**[006]** RNA represents another biopolymer that all living things require. RNA is canonically made up of four bases, but post-transcriptional modifications (PTMs) can dramatically expand the chemical diversity of RNA. So far, greater than 100 PTMs having been identified (See e.g., Frye et. al, 2018; Machnicka et. al, 2013; Nachtergaele, 2016). The use of non-canonical or non-natural nucleotides further adds to the chemical diversity of RNA. In addition to being messengers, RNAs can function as scaffolds, molecular decoys, enzymes, and network regulators across the nucleus and cytosol (See e.g., Cech and Steitz, 2014; Sharp, 2009; Wang and Chang, 2011).

**[007]** DNA is another biopolymer central to all known forms of life. DNA provides organisms with the instructions it needs to carry out functions for development, survival, and reproduction.

**[008]** RNA and DNA are both nucleic acids, though they have several differences. The bases they are canonically limited to differ. They also contain different sugars. DNA is traditionally confined to the nucleus of a cell, but RNA is capable of leaving the nucleus.

**[009]** There remains a need for therapeutic methods of and compositions for delivering nucleic acids to specific cells in the body of a subject.

## SUMMARY

**[0010]** The disclosure relates to novel conjugates between asparagine-linked (N-linked) glycans and nucleic acids (DNA, RNA) linked, e.g., via biorthogonal click chemistry. It is important to develop such novel conjugates, which may modulate the biophysical properties of the conjugates, for example, modulate the stability of the nucleic acids in biological systems (e.g., serum) and/or modulate delivery of the nucleic acids (e.g., targeted delivery to specific membranes, organelles). In one example, the present disclosure provides a pharmaceutical composition comprising a modified RNA comprising a glycan moiety. In some examples, the pharmaceutical composition comprises a modified RNA comprising a glycan moiety comprising at least 6 monosaccharides. In some examples, the pharmaceutical composition further comprises a pharmaceutically acceptable carrier. The pharmaceutical composition can comprise a glyconucleic acid comprising a nucleic acid and at least one glycan moiety comprising at least 6 monosaccharides conjugated to the nucleic acid, and a pharmaceutically acceptable carrier. The glycan moiety can comprise at least 8 monosaccharides. The glycan moiety can comprise at least 10 monosaccharides. The glycan moiety can comprise an N-linked glycan or an O-linked glycan.

**[0011]** The glycan moiety can comprise a bi-antennary glycan. The bi-antennary glycan can comprise a first terminal residue and a second terminal residue. The glycan moiety can comprise a tri-antennary glycan. The tri-antennary glycan can comprise a first terminal residue, a second terminal residue and a third terminal residue.

**[0012]** In some examples, the glycan moiety comprises sialic acid, fucose, or a combination thereof.

In some examples, the glycan moiety comprises GlcNAc, mannose, galactose, sialic acid, fucose, or a combination thereof. At least one of the first terminal residue, the second terminal residue and the third terminal residue, if present, can comprise sialic acid. At least one of the first terminal residue, the second terminal residue and the third terminal residue, if present, can comprise fucose. At least one of the first terminal residue, the second terminal residue and the third terminal residue, if present, can comprise GlcNAc. At least one of the first terminal residue, the second terminal residue and the third terminal residue, if present, can comprise mannose. At least one of the first terminal residue, the second terminal residue and the third terminal residue, if present, can comprise NeuNAc. At least one of the first terminal residue, the second terminal residue and the third terminal residue, if present, can comprise galactose.

**[0013]** The nucleic acid of the pharmaceutical composition can be an RNA. The nucleic acid of the pharmaceutical composition can be an siRNA. The nucleic acid of the pharmaceutical composition can be an mRNA. The nucleic acid of the pharmaceutical composition can be a circular RNA. The nucleic acid of the pharmaceutical composition can be a guide RNA. The nucleic acid of the pharmaceutical composition can be an aptamer RNA. The nucleic acid of the pharmaceutical composition can be an DNA.

