subjects. In yet another embodiment, the subject suffers from ischemic events.

[0014] In an aspect, the disclosure provides the use of a cysteamine, cystamine, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a subject suffering from ischemic injury or an acute ischemic event to reduce ischemic injury, wherein the subject has a thrombotic disorder, cancer, myeloproliferative disorder, multiple myeloma, surgery, trauma, heparin-induced thrombocytopenia, pregnancy, inflammatory bowel disease, nephrotic syndrome, paroxysmal nocturnal hemoglobinuria, hyperviscosity syndrome, or Waldenstrom's macroglobulinemia, or is immobilized, is using oral contraceptive, is taking thalidomide or its congeners optionally in combination with steroid, or wherein the ischemic injury is the result of a tissue injury, a disease or a stroke. In another ~~aspect~~embodiment, the disclosure provides the use of cysteamine, cystamine, or a pharmaceutically acceptable salt of any of the foregoing in the manufacture of a medicament for treating a subject at risk of thrombosis and ischemic injury resulting therefrom to reduce the risk of ischemic injury resulting from thrombosis. In another aspect, the disclosure provides the use of a cysteamine, cystamine, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a subject at risk of thrombosis to reduce the risk of ischemic injury due to thrombosis, wherein the subject has cancer, myeloproliferative disorder, multiple myeloma, surgery, trauma, heparin-induced thrombocytopenia, pregnancy, inflammatory bowel disease, nephrotic syndrome, paroxysmal nocturnal hemoglobinuria, hyperviscosity syndrome, or Waldenstrom's macroglobulinemia, or is immobilized, is using oral contraceptive, is taking thalidomide or its congeners optionally in combination with steroid, or wherein the ischemic injury is the result of a tissue injury, a disease or a stroke. In another aspect, the disclosure provides the use of a cysteamine, cystamine, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for increasing the ratio of low molecular weight (LMW) adiponectin levels to medium (MMW) and/or high molecular weight (HMW) adiponectin levels in a subject in need thereof, to increase the ratio of low molecular weight adiponectin levels compared to a baseline prior to contacting the subject with the cysteamine, cystamine, or a

pharmaceutically acceptable salt thereof, wherein the subject is not suffering from hypercholesterolemia or type II diabetes. In another aspect, the disclosure provides the use of a cysteamine, cystamine, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a subject having irregular or abnormal ratios of high molecular weight (HMW):medium molecular weight (MMW) adiponectin, HMW:low molecular weight (LMW) adiponectin, or MMW:LMW adiponectin, to improve adiponectin ratios in the subject compared to a subject that did not receive the cysteamine, cystamine, or a pharmaceutically acceptable salt thereof. In another aspect, the disclosure provides the use of a cysteamine, cystamine, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating an ischemic event in a subject, wherein the subject has improved behavioral outcome compared to a subject that did not receive the cysteamine, cystamine, or a pharmaceutically acceptable salt thereof, wherein the subject has a thrombotic disorder, cancer, myeloproliferative disorder, multiple myeloma, surgery, trauma, immobilization, oral contraceptive use, administration of thalidomide or its congeners optionally in combination with steroid, heparin-induced thrombocytopenia, pregnancy, inflammatory bowel disease, nephrotic syndrome, paroxysmal nocturnal hemoglobinuria, hyperviscosity syndrome, or Waldenstrom's macroglobulinemia, or wherein the ischemic event is the result of a tissue injury, a disease or a stroke. In another aspect, the disclosure provides the use of a cysteamine, cystamine, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for increasing adiponectin levels in a subject compared to a baseline prior to contacting the subject with the cysteamine, cystamine, or a pharmaceutically acceptable salt of any of the foregoing. The disclosure also provides a cysteamine, cysteamine derivative, cystamine, cystamine derivative or a pharmaceutically acceptable salt thereof for use in treating ischemia, ischemic injury, an acute ischemic event, thrombosis or ischemic injury resulting from thrombosis. In one embodiment, the ischemia or ischemic injury is the result of a thrombotic disorder. In another embodiment, the thrombotic disorder is sickle cell disease, deep vein thrombosis, pulmonary embolism, hypercoagulable state, thrombophilia, Factor V Leiden, Antithrombin III deficiency, Protein C deficiency, Protein S deficiency, Prothrombin gene

