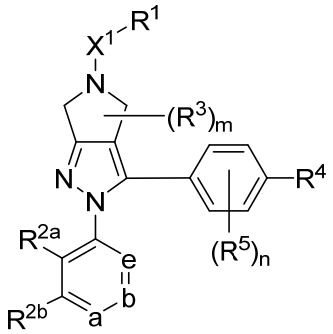
CLAIMS

1. A compound of Formula (**I**)



(I)

or a pharmaceutically acceptable salt thereof, wherein,

ring vertex a is N or C(R^{2c}), ring vertex b is N or C(R^{2d}), and ring vertex e is N or C(R^{2e}), wherein no more than one of a, b and e is N;

X^1 is selected from the group consisting of a bond, C_{1-8} alkylene, C(O), C(O)-C_{1-4} alkylene, and $S(O)_2$;

R^1 is selected from the group consisting of

a) 5- to 10-membered heteroaryl having from 1 to 4 heteroatoms as ring vertices selected from N, O and S;

b) C_{6-10} aryl;

c) C_{3-8} cycloalkyl;

d) 4- to 8-membered heterocycloalkyl having from 1 to 2 heteroatoms as ring vertices selected from N, O and S; and

e) C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} haloalkyl, –C(O)$NR^{1a}R^{1b}$, and –CO_2R^{1a}; wherein R^{1a} and R^{1b} are each independently selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{6-10} aryl, and –C_{1-6} alkylene–C_{6-10} aryl;

wherein the group –X^1-R^1 is optionally substituted with 1 to 5 R^x substituents;

R^{2a} and R^{2e} are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl,-O-C_{1-6} haloalkyl, -S-C_{1-6} alkyl, -C_{1-6} alkyl-O-C_{1-6} alkyl, -C_{1-6} alkyl-S-C_{1-6} alkyl, CN, and halogen, and at least one of R^{2a} and R^{2e} is other than hydrogen;

R^{2b}, R^{2c}, and R^{2d} are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, -O-C_{1-6} haloalkyl, -S-C_{1-6} alkyl, -C_{1-6} alkyl-O-C_{1-6} alkyl, -C_{1-6} alkyl-S-C_{1-6} alkyl, cyano, and halogen;

each R^3 is independently selected from the group consisting of hydroxyl, C_{1-4} alkyl, C_{1-4} haloalkyl and C_{1-4} hydroxyalkyl, and optionally two R^3 groups on the same carbon atom are combined to form oxo (=O), and optionally two R^3 groups and the carbon atoms they are attached to form a 3-6 membered ring with 0-2 hetereoatoms as ring members selected from O, N, and S;

R^4 is independently selected from the group consisting of –X^2-OR^{4a}, –X^2-$NR^{4a}R^{4b}$, –X^2-$CONR^{4a}R^{4b}$, –X^2-NR^{4a}-C(O)R^{4a}, -X^2-NR^{4a}-C(O)$NR^{4a}R^{4b}$, -X^2-NR^{4a}-C(O)OR^{4a}, -X^2-NR^{4a}-C(O)-C_{1-3} alkylene-OR^{4a} and –X^2-NR^{4a}-C(O)-C_{1-3} alkylene-$NR^{4a}R^{4b}$; wherein each X^2 is independently a bond, C(O), C_{1-4} alkylene, C(O)-C_{1-4} alkylene, and C_{1-4} alkylene-C(O), and each R^{4a} and R^{4b} is independently selected from the group consisting of hydrogen, C_{1-4} alkyl, and C_{1-4} haloalkyl;

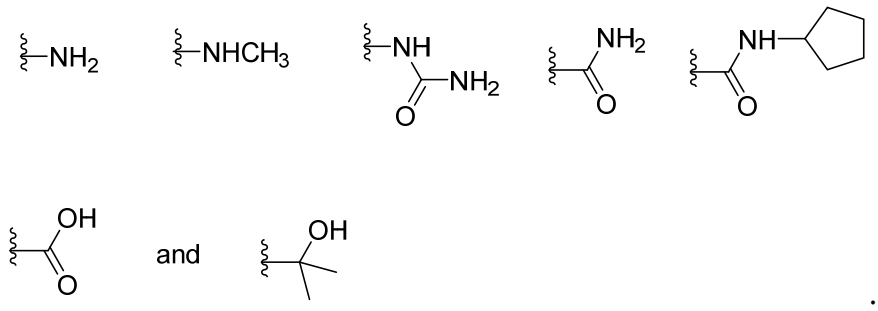
each R^5 is independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} haloalkyl, C_{1-8} haloalkoxy, C_{1-8} hydroxyalkyl, halogen, OH, CN, C(O)R^{5a} and CO_2R^{5a}; wherein each R^{5a} is independently selected from the group consisting of hydrogen, C_{1-4} alkyl, and C_{1-4} haloalkyl;