**[0014]** The at least one glycan moiety can comprise a compound of Table 2A or 2B. The modified nucleic acid can comprise a nucleic acid of Table 1. The at least one glycan moiety can be conjugated to the modified nucleic acid via a click-chemistry reaction. The nucleic acid can be conjugated to the glycan via a linker group covalently bound to a terminus of the nucleic acid. The nucleic acid can be conjugated to the glycan via a linker covalently bound to a chemically modified nucleotide in the middle of the nucleic acid. The nucleic acid can be conjugated to the glycan via a linker covalently bound to a chemically modified nucleotide that is not located at the 3' terminal or the 5' terminal of the nucleic acid. The nucleic acid can be conjugated to the glycan via a chemical handle inserted between two nucleotides of the nucleic acid. In examples, the two nucleotides do not include nucleotides at the 3' terminal or the 5' terminal of the nucleic acid.

**[0015]** In another example, provided herein are compounds of Formula (I):

A-L-B (I),

or a salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, or an isotopically enriched derivative thereof, wherein:

A is a nucleic acid of deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) comprising a first click-chemistry handle;

B is an asparagine-linked glycan (N-glycan) comprising a second click-chemistry handle; and

L comprises a linker formed by a biorthogonal click chemistry reaction between the first

click-chemistry handle and the second click-chemistry handle.

**[0016]** Also provided herein are methods of preparing a compound of Formula (I), the method comprising reacting nucleic acid A, comprising a first click-chemistry handle with compound B, which is an asparagine-linked glycan (N-glycan) comprising a second click-chemistry handle; wherein the reaction of the first step is carried out under biorthogonal click chemistry conditions.

**[0017]** The glyconucleic acid compound can have Formula (I): **A-L-B** (I), or a salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, or an isotopically enriched derivative thereof, wherein: **A** is a nucleic acid comprising a first click-chemistry handle; **B** is an asparagine-linked glycan (N-glycan) comprising a second click-chemistry handle; and **L** comprises a linker formed by a biorthogonal click chemistry reaction between the first click-chemistry handle and the second click-chemistry handle. A can be an RNA comprising a first click-chemistry handle. A can be an siRNA comprising a first click-chemistry handle. A can be an mRNA comprising a first click-chemistry handle. A can be a circular RNA comprising a first click-chemistry handle. A can be a DNA comprising a first click-chemistry handle.

**[0018]** A can comprise a first click-chemistry handle selected from those listed in Table 4 under "Reagent A", and B can comprise a second click-chemistry handle selected from those listed in Table 4 under "Reagent B". A can comprise a first click-chemistry handle selected from those listed in Table 4 under "Reagent B", and B can comprise a second click-chemistry handle selected from those listed in Table 4 under "Reagent A". B can be an asparagine linked glycan comprising a bi-antennary glycan, wherein the bi-antennary glycan comprises a first terminal residue and a second terminal residue. B can be an asparagine linked glycan comprising a tri-antennary glycan, wherein the tri-antennary glycan comprises a first terminal residue, a second terminal residue and a third terminal residue.

**[0019]** At least one of the first terminal residue, the second terminal residue and the third terminal residue, if present, can comprise sialic acid. At least one of the first terminal residue, the second terminal residue and the third terminal residue, if present, can comprise fucose. At least one of the first terminal residue, the second terminal residue and the third terminal residue, if present, can comprise GlcNAc. At least one of the first terminal residue, the second terminal residue and the third terminal residue, if present, can comprise mannose. At least one of the first terminal residue, the second terminal residue and the third terminal residue, if present, can comprise NeuNAc. At least one of the first terminal residue, the second terminal residue and the third terminal residue, if present, can comprise galactose.

**[0020]** The disclosure also relates to methods of treating a disease or condition comprising administering to a subject in need thereof a therapeutically effective amount of the pharmaceutical composition disclosed herein or the glyconucleic acid disclosed herein. The disease or condition can be selected from an inflammation disorder, an autoimmune disease, a cancer, a metabolic disease, a clotting disease, an anti-clotting disease, an allergy, a viral disease, and a microbial infection. In examples, the disease or

condition is inflammation. In examples, the disease or condition is cancer. In examples, the disease or condition is an autoimmune disease. In examples, the disease or condition is an IgE-mediated allergy. In examples, the disease or condition is systemic lupus erythematosus. In examples, the disease or condition is a microbial infection. In examples, the disease or condition is a viral infection. In examples, the disease or condition is a metabolic disease.

