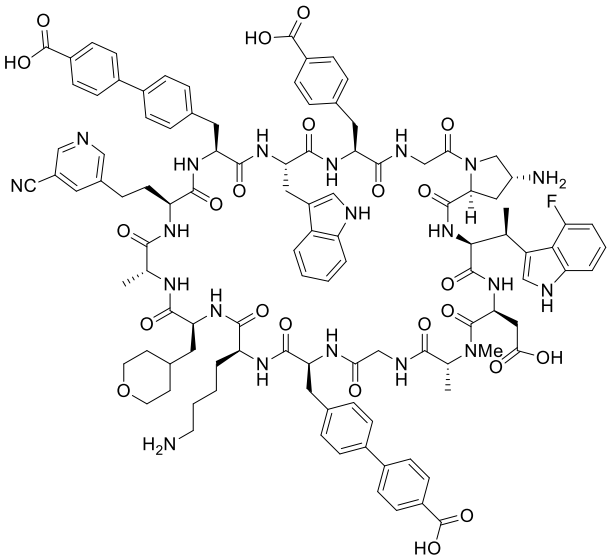
A^1 and A^2 are both HO_2C-; and

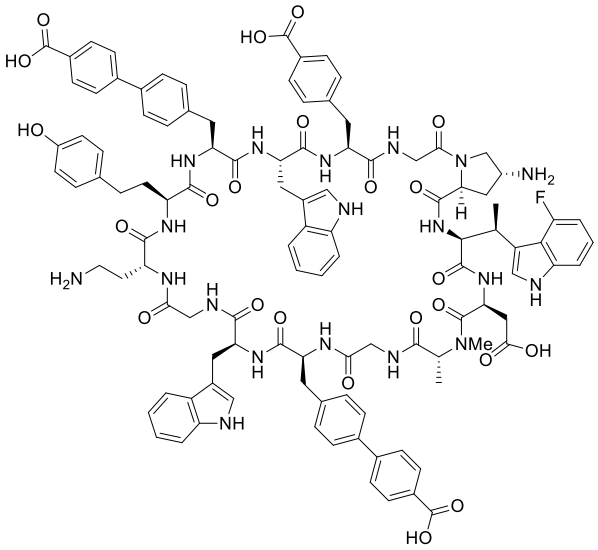
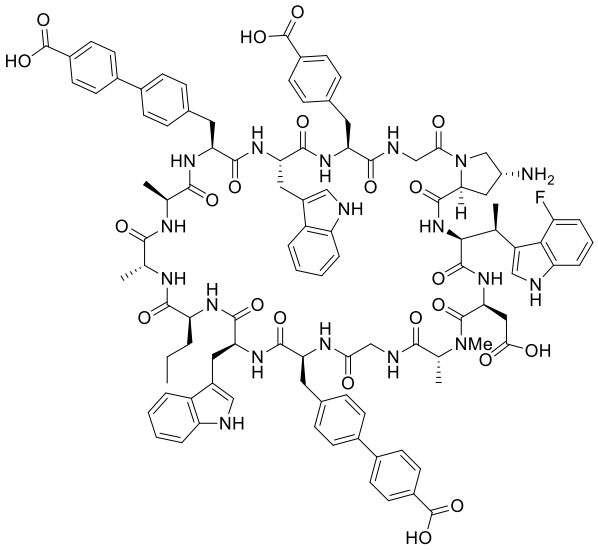
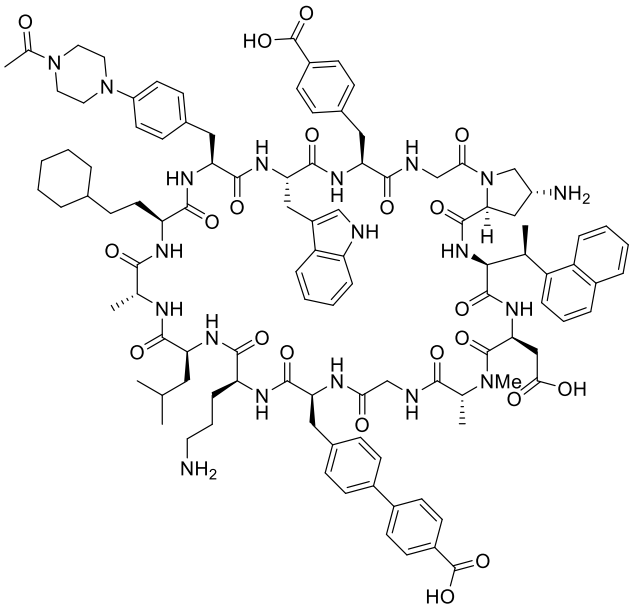
X^1, X^2, and X^3 are C(H).

