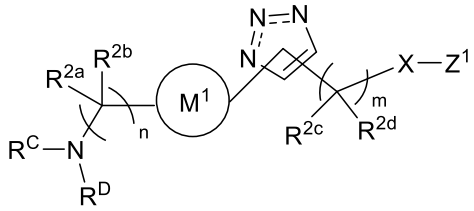
CLAIMS

1. A compound of Formula (II-c):



Formula (II-c), or a salt thereof, wherein:

Ring M^1 is aryl, each of which is optionally substituted with 1-5 R^3;

Z^1 is alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, each of which is optionally substituted by one or more R^5;

X is absent or O;

each of R^{2a}, R^{2b}, R^{2c}, and R^{2d} is independently hydrogen, alkyl, alkenyl, alkynyl, heteroalkyl, halo, cyano, nitro, amino, cycloalkyl, heterocyclyl, aryl, or heteroaryl;

or R^{2a} and R^{2b} or R^{2c} and R^{2d} are taken together to form an oxo group; R^C and R^D are independently hydrogen, alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein each of alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with 1-6 R^6;

or R^C and R^D, taken together with the nitrogen atom to which they are attached, form a ring (e.g., a 5-7 membered ring), optionally substituted with 1-6 R^6;

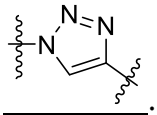
each of R^3, R^5, and R^6 is independently alkyl, alkenyl, alkynyl, heteroalkyl, halogen, cyano, azido, oxo, $–OR^{A1}$, $–C(O)OR^{A1}$, $–C(O)R^{B1}$,$–OC(O)R^{B1}$, $–N(R^{C1})(R^{D1})$, $–N(R^{C1})C(O)R^{B1}$, $–C(O)N(R^{C1})$, SR^{E1}, cycloalkyl, heterocyclyl, aryl, heteroaryl;

each of R^{10} and R^{11} is independently hydrogen, alkyl, alkenyl, alkynyl, heteroalkyl, halogen, $–C(O)R^{B1}$, $–N(R^{C1})C(O)R^{B1}$, $–C(O)N(R^{C1})$, SR^{E1}, $S(O)_x$, cycloalkyl, or heterocyclyl;

each R^{A1}, R^{B1}, R^{C1}, R^{D1}, and R^{E1} is independently hydrogen, alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, wherein each of alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl is optionally substituted with 1-6 R^7;

each R^7 is independently alkyl, alkenyl, alkynyl, heteroalkyl, halogen, cyano, oxo, hydroxyl, cycloalkyl, or heterocyclyl;

each m and n is independently 0, 1, 2, 3, 4, 5, or 6; and x is 1 or 2; and

wherein the triazolyl ring is .

2. The compound of claim 1, wherein M^2 is phenyl.

3. The compound of any one of the preceding claims, wherein each of R^{2a}, R^{2b}, R^{2c}, and R^{2d} is independently hydrogen or alkyl or one of R^{2a} and R^{2b} or R^{2c} and R^{2d} are taken together to form an oxo group.

4. The compound of claim 3, wherein each of R^{2a}, R^{2b}, R^{2c}, and R^{2d} is independently hydrogen.

5. The compound of any one of the preceding claims, wherein each of m and n is 1.

6. The compound of any one of the preceding claims, wherein Z^1 is heterocyclyl (e.g., 6-membered heterocyclyl).

7. The compound of claim 6, wherein Z^1 is a nitrogen-containing heterocyclyl, an oxygen-containing heterocyclyl, or a sulfur-containing heterocyclyl (e.g., oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, thiomorpholinyl-1,1-dioxide, piperidinyl, piperazinyl, or pyrrolidinyl).

8. The compound of any one of claims 1-5, wherein Z^1 is aryl (e.g., phenyl).

9. The compound of claim 8, wherein Z^1 is monosubstituted phenyl (e.g., with 1 R^5).

10. The compound of claim 8, wherein Z^1 is monosubstituted phenyl, wherein the 1 R^5 an amine-containing group (e.g., NH_2) or an oxygen-containing group (e.g., OCH_3).