**[0021]** In another example, provided are glycosylated ribonucleic acid (glycoRNA)-related methods and compositions. In certain examples, provided are methods for reducing interaction between glycan binding protein (GBP)-expressing cells and cells displaying cell surface glycosylated ribonucleic acids (glycoRNAs). In some examples, such methods comprise contacting the GBP-expressing cells and/or the cells displaying cell surface glycoRNAs with an agent that binds the GBP and/or cell surface glycoRNAs such that interaction between the GBP-expressing cells and the cells displaying cell surface glycoRNAs is reduced. Such methods may be performed in vitro, in vivo or ex vivo. Also provided are conjugates, fusion proteins and compositions that find use, e.g., in practicing the methods of the present disclosure. Methods of targeting an agent to GBP-expressing cells, and methods of assessing a biological sample for glycoRNAs are also provided.

**[0022]** The disclosure further relates to methods for reducing interaction between glycan binding protein (GBP)-expressing cells and cells displaying cell surface glycosylated ribonucleic acids (glycoRNAs), comprising: contacting the GBP-expressing cells with soluble glycoRNAs which bind to GBP expressed on the surface of the GBP-expressing cells, in an amount effective to reduce interaction between the GBP-expressing cells and the cells displaying cell surface glycoRNAs.

**[0023]** The soluble glycoRNAs can comprise RNAs from the Y RNA family. The soluble glycoRNAs can comprise Y5 RNAs. The soluble glycoRNAs can comprise snoRNAs, tRNAs, snRNAs, rRNAs, or any combination thereof. The soluble glycoRNAs can comprise soluble sialylated RNAs. The soluble sialylated RNAs can comprise Neu5Ac, Neu5Gc, or a combination thereof. The soluble glycoRNAs are conjugated to one or more agents. The one or more agents can comprise a therapeutic agent. The one or more agents comprise a detectable label. The GBPs comprise sialic acid-binding immunoglobulin-like lectins (Siglecs). The Siglecs can comprise Siglec-11. The Siglecs can comprise Siglec-14. The GBPs can comprise C-type lectins. The GBPs can comprise galectins. The GBPs can comprise selectins.

**[0023a]** Accordingly, in one aspect, the present disclosure provides a pharmaceutical composition comprising: a) a glyconucleic acid or salt thereof, the glyconucleic acid comprising: i) a short interfering RNA (siRNA)nucleic acid; and ii) at least one oligosaccharide glycan moiety comprising at least 6 monosaccharides, conjugated to the nucleic acida multiple antennary complex type N-glycan comprising at least one GlcNAc residue attached to the Manal-3 arm and at least one GlcNAc attached to the Manal-6 arm of a trimannose core; and b) a pharmaceutically acceptable carrier.

**[0023b]** In another aspect, the present disclosure provides a pharmaceutical composition comprising: a) a glyconucleic acid or salt thereof, the glyconucleic acid comprising: i) a short interfering RNA (siRNA); and ii) at least one oligosaccharide moiety comprising a hybrid type N-glycan comprising a trimannose core, at least one GlcNAc residue on the terminal end of the α1,3 mannose (Man α1,3) arm of the trimannose core and zero or more mannoses on the α1,6 mannose (Man α1,3) arm of the trimannose core, covalently bound to the siRNA; and b) a pharmaceutically acceptable carrier.

**[0023c]** In another aspect, the present disclosure provides a pharmaceutical composition comprising: a) a glyconucleic acid or salt thereof, the glyconucleic acid comprising: i) a short interfering RNA (siRNA); and ii) at least one oligosaccharide moiety comprising a high-mannose type N-glycan comprising four or more mannose residues on a di-GlcNAc oligosaccharide structure, covalently bound to the siRNA; and b) a pharmaceutically acceptable carrier.

**[0023d]** In another aspect, the present disclosure provides a method of making a glyconucleic acid of Formula (I): **A-L-B** (I), or a salt thereof, wherein: **A** is an siRNA; **B** is a multiple antennary complex type N-glycan, hybrid type N-glycan or a high mannose glycan; and **L** comprises a linker formed by a biorthogonal click chemistry reaction between: **a)** a polynucleotide that comprises the **A** and a first click-chemistry handle, and **b)** an oligosaccharide moiety that comprises **B** and a second click chemistry handle; the method comprising reacting a polynucleotide that comprises **A** and a first click-chemistry handle with a oligosaccharide moiety that comprises **B** and a second click-chemistry handle; wherein the reaction of the first step is carried out under biorthogonal click chemistry conditions.