each R^x is independently selected from the group consisting of halogen, CN, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{1-4} hydroxy, C_{2-4} alkenyl, C_{3-6} cycloalkyl, CO_2-C_{1-4} alkyl, and $CONH_2$;

the subscript m is 0, 1, 2, 3 or 4; and

the subscript n is 0, 1, 2 or 3.

2. The compound of claim **1**, or a pharmaceutically acceptable salt thereof, wherein R^4 is selected from the group consisting of



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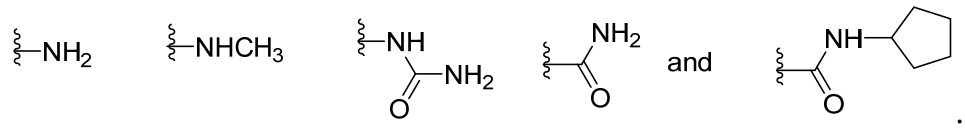
3. The compound of any one of claims **1** or **2**, or a pharmaceutically acceptable salt thereof, wherein R^4 is selected from the group consisting of



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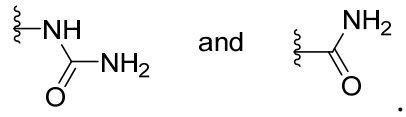
4. The compound of any one of claims **1** to **3**, or a pharmaceutically acceptable salt thereof, wherein R^4 is selected from the group consisting of



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5. The compound of any one of claims **1** to **4**, or a pharmaceutically acceptable salt thereof, wherein X^1 is a bond.

6. The compound of any one of claims **1** to **4**, or a pharmaceutically acceptable salt thereof, wherein X^1 is C(O).

7. The compound of any one of claims **1** to **4**, or a pharmaceutically acceptable salt thereof, wherein X^1 is C_{1-8} alkylene.

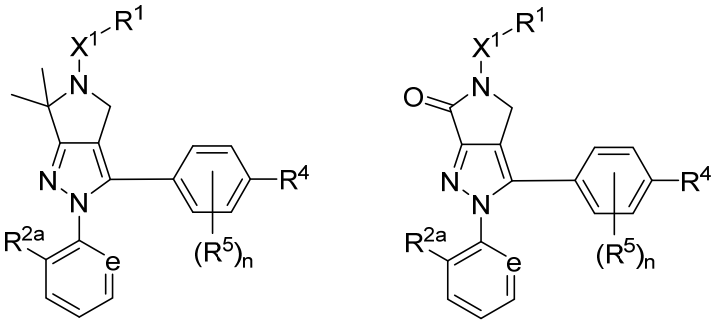
8. The compound of any one of claims **1** to **4**, or a pharmaceutically acceptable salt thereof, wherein X^1 is C(O)-C_{1-4} alkylene or $S(O)_2$.

9. The compound of any one of claims **1** to **8**, or a pharmaceutically acceptable salt thereof, wherein R^1 is a 5- to 10-membered heteroaryl having from 1 to 4

heteroatoms as ring vertices selected from N, O and S; and wherein the group $–X^1$-R^1 is optionally substituted with 1 to 4 R^x substituents.

10. The compound of claim **9**, wherein R^1 is selected from the group consisting of pyrazolyl, pyridyl, pyrimidinyl, imidazolyl, thiazolyl, thiadiazolyl and pyrazinyl; and wherein the group $–X^1$-R^1 is optionally substituted with 1 to 4 R^x substituents.

11. The compound of any one of claims **1** to **10**, or a pharmaceutically acceptable salt thereof, having formula (Ia) or (Ib):



(Ia) (Ib).

12. The compound of any one of claims **1** to **8**, or a pharmaceutically acceptable salt thereof, wherein R^1 is C_{6-10} aryl; and wherein the group $–X^1$-R^1 is optionally substituted with 1 to 4 R^x substituents.

