CLAIMS

What is claimed is:

1. A small activating nucleic acid molecule targeting a promoter of THPO, a nucleic acid molecule encoding the small activating nucleic acid molecule, or a composition or formulation comprising the small activating nucleic acid molecule for use in the treatment of ~~method for treating~~ thrombocytopenia and/or a disease and condition related to insufficient or decreased expression of THPO protein in a subject~~, comprising administering to the subject a curative dose of a small activating nucleic acid molecule targeting a promoter of *THPO*, a nucleic acid molecule encoding the small activating nucleic acid molecule, or a composition or formulation comprising the small activating nucleic acid molecule~~.

2. The small activating nucleic acid molecule targeting a promoter of THPO, the nucleic acid molecule encoding the small activating nucleic acid molecule, or the composition or formulation comprising the small activating nucleic acid molecule for use ~~method~~ of claim 1, wherein the thrombocytopenia comprises thrombocytopenia caused ~~by various causes, such as~~ congenital (hereditary) or acquired thrombocytopenia, preferably thrombocytopenia caused by myelo-thrombocytopenia, increased peripheral platelet destruction, or splenic sequestration.

3. The small activating nucleic acid molecule targeting a promoter of THPO, the nucleic acid molecule encoding the small activating nucleic acid molecule, or the composition or formulation comprising the small activating nucleic acid molecule for use ~~method~~ of claim 1, wherein the thrombocytopenia includes~~, but is not limited to,~~ thrombocytopenia related to insufficient or decreased expression of THPO protein, thrombocytopenia caused by ~~various causes such as~~ immune thrombocytopenia, drug-induced thrombocytopenia, thrombotic thrombocytopenia purpura, or hereditary thrombocytopenia.

4. The small activating nucleic acid molecule targeting a promoter of THPO, the nucleic acid molecule encoding the small activating nucleic acid molecule, or the composition or formulation comprising the small activating nucleic acid molecule for use ~~method~~ of any one of claims 1 to 3, wherein the individual is a mammal.

5. The small activating nucleic acid molecule targeting a promoter of THPO, the nucleic acid

molecule encoding the small activating nucleic acid molecule, or the composition or formulation comprising the small activating nucleic acid molecule for use ~~method~~ of claim 4, wherein the individual is a human.

6. The small activating nucleic acid molecule targeting a promoter of THPO, the nucleic acid molecule encoding the small activating nucleic acid molecule, or the composition or formulation comprising the small activating nucleic acid molecule for use ~~method~~ of any one of claims 1 to 3, wherein the small activating nucleic acid molecule comprises a first nucleic acid strand and a second nucleic acid strand, the first nucleic acid strand having at least 75% (e.g., at least about 79%, about 80%, about 85%, about 90%, about 95%, about 99% or about 100%) homology or complementarity to continuous 16 to 35 nucleotides in length of any one of SEQ ID NO: 601 to SEQ ID NO: 605, and the first nucleic acid strand and the second nucleic acid strand complementarily form a double-stranded nucleic acid structure capable of activating the expression of *THPO* gene in a cell.

7. The small activating nucleic acid molecule targeting a promoter of THPO, the nucleic acid molecule encoding the small activating nucleic acid molecule, or the composition or formulation comprising the small activating nucleic acid molecule for use ~~method~~ of claim 6, wherein the first nucleic acid strand of the small activating nucleic acid molecule comprises or is selected from any nucleotide sequence selected from SEQ ID NOs: 1048 to SEQ ID NOs: 1489, and the second nucleic acid strand comprises or is selected from any nucleotide sequence selected from SEQ ID NOs: 1490 to SEQ ID NOs: 1931.

8. The small activating nucleic acid molecule targeting a promoter of THPO, the nucleic acid molecule encoding the small activating nucleic acid molecule, or the composition or formulation comprising the small activating nucleic acid molecule for use ~~method~~ of claim 6, wherein the first nucleic acid strand and the second nucleic acid strand are present on two different nucleic acid strands.

9. The small activating nucleic acid molecule targeting a promoter of THPO, the nucleic acid molecule encoding the small activating nucleic acid molecule, or the composition or formulation comprising the small activating nucleic acid molecule for use ~~method~~ of claim 6, wherein the first nucleic acid strand and the second nucleic acid strand are present on the same nucleic acid strand, preferably, the small activating nucleic acid molecule is a hairpin single-stranded nucleic acid

molecule, wherein the first nucleic acid strand and the second nucleic acid strand comprise complementary regions forming a double-stranded nucleic acid structure.

10. The small activating nucleic acid molecule targeting a promoter of THPO, the nucleic acid molecule encoding the small activating nucleic acid molecule, or the composition or formulation comprising the small activating nucleic acid molecule for use ~~method~~ of claim 1, wherein at least one strand of the small activating nucleic acid molecule has an overhang of 0 to 6 nucleotides in length at 3' terminus.