**[0023e]** In another aspect, the present disclosure provides a pharmaceutical composition comprising a glyconucleic acid or salt thereof made by the method of the disclosure.

**[0023f]** In another aspect, the present disclosure provides a use of the pharmaceutical composition of the disclosure in the manufacture of a medicament for treating a disease or a condition, wherein the disease or condition is selected from an inflammation disorder, an autoimmune disease, a cancer, a metabolic disease, a clotting disease, an anti-clotting disease, an allergy, a viral disease, and a microbial infection.

**[0023g]** In another aspect, the present disclosure provides a pharmaceutical composition of the disclosure for use in therapy.

## BRIEF DESCRIPTION OF THE DRAWINGS

**[0024] FIGs. 1A-1D** are a schematic and blot images showing that $Ac_4$ManNAz, a glycan reporter, incorporates into mammalian cellular RNA. **FIG. 1A** is a schematic of an RNA extraction protocol. $Ac_4$ManNAz = peracetylated *N*-azidoacetylmannosamine. Prot.K = proteinase K. DBCO = dibenzocyclooctyne. **FIG. 1B** is an RNA blotting of RNA from HeLa cells treated with 100 μM

## CLAIMS

WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising:

a) a glyconucleic acid or salt thereof, the glyconucleic acid comprising:

i) a short interfering RNA (siRNA); and

ii) at least one oligosaccharide moiety comprising a multiple antennary complex type N-glycan comprising at least one GlcNAc residue attached to the Manal-3 arm and at least one GlcNAc attached to the Manal-6 arm of a trimannose core; and

b) a pharmaceutically acceptable carrier.

2. A pharmaceutical composition comprising:

a) a glyconucleic acid or salt thereof, the glyconucleic acid comprising:

i) a short interfering RNA (siRNA); and

ii) at least one oligosaccharide moiety comprising a hybrid type N-glycan comprising a trimannose core, at least one GlcNAc residue on the terminal end of the α1,3 mannose (Man α1,3) arm of the trimannose core and zero or more mannoses on the α1,6 mannose (Man α1,3) arm of the trimannose core, covalently bound to the siRNA; and

b) a pharmaceutically acceptable carrier.

3. A pharmaceutical composition comprising:

a) a glyconucleic acid or salt thereof, the glyconucleic acid comprising:

i) a short interfering RNA (siRNA); and

ii) at least one oligosaccharide moiety comprising a high-mannose type N-glycan comprising four or more mannose residues on a di-GlcNAc oligosaccharide structure, covalently bound to the siRNA; and

b) a pharmaceutically acceptable carrier.

4. The pharmaceutical composition of any one of claims 1-3, wherein the at least one oligosaccharide moiety comprises at least 6 monosaccharides.

5. The pharmaceutical composition of any one of claims 1-3, wherein the at least one oligosaccharide moiety comprises at least 8 monosaccharides.

6. The pharmaceutical composition of any one of claims 1-2, wherein the at least one oligosaccharide moiety comprises at least 10 monosaccharides.

7. The pharmaceutical composition of any one of claims 1-3, wherein at least one of the terminal residue of the multiple antennary complex type N-glycan or the hybrid type N-glycan comprises a monosaccharide selected from sialic acid, fucose, GlcNAc, mannose, and galactose.

8. The pharmaceutical composition of any one of claims 1-3, wherein the at least one oligosaccharide moiety is covalently bound to the siRNA via a click-chemistry reaction.

9. The pharmaceutical composition of any one of claims 1-3, wherein the siRNA is covalently bound to the oligosaccharide moiety via a linker group covalently bound to a terminus of the siRNA.

10. The pharmaceutical composition of any one of claims 1-3, wherein the siRNA is covalently bound to the oligosaccharide moiety via a linker covalently bound to a chemically modified nucleotide in the middle of the siRNA.

11. The pharmaceutical composition of any one of claims 1-3, wherein the siRNA is covalently bound to the oligosaccharide moiety via a chemical handle inserted between two nucleotides of the siRNA.

12. The pharmaceutical composition of claim 1, wherein the at least one-oligosaccharide moiety comprises a tetra-antennary complex type N-glycan, comprising a first terminal residue, a second terminal residue, a third terminal residue, and a fourth terminal residue.