13. The compound of claim **12**, wherein R^1 is phenyl; and wherein the group $–X^1$-R^1 is optionally substituted with 1 to 4 R^x substituents.

14. The compound of any one of claims **1** to **8**, or a pharmaceutically acceptable salt thereof, wherein R^1 is C_{3-8} cycloalkyl; and wherein the group $–X^1$-R^1 is optionally substituted with 1 to 4 R^x substituents.

15. The compound of claim **14**, wherein R^1 is selected from the group consisting of cyclobutyl, cyclopentyl and cyclohexyl; and wherein the group $–X^1$-R^1 is optionally substituted with 1 to 4 R^x substituents.

16. The compound of any one of claims **1** to **8**, or a pharmaceutically acceptable salt thereof, wherein R^1 is a 4- to 8-membered heterocycloalkyl having from 1 to 2 heteroatoms as ring vertices selected from N, O and S; and wherein the group $–X^1$-R^1 is optionally substituted with 1 to 4 R^x substituents.

17. The compound of claim **16**, wherein R^1 is selected from the group consisting of oxetanyl, tetrahydrofuranyl, tetrahydropyranyl and morpholinyl; and wherein the group $–X^1$-R^1 is optionally substituted with 1 to 4 R^x substituents.

18. The compound of any one of claims **1** to **8**, or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} haloalkyl, $–C(O)NR^{1a}R^{1b}$, and $–CO_2R^{1a}$; wherein R^{1a} and R^{1b} are each independently selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{6-10} aryl, and $–C_{1-6}$ alkylene$–C_{6-10}$ aryl; and wherein the group $–X^1$-R^1 is optionally substituted with 1 to 4 R^x substituents.

19. The compound of any one of claims **1** to **8**, or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from the group consisting of phenyl, pyridyl, pyrimidinyl, and pyrazinyl; and wherein the group $–X^1$-R^1 is optionally substituted with 1 to 4 R^x substituents.

20. The compound of any one of claims **1** to **19**, or a pharmaceutically acceptable salt thereof, wherein ring vertices a and b are CH; R^{2b} is H; ring vertex e is $C(R^{2e})$, and R^{2a} and R^{2e} are independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl,-O-C_{1-6} haloalkyl, -S-C_{1-6} alkyl, -C_{1-6} alkyl-O-C_{1-6} alkyl, -C_{1-6} alkyl-S-C_{1-6} alkyl, CN, and halogen.

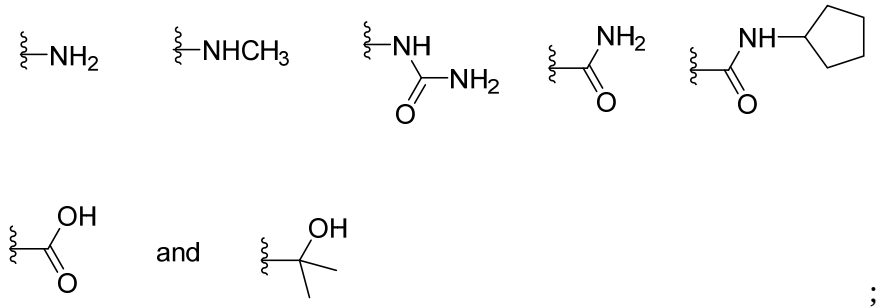
21. The compound of any one of claims **1** to **19**, or a pharmaceutically acceptable salt thereof, wherein ring vertices a and b are CH; R^{2b} is H; ring vertex e is $C(R^{2e})$, and R^{2a} and R^{2e} are independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} alkoxy and halogen.

22. The compound of any one of claims **1** to **21**, or a pharmaceutically acceptable salt thereof, wherein n is 0, 1 or 2 and each R^5, when present, is selected from the group consisting of F, Cl, CN, C_{1-4} alkyl and C_{1-4} alkoxy.

23. The compound of any one of claims **1** to **21**, or a pharmaceutically acceptable salt thereof, wherein n is 0, 1 or 2 and each R^5, when present, is selected from the group consisting of F, Cl, CN, CH_3 and OCH_3.

24. The compound of any one of claims **1** to **21**, or a pharmaceutically acceptable salt thereof, wherein m is 0, 1 or 2 and each R^3, when present, is C_{1-4} alkyl.