11. The small activating nucleic acid molecule targeting a promoter of THPO, the nucleic acid molecule encoding the small activating nucleic acid molecule, or the composition or formulation comprising the small activating nucleic acid molecule for use ~~method~~ of claim 10, wherein both strands of the small activating nucleic acid molecule have an overhang of 0 to 6 nucleotides in length at the 3' terminus, preferably an overhang of 2 or 3 nucleotides in length.

12. The small activating nucleic acid molecule targeting a promoter of THPO, the nucleic acid molecule encoding the small activating nucleic acid molecule, or the composition or formulation comprising the small activating nucleic acid molecule for use ~~method~~ of claim 6 or 7, wherein the first nucleic acid strand and the second nucleic acid strand independently have 16 to 35 nucleotides in length.

13. The small activating nucleic acid molecule targeting a promoter of THPO, the nucleic acid molecule encoding the small activating nucleic acid molecule, or the composition or formulation comprising the small activating nucleic acid molecule for use ~~method~~ of any of claims 1 to 12, wherein the small activating nucleic acid molecule comprises only natural non-chemically modified nucleotides, or wherein the small activating nucleic acid molecule for use comprises at least one modification, preferably, the modification is a chemical modification.

14. The small activating nucleic acid molecule targeting a promoter of THPO, the nucleic acid molecule encoding the small activating nucleic acid molecule, or the composition or formulation comprising the small activating nucleic acid molecule for use ~~method~~ of claim 13, wherein the chemical modification comprises or is selected from one or more modifications selected from the group consisting of:

(1) modification of a phosphodiester bond connecting nucleotides in the nucleotide sequence of

the small activating nucleic acid molecule;

(2) modification of 2'-OH of a ribose in the nucleotide sequence of the small activating nucleic acid molecule;

(3) modification of a base in the nucleotide sequence of the small activating nucleic acid molecule; and

(4) at least one nucleotide in the nucleotide sequence of the small activating nucleic acid molecule being a locked nucleic acid.

15. The small activating nucleic acid molecule targeting a promoter of THPO, the nucleic acid molecule encoding the small activating nucleic acid molecule, or the composition or formulation comprising the small activating nucleic acid molecule for use ~~method~~ of claim 13, wherein the chemical modification comprises one or more rmodifications selected from the group consisting of: 2'-fluoro modification, 2'-oxymethyl modification, 2'-oxyethylidene methoxy modification, 2,4'-dinitrophenol modification, locked nucleic acid (LNA), 2'-amino modification, 2'-deoxy modification, 5'-bromouracil modification, 5'-iodouracil modification, N-methyluracil modification, 2,6-diaminopurine modification, phosphorothioate modification, and boranophosphate modification.

16. The small activating nucleic acid molecule targeting a promoter of THPO, the nucleic acid molecule encoding the small activating nucleic acid molecule, or the composition or formulation comprising the small activating nucleic acid molecule for use ~~method~~ of claim 3, wherein the acquired thrombocytopenia includes~~, but is not limited to, thrombocytopenia~~ is caused by aplastic anemia, myelodysplastic syndrome, leukemia, drugs, infection, tumor diseases, radiotherapy, bone marrow transplantation and chronic liver diseases, ~~and~~ or immune thrombocytopenia, wherein the factors causing increased peripheral platelet destruction comprise thrombotic thrombocytopenia, heparin-induced thrombocytopenia, drug-induced thrombocytopenia, ITP, ~~and~~ or thrombotic thrombocytopenia purpura.

17. A small activating nucleic acid molecule targeting a promoter of THPO, a nucleic acid molecule encoding the small activating nucleic acid molecule, or a composition or formulation comprising the small activating nucleic acid molecule for use in ~~method for~~ activating/up-regulating the expression of *THPO* gene in a subject or a cell, ~~comprising~~ wherein ~~administering a~~ the small activating nucleic acid molecule~~ of the present invention~~, ~~a~~ the nucleic acid coding the

small activating nucleic acid molecule ~~of the present invention~~, or ~~a~~ the composition or formulation comprising the small activating nucleic acid molecule ~~of the present invention~~ is to be administered to the subject or the cell.

18. A nucleic acid coding the small activating nucleic acid molecule of any one of claims 1 to 17~~9~~.

19. A cell comprising the small activating nucleic acid molecule of any one of claims 1 to 17~~9~~ or a nucleic acid encoding the small activating nucleic acid molecule of any one of claims 1 to 17~~9~~.

~~20. A composition comprising the small activating nucleic acid molecule of any one of claims 1 to 9.~~

20.~~21.~~ A formulation comprising the small activating nucleic acid molecule of any one of claims 1 to 17~~9~~, wherein the formulation comprises a liposome, preferably an LNP-entrapped small activating nucleic acid molecule.