mutation (G20210A), Hyperhomcysteinemia, antiphospholipid antibody syndrome (APS), anticardiolipin antibody (ACLA) thrombosis syndrome, or lupus anticoagulant (LA) syndrome. In yet another embodiment, the cysteamine, cysteamine derivative, cystamine, cystamine derivative or a pharmaceutically acceptable salt thereof is cysteamine, a cysteamine derivative, or a pharmaceutically acceptable salt thereof. In yet a further embodiment, the ischemia is caused by a risk factor selected from the group consisting of high blood pressure, tobacco use, carotid or other artery disease, peripheral artery disease, atrial fibrillation, other heart disease, transient ischemic attacks (TIAs), a blood disorders, high blood cholesterol, physical inactivity, obesity, excessive alcohol use, illegal drug use, a prior stroke, Sickle Cell Anemia and prior heart attack. In another embodiment, the cysteamine, cysteamine derivative, cystamine, cystamine derivative or a pharmaceutically acceptable salt thereof is formulated for intraperitoneal administration. In any of the foregoing embodiments, the cysteamine, cysteamine derivative, cystamine, cystamine derivative or a pharmaceutically acceptable salt thereof is administered intravascularly. In yet a further embodiment of any of the foregong, the cysteamine, cysteamine derivative, cystamine, cystamine derivative or a pharmaceutically acceptable salt thereof is formulated for oral administration. In a further embodiment, the cysteamine, cysteamine derivative, cystamine, cystamine derivative or a pharmaceutically acceptable salt thereof is

Claims:

1. Use of a cysteamine, cystamine, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a subject suffering from ischemic injury or an acute ischemic event to reduce ischemic injury, wherein the subject has a thrombotic disorder, cancer, myeloproliferative disorder, multiple myeloma, surgery, trauma, heparin-induced thrombocytopenia, pregnancy, inflammatory bowel disease, nephrotic syndrome, paroxysmal nocturnal hemoglobinuria, hyperviscosity syndrome, or Waldenstrom's macroglobulinemia, or is immobilized, is using oral contraceptive, is taking thalidomide or its congeners optionally in combination with steroid, or wherein the ischemic injury is the result of a tissue injury, a disease or a stroke.

2. The use of claim 1 wherein the ischemic injury is the result of a thrombotic disorder.

3. The use of claim 2, wherein the thrombotic disorder is sickle cell disease, deep vein thrombosis, pulmonary embolism, cardiac embolism, hypercoagulable state, thrombophilia, Factor V Leiden, Antithrombin III deficiency, Protein C deficiency, Protein S deficiency, Prothrombin gene mutation (G20210A), Hyperhomcysteinemia, antiphospholipid antibody syndrome (APS), anticardiolipin antibody (ACLA) thrombosis syndrome, or lupus anticoagulant (LA) syndrome.

4. The use of any of claims 1 to 3, wherein the amount of a cysteamine, cystamine, or a pharmaceutically acceptable salt thereof is effective to reduce the risk of ischemic injury resulting from thrombosis.

5. Use of cysteamine, cystamine, or a pharmaceutically acceptable salt of any of the foregoing in the manufacture of a medicament for treating a subject at risk of thrombosis and ischemic injury resulting therefrom to reduce the risk of ischemic injury resulting from thrombosis.

~~6. The use of claim 4 or 5, wherein the subject has cancer, myeloproliferative disorder, multiple myeloma, surgery, trauma, immobilization, oral contraceptive use, administration of thalidomide or its congeners optionally in combination with steroid, heparin induced thrombocytopenia, pregnancy, inflammatory bowel disease, nephrotic syndrome, paroxysmal nocturnal~~

~~hemoglobinuria, hyperviscosity syndrome, or Waldenstrom's macroglobulinemia.~~

~~7~~6. Use of a cysteamine, cystamine, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a subject at risk of thrombosis to reduce the risk of ischemic injury due to thrombosis, wherein the subject has cancer, myeloproliferative disorder, multiple myeloma, surgery, trauma, heparin-induced thrombocytopenia, pregnancy, inflammatory bowel disease, nephrotic syndrome, paroxysmal nocturnal hemoglobinuria, hyperviscosity syndrome, or Waldenstrom's macroglobulinemia, or is immobilized, is using oral contraceptive, is taking thalidomide or its congeners optionally in combination with steroid, or wherein the ischemic injury is the result of a tissue injury, a disease or a stroke.

~~8. The use of claim 7, wherein the subject has cancer, myeloproliferative disorder, multiple myeloma, surgery, trauma, immobilization, oral contraceptive use, administration of thalidomide or its congeners optionally in combination with steroid, heparin-induced thrombocytopenia, pregnancy, inflammatory bowel disease, nephrotic syndrome, paroxysmal nocturnal hemoglobinuria, hyperviscosity syndrome, or Waldenstrom's macroglobulinemia.~~

~~9. The use of claims 1 or 7, wherein the ischemic injury is the result of a tissue injury, a disease or a stroke.~~

~~10~~7. The use of claim ~~9~~1 or 6, wherein the injury is a reperfusion injury.

~~11~~8. The use of claim ~~10~~7, wherein the reperfusion injury is a result of surgery or organ transplant.

~~12~~9. The use of claim ~~9~~1 or 6, wherein the disease is Sickle Cell Disease.