25. The compound of claim **1**, or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from the group consisting of phenyl or pyridyl, wherein the group $–X^1$-R^1 is optionally substituted with 1 to 4 R^x substituents; ring vertices a and b are CH; R^{2b} is H; ring vertex e is $C(R^{2e})$, and R^{2a} and R^{2e} are independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} alkoxy and halogen; m is 0, 1 or 2 and each R^3, when present, is CH_3; R^4 is selected from the group consisting of



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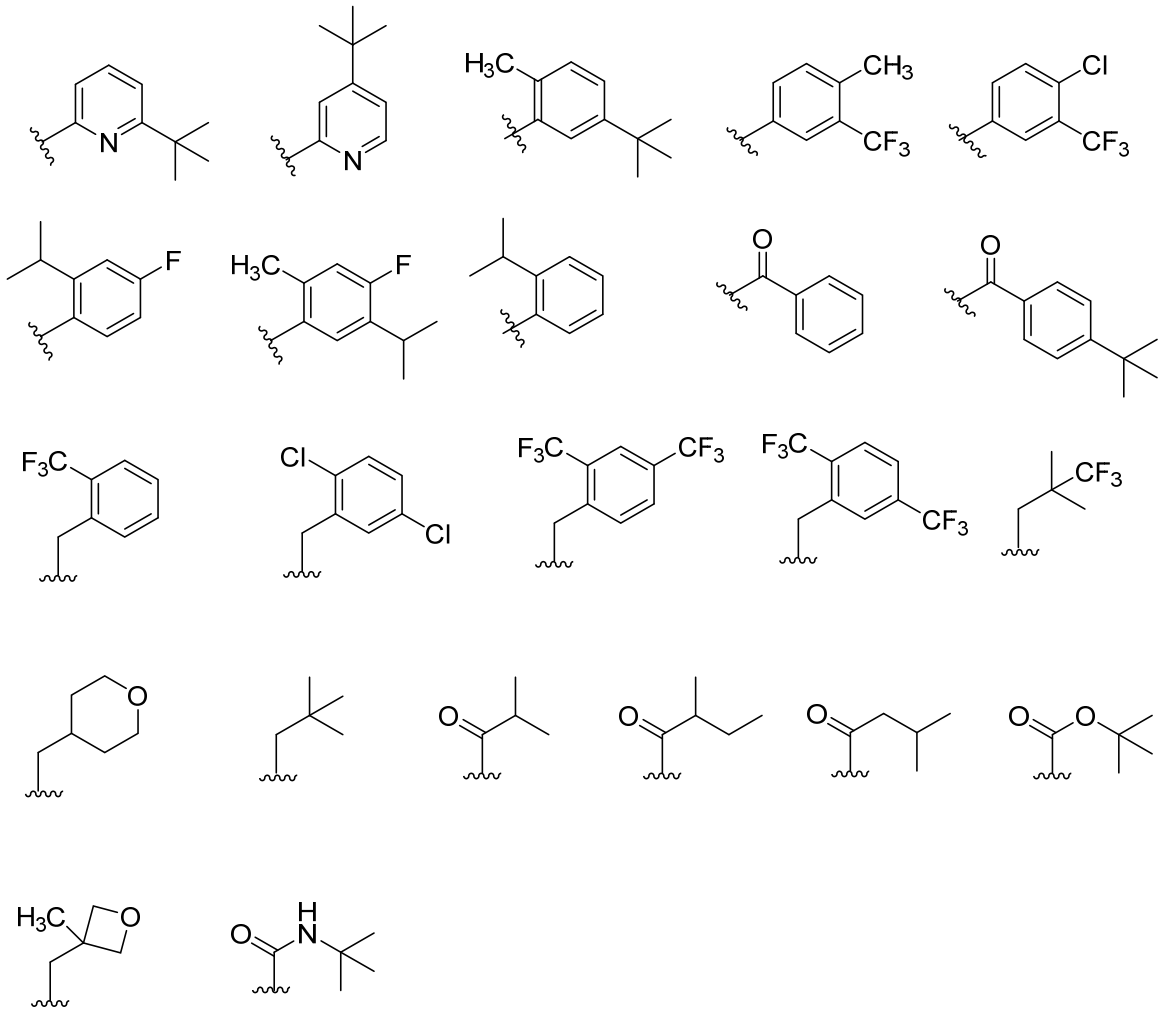
n is 0, 1 or 2 and each R^5, when present, is selected from the group consisting of F, Cl, CN, CH_3 and OCH_3.