13. The pharmaceutical composition of claim 12, wherein at least one of the first terminal residue, the second terminal residue, the third terminal residue, and the fourth terminal residue comprises a monosaccharide selected from sialic acid, GlcNAc, and galactose.

14. The pharmaceutical composition of claim 12, wherein at least one of the first terminal residue, the second terminal residue, the third terminal residue, and the fourth terminal residue comprises galactose.

15. The pharmaceutical composition of claim 12, wherein the at least one oligosaccharide moiety comprises a fucose linked to a GlcNAc residue in a core or a base region of the complex type N-glycan.

16. The pharmaceutical composition of claim 1, wherein the at least one oligosaccharide moiety comprises a bisecting complex type N-glycan.

17. The pharmaceutical composition of any one of claims 1-3, wherein the at least one oligosaccharide moiety comprises a fucose linked to a GlcNAc residue in a core or a base region of the complex type N-glycan, in a core or base region of the hybrid type N-glyncan, or in a core or base region of the high-mannose type N-glycan.

18. The pharmaceutical composition of claim 12, wherein at least one of the first terminal residue, the second terminal residue, the third terminal residue, and the fourth terminal residue comprises sialic acid.

19. The pharmaceutical composition of claim 12, wherein at least one of the first terminal residue, the second terminal residue, the third terminal residue, and the fourth terminal residue comprises GlcNAc.

20. The pharmaceutical composition of claim 12, wherein at least one of the first terminal residue, the second terminal residue, the third terminal residue, and the fourth terminal residue comprises mannose.

21. The pharmaceutical composition of any one of claims 1-3, wherein the at least one oligosaccharide moiety comprises a bi-antennary complex type N-glycan comprising a first terminal residue and a second terminal residue, a bi-antennary complex hybrid type N-glycan comprising a first terminal residue and a second terminal residue, or a bi-antennary complex high-mannose type N-glycan comprising a first terminal residue and a second terminal residue.

22. The pharmaceutical composition of claim 21, wherein at least one of the first terminal residue and the second terminal residue comprises a monosaccharide selected from sialic acid, GlcNAc and galactose.

23. The pharmaceutical composition of claim 21, wherein at least one of the first terminal residue and the second terminal residue comprises sialic acid.

24. The pharmaceutical composition of claim 21, wherein at least one of the first terminal residue and the second terminal residue comprises GlcNAc.

25. The pharmaceutical composition of claim 21, wherein at least one of the first terminal residue and the second terminal residue comprises mannose.

26. The pharmaceutical composition of claim 21, wherein the at least one oligosaccharide moiety comprises a fucose linked to a GlcNAc residue in a core or a base region of the bi-antennary N-glycan.

27. The pharmaceutical composition of any one of claims 1-3, wherein the at least one oligosaccharide moiety comprises a tri-antennary complex type N-glycan comprising a first terminal residue, a second terminal residue, and a third terminal residue, a tri-antennary complex hybrid type N-glycan comprising a first terminal residue, a second terminal residue, and a third terminal residue, or a tri-antennary complex high-mannose type N-glycan comprising a first terminal residue, a second terminal residue, and a third terminal residue.

28. The pharmaceutical composition of claim 27, wherein at least one of the first terminal residue and the second terminal residue comprises a monosaccharide selected from sialic acid, GlcNAc, and galactose.

29. The pharmaceutical composition of claim 27, wherein at least one of the first terminal residue, the second terminal residue, and the third terminal residue comprises sialic acid.

30. The pharmaceutical composition of claim 27, wherein at least one of the first terminal residue, the second terminal residue, and the third terminal residue comprises GlcNAc.

31. The pharmaceutical composition of claim 27, wherein at least one of the first terminal residue, the second terminal residue, and the third terminal residue comprises galactose.

32. The pharmaceutical composition of claim 27, wherein the at least one oligosaccharide moiety comprises a fucose linked to a GlcNAc residue in a core or a base region of the tri-antennary complex type N-glycan.