11. The compound of any one of claims 9-10, wherein the 1 R^5 is in the ortho position or the para position.

12. The compound of any one of the preceding claims, wherein the compound (e.g., the compound of Formula (I)) is disposed on a surface, e.g., an inner or outer surface, of a device.

13. The compound of any one of the preceding claims, wherein the compound is selected from a compound depicted in any one of Figures 1-6, or a pharmaceutically acceptable salt thereof.

14. A pharmaceutical composition comprising a compound of any one of the preceding claims and a pharmaceutically acceptable excipient.

15. A composition for use in treating a disease, disorder, or condition, or modulating an immune response in a subject, e.g., at a site in the subject, e.g., the site of an implantable element (e.g., a device or material), comprising a compound of any one of claims 1-13 or a composition of claim 14.

16. The composition of claim 15, wherein the composition comprises an implantable element (e.g., a device or material, e.g., described herein).

17. The composition of any one of claims 15-16, wherein the composition is to be provided systemically or locally.

18. The composition of any one of claims 15-17, wherein the disorder or condition is, e.g., a condition characterized by unwanted immune response.

19. The composition of any one of claims 15-18, wherein the disorder or condition is, e.g., a condition characterized by an inadequate immune response.

20. The composition of any one of claims 15-19, wherein the composition is to be provided to downregulate an immune response.

21. The composition of any one of claims 15-19, wherein the composition is to be provided to upregulate an immune response.

22. The composition of any one of claim 15-21, wherein the composition reduces or is capable of reducing an unwanted reaction to the implantable element, e.g., reducing fibrosis or, inflammation at, or inactivation of, the implanted device or cell.

23. The composition of claim 16, wherein the implantable element (e.g., device or material) comprises a cell, e.g., a recombinant cell, which provides a substance, e.g., a therapeutic agent.

24. The composition of claim 23, wherein the cell is a retinal epithelial cell (e.g., a human RPE cell) or an RPE-like cell.

25. The composition of claims 22-24, wherein the cell comprises an exogenous nucleic acid (e.g., RNA (e.g., an mRNA) or DNA).

26. The composition of claim 25, wherein the exogenous nucleic acid encodes a polypeptide.

27. The composition of claim 26, wherein the polypeptide comprises an antibody (e.g., anti-nerve growth factor antibody).

28. The composition of claim 26, wherein the polypeptide is an enzyme (e.g., alpha-galactosidase).

29. The composition of claim 26, wherein the polypeptide comprises a clotting factor (e.g., a blood clotting factor, e.g., an activated blood clotting factor).

30. The composition of claim 26, wherein the polypeptide comprises Factor I, Factor II, Factor V, Factor VII, Factor VIII, Factor IX, Factor X, Factor XI, or Factor XIII.

31. The composition of claim 26, wherein the sequence of the polypeptide comprises at least one amino acid deletion, addition, or substitution relative to the sequence (e.g., naturally occurring human sequence) of Factor I, Factor II, Factor V, Factor VII, Factor VIII, Factor IX, Factor X, Factor XI, or Factor XIII.

32. The composition of claim 26, wherein the polypeptide is a replacement therapy or a replacement protein (e.g., a clotting factor, an enzyme, or an antibody).

33. The composition of any one of claims 26-32, wherein the disease is a blood clotting disease or a lysosomal storage disease (e.g., a hemophilia (e.g., Hemophilia A or Hemophilia B), Fabry Disease, Gaucher Disease, Pompe Disease, or MPS I).

34. The composition of claims 16-33, wherein the implantable element is to be provided as a prophylactic treatment.

35. The composition of claims 16-34, wherein the implantable element is formulated for injection into a subject (e.g., intraperitoneal, intramuscular, or subcutaneous injection).

36. The composition of claims 16-34, wherein the implantable element is formulated for implantation into a subject (e.g., into the peritoneal cavity, e.g., the lesser sac).

37. The composition of claims 16-36, wherein the implantable element is to be implanted or injected into the lesser sac, into the omentum, or into the subcutaneous fat of a subject.