~~13~~10. The use of any one of claims 1 to ~~12~~9, wherein the cysteamine, cystamine, or a pharmaceutically acceptable salt thereof is administered within 72 hours after an ischemic event.

~~14~~11. The use of any one of claims 1 to ~~13~~10, wherein the cysteamine, cystamine,

or a pharmaceutically acceptable salt thereof is administered continuously after an ischemic event.

~~15~~12. The use of any one of claim 1 to ~~12~~9, wherein the cysteamine, cystamine, or a pharmaceutically acceptable salt thereof is administered continuously to a subject at risk of an ischemic event.

~~16~~13. Use of a cysteamine, cystamine, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for increasing the ratio of low molecular weight (LMW) adiponectin levels to medium (MMW) and/or high molecular weight (HMW) adiponectin levels in a subject in need thereof, to increase the ratio of low molecular weight adiponectin levels compared to a baseline prior to contacting the subject with the cysteamine, cystamine, or a pharmaceutically acceptable salt thereof, wherein the subject is not suffering from hypercholesterolemia or type II diabetes.

~~17~~14. Use of a cysteamine, cystamine, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a subject having irregular or abnormal ratios of high molecular weight (HMW):medium molecular weight (MMW) adiponectin, HMW:low molecular weight (LMW) adiponectin, or MMW:LMW adiponectin, to improve adiponectin ratios in the subject compared to a subject that did not receive the cysteamine, cystamine, or a pharmaceutically acceptable salt thereof.

~~18~~15. The use of claim 1, 5, ~~7~~6, ~~16~~13 or ~~17~~14, wherein the subject has a risk factor for ischemia selected from the group consisting of high blood pressure, tobacco use, carotid or other artery disease, peripheral artery disease, atrial fibrillation, other heart disease, transient ischemic attacks (TIAs), a blood disorders, high blood cholesterol, physical inactivity, obesity,

excessive alcohol use, illegal drug use, a prior stroke, Sickle Cell Anemia and prior heart attack.

~~19~~16. The use of claim ~~16~~13 or ~~17~~14, wherein the subject has previously suffered from an ischemic event.

~~20~~17. The use of any of the preceding claims, wherein cysteamine or a pharmaceutically acceptable salt thereof is to be administered.

~~21~~18. The use of any of the preceding claims, wherein the cysteamine, cystamine, or a pharmaceutically acceptable salt of any of the foregoing, is to be administered at a concentration in the range of about 0.5-20 mg/kg of body weight of said subject.

~~22~~19. The use of any of claims 1-~~20~~17, wherein the total daily dose of the cysteamine, cystamine, or a pharmaceutically acceptable salt of any of the foregoing, is about 0.5-4.0 g/m^2.

~~23~~20. The use of any of the preceding claims, wherein the cysteamine, cystamine, or a pharmaceutically acceptable salt of any of the foregoing, is to be administered orally.

~~24~~21. The use of claim ~~23~~20, wherein the cysteamine, cystamine or a pharmaceutically acceptable salt of any of the foregoing, is a delayed or controlled release dosage form.

~~25~~22. The use of any of claims 1-~~22~~19, wherein the cysteamine, cystamine or a pharmaceutically acceptable salt of any of the foregoing, is to be administered intraperitoneally.

~~26~~23. The use of claim ~~25~~22, wherein the cysteamine, cystamine or a pharmaceutically acceptable salt of any of the foregoing, is to be administered intravenously or intra-arterially.

~~27~~24. The use of any one of claims 1 to ~~26~~23, wherein the medicament results in a reduction in ischemia reperfusion injury or inflammation from an ischemic event.

~~28~~25. The use of any one of claims 1 to ~~27~~24, wherein the medicament further comprises one or more additional agents useful to treat ischemia.

~~29~~26. The use of claim ~~28~~25, wherein the one or more additional agents is selected from the group consisting of a reperfusion agent, a free-radical scavenger agent, and a spin trap agent, a neuroprotective agent, an anticoagulant, an antiplatelet agent, nimodipine, and naloxone.

~~30~~27. The use of any one of claims 1 to ~~29~~26, wherein the medicament further comprises one or more agents useful to treat a thrombotic disorder, optionally an anticoagulant, heparin, a vitamin K antagonist, 4-hydroxycoumarin derivatives, warfarin, acenocoumarol, dicumarol, ethyl biscoumacetate, phenprocoumon, streptokinase, urokinase, tissue plasminogen activator (tPA), alteplase (recombinant tPA), reteplase, tenecteplase, and argatroban.

~~31~~28. The use of any one of claims ~~23–~~20 or ~~24~~21, wherein the cysteamine, cystamine or a pharmaceutically acceptable salt of any of the foregoing, is to be administered less than four times per day.