33. The pharmaceutical composition of claim 1, wherein the at least one oligosaccharide moiety comprises a glycan selected from G-1 (GlcNAc(b1-2)Man(a1-3)[GlcNAc(b1-2)Man(a1-6)]Man(b1-4)GlcNAc(b1-4)[Fuc(a1-6)]GlcNAc(b1-), G-2 (Neu5Ac(a2-6)Gal(b1-4)GlcNAc(b1-2)Man(a1-3)[Neu5Ac(a2-6)Gal(b1-4)GlcNAc(b1-2)Man(a1-6)]Man(b1-4)GlcNAc(b1-4)[Fuc(a1-6)]GlcNAc(b1-), G-4 (Gal(b1-4)GlcNAc(b1-2)Man(a1-3)[Gal(b1-4)GlcNAc(b1-2)Man(a1-6)][GlcNAc(b1-4)]Man(b1-4)GlcNAc(b1-4)GlcNAc(b1), G-5 (NeuNAc(a2-3)Gal(b1-4)GlcNAc(b1-2)Man(a1-3)[NeuNAc(a2-3)Gal(b1-4)GlcNAc(b1-2)Man(a1-6)]Man(b1-4)GlcNAc(b1-4)GlcNAc(b1-), G-8 (GlcNAc(b1-2)Man(a1-3)[GlcNAc(b1-2)Man(a1-6)]Man(b1-4)GlcNAc(b1-4)GlcNAc(b1-), G-9 (Gal(b1-4)GlcNAc(b1-2)Man(a1-3)[Gal(b1-4)GlcNAc(b1-2)Man(a1-6)]Man(b1-4)GlcNAc(b1-4)GlcNAc(b1-), G-10 (Neu5Ac(a2-6)Gal(b1-4)GlcNAc(b1-2)Man(a1-3)[Neu5Ac(a2-6)Gal(b1-4)GlcNAc(b1-2)Man(a1-6)]Man(b1-4)GlcNAc(b1-4)GlcNAc(b1-), G-11 (Gal(b1-4)GlcNAc(b1-2)Man(a1-3)[Gal(b1-4)GlcNAc(b1-2)Man(a1-6)]Man(b1-4)GlcNAc(b1-4)[Fuc(a1-6)]GlcNAc(b1-), and G-34 (Neu5Ac(a2-3)Gal(b1-4)GlcNAc(b1-2)Man(a1-3)[Neu5Ac(a2-3)Gal(b1-4)GlcNAc(b1-2)Man(a1-6)]Man(b1-4)GlcNAc(b1-4)GlcNAc(b1-).

34. A method of making a glyconucleic acid of Formula (I):

**A-L-B** (I),

or a salt thereof, wherein:

**A** is an siRNA;

**B** is a multiple antennary complex type N-glycan, hybrid type N-glycan or a high mannose glycan; and

**L** comprises a linker formed by a biorthogonal click chemistry reaction between:

**a)** a polynucleotide that comprises the **A** and a first click-chemistry handle, and

**b)** an oligosaccharide moiety that comprises **B** and a second click chemistry handle;

the method comprising reacting a polynucleotide that comprises **A** and a first click-chemistry handle with a oligosaccharide moiety that comprises **B** and a second click-chemistry handle; wherein the reaction of the first step is carried out under biorthogonal click chemistry conditions.

35. A pharmaceutical composition comprising a glyconucleic acid or salt thereof made by the method of claim 34.

36. The pharmaceutical composition of claim 3, wherein the at least one oligosaccharide moiety comprises a bi-antennary high-mannose type N-glycan comprising a first terminal residue and a second terminal residue.

37. The pharmaceutical composition of claim 3, wherein the at least one oligosaccharide moiety comprises a tri-antennary high-mannose type N-glycan comprising a first terminal residue, a second terminal residue, and a third terminal residue.

38. The pharmaceutical composition of claim 3, wherein the at least one oligosaccharide moiety comprises glycan Man(a1-6)[Man(a1-3)]Man(a1-6)[Man(a1-3)]Man(b1-4)GlcNAc(b1-4)GlcNAc(b1- (“G-7”).

39. Use of the pharmaceutical composition of any one of claims 1-33, or 35 to 38 in the manufacture of a medicament for treating a disease or a condition, wherein the disease or condition is selected from an inflammation disorder, an autoimmune disease, a cancer, a metabolic disease, a clotting disease, an anti-clotting disease, an allergy, a viral disease, and a microbial infection.

40. The pharmaceutical composition of any one of claims 1-33, or 35 to 38 for use in therapy.