CLAIMS

1. A composition which comprises an apyrase and an annexin that binds phosphatidyl serine(PS) on the surface of activated platelets, said apyrase and annexin are present in amounts that are together effective to inhibit thrombosis without increasing bleeding.

2. The composition of claim 1 wherein the apyrase and annexin are present in equimolar amounts.

3. The composition of claim 2 wherein the apyrase and annexin are covalently coupled.

4. The composition of any of claims 1-3 wherein the apyrase is soluble CD39L3 or a modified form thereof with enhanced ADPase activity.

5. The composition of claim 4 wherein the apyrase is soluble CD39L3 in modified form wherein said modification consists of substitutions at amino acid positions 67 and 69.

6. The composition of claim 4 wherein said substitutions are R67G and T69R.

7. The composition of claim 6 wherein the apyrase is APT102 (SEQ ID NO:2).

8. The composition of any of claims 1-7 wherein the annexin is annexin IV or V.

9. The composition of any of claims 3-8 wherein the apyrase and annexin are covalently coupled through a linker peptide to form a fusion protein.

10. The composition of claim 9 wherein the linker peptide contains 3-30 amino acids.

11. The composition of claim 10 wherein the linker peptide contains 15-25 amino acids.

12. The composition of any of claims 9-11 wherein the linker peptide is resistant to hydrolysis in plasma and/or in cell culture supernatant.

13. The composition of claim 12 wherein the linker peptide has the amino acid sequence of SEQ ID NO:6.

14. The composition of claim 13 wherein the fusion protein is APT 402 (SEQ ID NO:10).

15. A nucleic acid that encodes the fusion protein as defined in any of claims 3-14.

16. The nucleic acid of claim 15 further comprising control sequences for expression.

17. Recombinant host cells or vectors that contain the nucleic acid of claim 16.

18. A method to produce a fusion protein that comprises apyrase and annexin covalently coupled through a linker peptide, which method comprises culturing the host cells of claim ~~15~~ 17 and recovering the fusion protein from the culture.

19. A fusion protein that comprises apyrase and annexin covalently coupled through a linker peptide produced by the method of claim 18.

20. ~~A~~ Use of a composition as defined in any of claims 1-14 or a fusion protein as defined in claim 19 in the manufacture of a medicament~~method~~ to treat a subject experiencing thrombosis or a subject undergoing surgery at risk for excessive bleeding ~~which method comprises administering to said subject an effective amount of the composition of any of claims 1-14 or the fusion protein of claim 19~~.

21. The ~~method~~ use of claim ~~18~~ 20 wherein ~~which method comprises administering to said subject~~ an effective amount of APT 402 (SEQ ID NO:10) is to be administered to said subject.

22. The use ~~method~~ of claim 21 wherein the medicament is to be administered ~~said administering is~~ intravenously ~~(IV)~~.

23. The use ~~method~~ of claim 22 wherein the medicament is to be administered by ~~said method is~~ bolus injection followed by intraveneous ~~IV~~ infusion.

24. ~~A~~Use of a combination of an apyrase and an annexin that binds phosphatidyl serine(PS) on the surface of activated platelets in the manufacture of a medicament ~~method~~ to treat a subject experiencing thrombosis or a subject undergoing surgery at risk for excessive bleeding, wherein said apyrase and annexin are to be administered in amounts that are together effective to inhibit thrombosis without increasing bleeding ~~which method comprises administering to said subject an effective amount of a combination of an apyrase and an annexin that binds phosphatidyl serine(PS) on the surface of activated platelets, in amounts of said apyrase and annexin that are together effective to inhibit thrombosis without increasing bleeding~~.

25. The ~~method~~ use of claim 24 wherein the apyrase is APT 102 (SEQ ID NO:2) and the annexin is annexin V.

26. The use ~~method~~ of claim 24 wherein ~~the administering is~~ said apyrase and annexin are to be administered simultaneously.

27. The use ~~method~~ of claim 24 wherein ~~the administering is~~ said apyrase and annexin are to be administered sequentially.