~~32~~29. The use of any one of claims ~~31~~28, wherein the cysteamine, cystamine or pharmaceutically acceptable salt is to be administered twice daily.

~~33~~30. The use of any of the foregoing claims, wherein the cysteamine, cystamine, or a pharmaceutically acceptable salt thereof is to be administered continuously for a period of days, weeks or months.

~~34~~31. Use of a cysteamine, cystamine, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating an ischemic event in a subject, wherein the subject has improved behavioral outcome compared to a subject that did not receive the cysteamine, cystamine, or a pharmaceutically acceptable salt thereof, wherein the subject has a thrombotic disorder, cancer, myeloproliferative disorder, multiple myeloma, surgery, trauma, heparin-induced thrombocytopenia, pregnancy, inflammatory bowel disease, nephrotic syndrome, paroxysmal nocturnal hemoglobinuria, hyperviscosity syndrome, or Waldenstrom's macroglobulinemia, or is immobilized, is using oral contraceptive, is taking thalidomide or its congeners optionally in combination with steroid, or wherein the ischemic event is the result of a tissue injury, a disease or a stroke.

~~35~~32. The use of claim ~~34~~31, wherein the medicament increases the subject's adiponectin levels.

~~36~~33. The use of claim ~~34~~31 or ~~35~~32, wherein the total daily dose of the cysteamine, cystamine, or a pharmaceutically acceptable salt thereof is about 0.5-4.0 g/m^2.

~~37~~34. The use of any of claims ~~34~~31 to ~~36~~33, wherein the cysteamine, cystamine, or a pharmaceutically acceptable salt thereof is to be administered intraperitoneally.

~~38~~35. The use of any of claims ~~34~~31 to ~~37~~34, wherein cysteamine, cystamine, or a pharmaceutically acceptable salt thereof is to be administered orally.

~~39~~36. The use of any of claims ~~34~~31 to ~~38~~35, wherein the cysteamine, cystamine, or a pharmaceutically acceptable salt thereof is a delayed or controlled release dosage form that provides increased delivery of the

cysteamine, cystamine, or a pharmaceutically acceptable salt thereof to the small intestine.

~~40~~37. The use of claim ~~39~~36, wherein the delayed or controlled release dosage form comprises an enteric coating that releases the cysteamine, cystamine, or a pharmaceutically acceptable salt thereof when the cysteamine, cystamine, or a pharmaceutically acceptable salt thereof reaches the small intestine or a region of the gastrointestinal tract of a subject in which the pH is greater than about pH 4.5.

~~41~~38. The use of claim ~~42~~37, wherein the enteric coating is a coating selected from the group consisting of polymerized gelatin, shellac, methacrylic acid copolymer type C NF, cellulose butyrate phthalate, cellulose hydrogen phthalate, cellulose proprionate phthalate, polyvinyl acetate phthalate (PVAP), cellulose acetate phthalate (CAP), cellulose acetate trimellitate (CAT), hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate, dioxypropyl methylcellulose succinate, carboxymethyl ethylcellulose (CMEC), hydroxypropyl methylcellulose acetate succinate (HPMCAS) , and acrylic acid polymers and copolymers, typically formed from methyl acrylate, ethyl acrylate, methyl methacrylate and/or ethyl methacrylate with copolymers of acrylic and methacrylic acid esters.

~~42~~39. The use of any of the foregoing claims, wherein when the cysteamine, cystamine, or a pharmaceutically acceptable salt thereof is to be administered orally, the cysteamine, cystamine, or a pharmaceutically acceptable salt thereof is to be administered with a bioavailable iron formulation.

~~43~~40. The use of any of the foregoing claims, wherein the medicament results in a reduction in inflammation from the ischemic event.

~~44~~41. The use of claim ~~18~~15, wherein the cysteamine, cystamine, or a pharmaceutically acceptable salt thereof is to be administered chronically.

~~45~~42. The use of claim 1, 5, ~~7~~6, ~~16~~13 or ~~17~~14, wherein the cysteamine, cystamine, or a pharmaceutically acceptable salt thereof is to be administered acutely.

~~46~~43. Use of a cysteamine, cystamine, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for increasing adiponectin levels in a subject compared to a baseline prior to contacting the subject with the cysteamine, cystamine, or a pharmaceutically acceptable salt of any of the foregoing.

~~47~~44. The use of claim ~~46~~43, wherein the total adiponectin levels are increased.

~~48~~45. The use of claim ~~46~~43, wherein the ratio of lower molecular weight adiponectin is increased.

~~49~~46. The use of claim ~~48~~45, wherein the subject is obese and has low LMW adiponectin levels compared to healthy subjects.

~~50~~47. The use of claim ~~48~~45, wherein the subject has diabetes and has low LMW adiponectin levels compared to healthy subjects.

~~51~~48. The use of claim ~~46~~43, wherein the subject suffers from ischemic events.