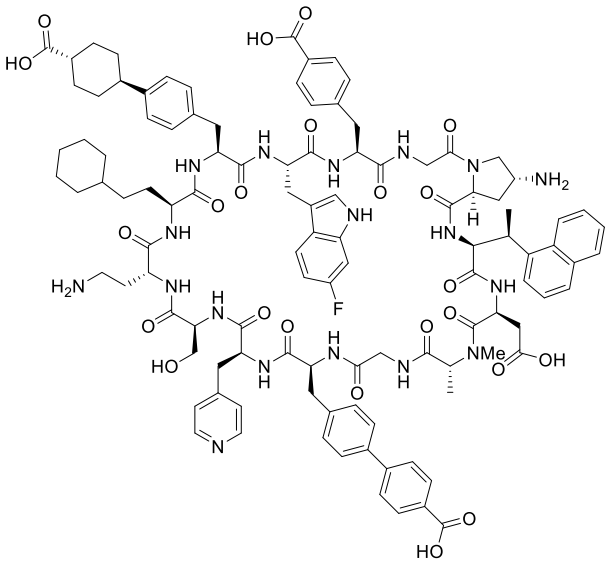
22. The compound of claim 1 selected from the group consisting of SEQ ID NOS: 1-215, or a pharmaceutically acceptable salt thereof.

23. The compound of claim 1 selected from the group consisting of (SEQ ID NOS 78, 71-72, 67, 65, 70, 69, 68, 66, 64, 77, 79, 209, 193, 215, 212, and 210 respectively, in order of appearance):

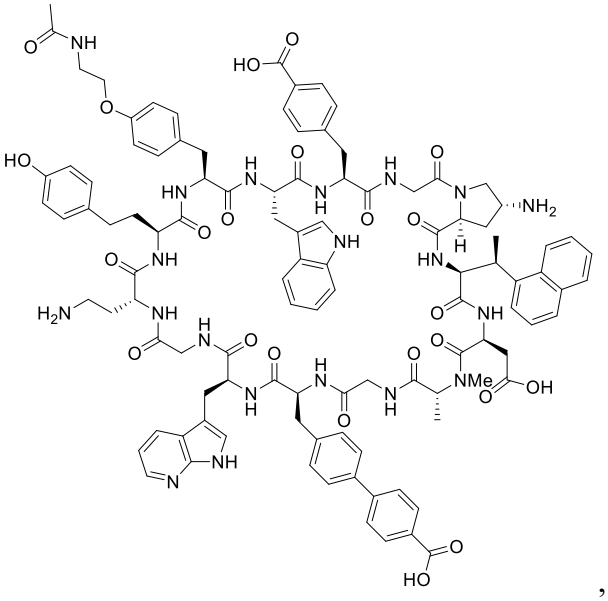

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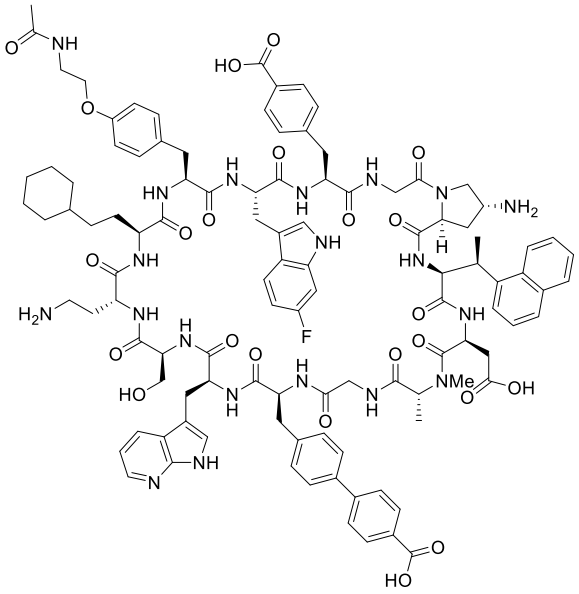

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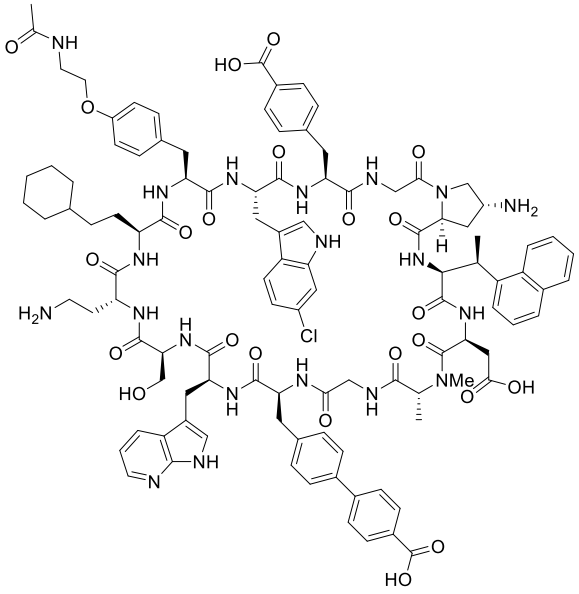
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, and



, or a pharmaceutically acceptable salt thereof.

24. A pharmaceutical composition comprising the compound of any one of claims 1-23 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

25. A compound of any one of claims 1-23 or a pharmaceutically acceptable salt thereof for use in therapy.

26. Use of a compound of any one of claims 1-23 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating atherosclerosis.

27. Use of a compound of any one of claims 1-23 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating vascular inflammation.

28. Use of a compound of any one of claims 1-23 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating an inflammatory disorder.

29. The use of any one of claims 26 to 28, wherein the compound is to be orally administered.