26. The compound of claim **1**, or a pharmaceutically acceptable salt thereof, wherein $–X^1$-R^1 is selected from the group consisting of:



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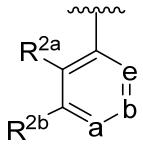
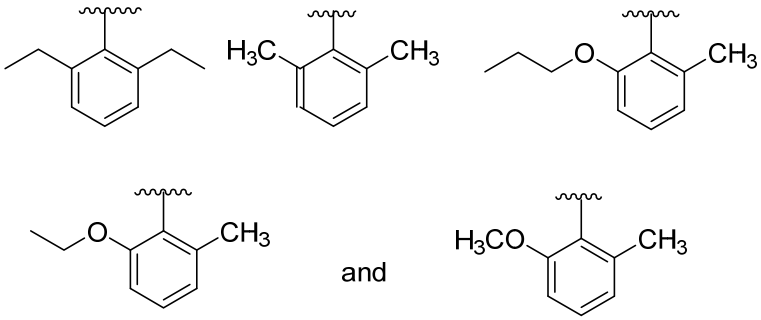
27. The compound of any one of claims **1** to **26**, or a pharmaceutically acceptable salt thereof, wherein  is selected from the group consisting of



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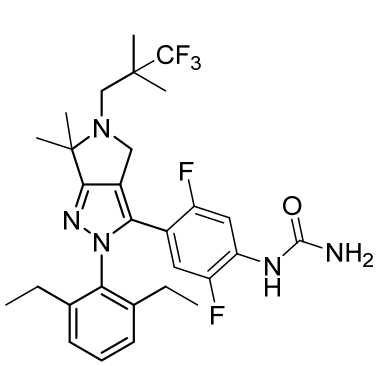
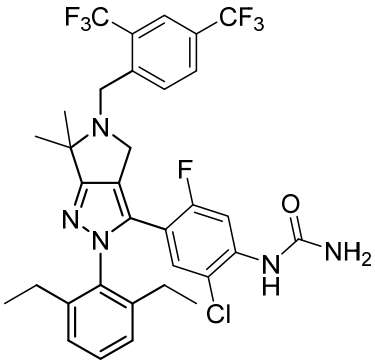
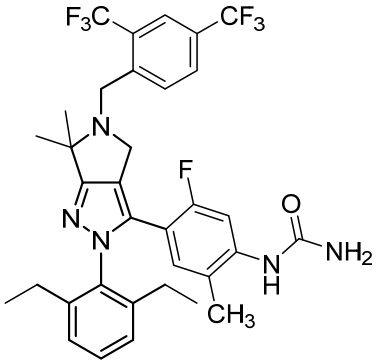
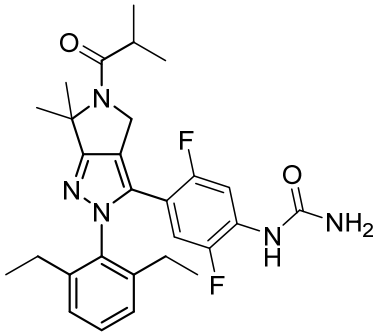
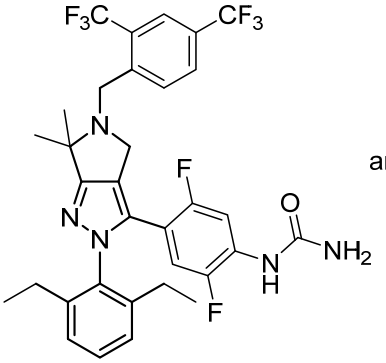
28. The compound of any one of claims **1** to **27**, or a pharmaceutically acceptable salt thereof, wherein n is 0.

29. The compound of any one of claims **1** to **27**, or a pharmaceutically acceptable salt thereof, wherein n is 2 and the two R^3 groups are on the same carbon atom and are combined to form oxo (=O).

30. The compound of claim **1**, or a pharmaceutically acceptable salt thereof, wherein said compound is selected from the group consisting of: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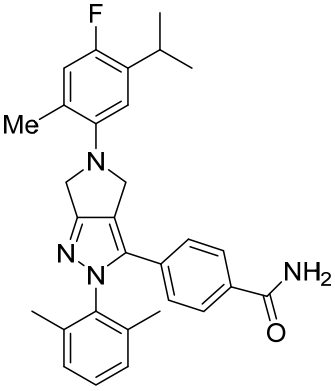
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31. A pharmaceutical composition comprising a compound of any one of claims **1** to **30** or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

32. Use of the compound of any one of claims **1** to **30** or the pharmaceutical composition of claim 31 in the preparation of a medicament for the treatment of a human

suffering from or susceptible to a disease or disorder involving pathologic activation of C5a receptors.