38. The composition of claims 16-37, wherein the implantable element is to be administered to a first subject having less than about 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 2%, or 1% of the polypeptide (e.g., a blood clotting factor, e.g., Factor I, Factor II, Factor V, Factor VII, Factor VIII, Factor IX, Factor X, Factor XI, or Factor XIII) relative to a second subject (e.g., a healthy subject), e.g., as determined by a blood test.

39. The composition of claims 16-38, wherein the level of a biomarker (e.g., a serum biomarker) in a subject is to be monitored, e.g., in order to determine the level of efficacy of treatment.

40. An implantable element (e.g., a device or a material) comprising a compound of any one of claims 1-13 or a composition of claim 14.

41. A device comprising a compound of any one of claims 1-13 or a composition of claim 14.

42. The device of claim 41, wherein the compound is disposed on a surface, e.g., an inner or outer surface, of the device.

43. The device of any one of claims 41-42, wherein the compound is distributed evenly across the surface.

44. The device of any one of claims 41-42, wherein the compound is distributed unevenly across the surface.

45. The device of any one of claims 41-44, wherein the device is to be administered or to be provided to a subject for the treatment of a disease, disorder, or condition.

46 The device of any one of claims 41-45, wherein a first portion of the surface of the device comprises a compound of Formula (I) that modulates, e.g., down regulates or upregulates, an immune response and a second portion of the device lacks the compound, or has substantially lower density of the compound.

47. The device of any one of claims 41-45, wherein a first portion of the surface of the device comprises a compound of Formula I that modulates, e.g., down regulates, an immune response and a second portion of the surface comprises a second compound of Formula I, e.g., that

upregulates the immune response, second portion of the device lacks the compound, or has substantially lower density of the compound.

48. The device of any one of claims 41-47, wherein the device comprises a cell, e.g., a recombinant cell, which provides a substance, e.g., a therapeutic agent

49. The device of claim 48, wherein the cell is a retinal epithelial cell (e.g., a human RPE cell) or an RPE-like cell.

50. The device of claims 48-49 wherein the cell comprises an exogenous nucleic acid (e.g., RNA (e.g., an mRNA) or DNA).

51. The device of claim 50, wherein the exogenous nucleic acid encodes a polypeptide.

52. The device of claim 51, wherein the polypeptide comprises an antibody (e.g., anti-nerve growth factor antibody).

53. The device of claim 51, wherein the polypeptide is an enzyme (e.g., alpha-galactosidase).

54. The device of claim 51, wherein the polypeptide comprises a clotting factor (e.g., a blood clotting factor, e.g., an activated blood clotting factor).

55. The device of claim 51, wherein the polypeptide comprises Factor I, Factor II, Factor V, Factor VII, Factor VIII, Factor IX, Factor X, Factor XI, or Factor XIII.

56. The device of claim 51, wherein the sequence of the polypeptide comprises at least one amino acid deletion, addition, or substitution relative to the sequence (e.g., naturally occurring human sequence) of Factor I, Factor II, Factor V, Factor VII, Factor VIII, Factor IX, Factor X, Factor XI, or Factor XIII.

57. The device of claim 51, wherein the polypeptide is a replacement therapy or a replacement protein (e.g., a clotting factor, an enzyme, or an antibody).

58. The device of any one of claims 45-57, wherein the disease is a blood clotting disease or a lysosomal storage disease (e.g., a hemophilia (e.g., Hemophilia A or Hemophilia B), Fabry Disease, Gaucher Disease, Pompe Disease, or MPS I).

59. The device of claims 41-58, wherein the device is to be provided as a prophylactic treatment.

60. The device of claims 41-59, wherein the device is formulated for injection into a subject (e.g., intraperitoneal, intramuscular, or subcutaneous injection).

61. The device of claims 41-59 wherein the device is formulated for implantation into a subject (e.g., into the peritoneal cavity, e.g., the lesser sac).

62. The device of claims 41-61, wherein the device is to be implanted or to be injected into the lesser sac, into the omentum, or into the subcutaneous fat of a subject.