33. The use of claim **32**, wherein the disease or disorder is an inflammatory disease or disorder, an autoimmune disease, or an oncologic disease or disorder.

34. The use of claim **32**, wherein the disease or disorder is a cardiovascular or cerebrovascular disorder.

35. The use of claim **32**, wherein the disease or disorder is selected from the group consisting of neutropenia, neutrophilia, Wegener's granulomatosis, microscopic polyangiitis, C3-glomerulopathy, C3-glomerulonephritis, dense deposit disease, membranoproliferative glomerulonephritis, Kawasaki disease, sepsis, septic shock, Hemolytic uremic syndrome, atypical hemolytic uremic syndrome (aHUS), Alzheimer's disease, multiple sclerosis, stroke, inflammatory bowel disease, chronic obstructive pulmonary disorder, inflammation associated with burns, lung injury, osteoarthritis, atopic dermatitis, chronic urticaria, ischemia-reperfusion injury, acute respiratory distress syndrome, systemic inflammatory response syndrome, multiple organ dysfunction syndrome, Uveitis, tissue graft rejection, hyperacute rejection of transplanted organs, myocardial infarction, coronary thrombosis, vascular occlusion, post-surgical vascular reocclusion, artherosclerosis, polypoidal choroidal vasculopathy, traumatic central nervous system injury, ischemic heart disease, rheumatoid arthritis, systemic lupus erythematosus, Guillain- Barre syndrome, pancreatitis, lupus nephritis, lupus glomerulonephritis, psoriasis, Crohn's disease, vasculitis, ANCA vasculitis, irritable bowel syndrome, dermatomyositis, multiple sclerosis, bronchial asthma, pemphigus, pemphigoid, scleroderma, myasthenia gravis, autoimmune hemolytic and thrombocytopenic states, Goodpasture's syndrome, immuno vasculitis, Graft versus host disease, Paroxysmal nocturnal hemoglobinuria, Sjoegrens syndrome, insulin-dependent diabetes, mellitus, lupus nephropathy, Heyman nephritis, membranous nephritis, glomerulonephritis, IGA nephropathy, Membranoproliferative glomerulonephritis, Antiphospholipid syndrome, Age related macular degeneration; Dry age related macular degeneration, Wet age related macular degeneration, Motor neurone disease, contact sensitivity responses, hidradenitis suppurativa, and inflammation resulting from contact of blood with artificial surfaces.

36. The use of claim **32**, wherein the disease or disorder is selected from the group consisting of neutropenia, neutrophilia, Wegener's granulomatosis, microscopic polyangiitis, C3-glomerulopathy, C3-glomerulonephritis, dense deposit disease, membranoproliferative glomerulonephritis, Kawasaki disease, Hemolytic uremic syndrome, atypical hemolytic uremic syndrome (aHUS), tissue graft rejection, hyperacute rejection of transplanted organs, rheumatoid arthritis, systemic lupus erythematosus, lupus nephritis, lupus glomerulonephritis, vasculitis, ANCA vasculitis, autoimmune hemolytic and thrombocytopenic states, immuno vasculitis, Graft versus host disease, lupus nephropathy, Heyman nephritis, membranous nephritis, glomerulonephritis, IGA nephropathy, hidradenitis suppurativa, and Membranoproliferative glomerulonephritis.

37. The use of claim **32**, wherein the disease or disorder is selected from the group consisting of melanoma, lung cancer, lymphoma, sarcoma, carcinoma, fibrosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, angiosarcoma, lymphangiosarcoma, synovioma, mesothelioma, meningioma, leukemia, lymphoma, leiomyosarcoma, rhabdomyosarcoma, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, papillary carcinoma, cystadenocarcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatocellular carcinoma, transitional cell carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, wilm's tumor, pleomorphic adenoma, liver cell papilloma, renal tubular adenoma, cystadenoma, papilloma, adenoma, leiomyoma, rhabdomyoma, hemangioma, lymphangioma, osteoma, chondroma, lipoma and fibroma.