Claims:

1. A double-stranded nucleic acid molecule comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand are selected from the ~~a sense strand and an antisense strand, wherein the sense strand and the antisense strand are selected from an~~ oligonucleotides described as RHOA_48 (SEQ ID NOS: 79 and 113) or the oligonucleotides described as RHOA_48u (SEQ ID NOS: 80 and 114); or a pharmaceutically acceptable salt of such nucleic acid molecule;

wherein the double-stranded nucleic acid molecule has the structure:

5′ UGUAGCAAGAUGACUUCUG -Z 3′ (antisense SEQ ID NO:113)
||||||||||||||||||||
3′ Z′-ACAUCGUUCUACUGAAGAC -z″ 5′ (sense SEQ ID NO:79)

or

5′ AGUAGCAAGAUGACUUCUG -Z 3′ (antisense SEQ ID NO:114)
||||||||||||||||||||
3′ Z′-UCAUCGUUCUACUGAAGAC -z″ 5′ (sense SEQ ID NO:80)

wherein each "|" represents base pairing;

wherein each of A, C, G and U is independently an unmodified ribonucleotide, a modified ribonucleotide, or an unconventional moiety;

wherein each of Z and Z′ is independently 1-5 consecutive nucleotides or non-nucleotide moieties or a combination thereof covalently attached at the 3′ terminus of the strand in which it is present;

wherein z″ is a capping moiety covalently attached at the 5′ terminus of the sense strand.

~~2. The double-stranded nucleic acid molecule of claim 1 described as RHOA_48, wherein the antisense strand comprises the sequence 5′ UGUAGCAAGAUGACUUCUG 3′ (SEQ ID NO: 113) and wherein the sense strand comprises the sequence 5′ CAGAAGUCAUCUUGCUACA 3′ (SEQ ID NO: 79), or a pharmaceutically acceptable salt of such nucleic acid molecule.~~

~~3. The double-stranded nucleic acid of claim 2, having the structure:~~

~~**5' UGUAGCAAGAUGACUUCUG -Z 3' (antisense SEQ ID NO:113)**~~

~~3' Z'-ACAUCGUUCUACUGAAGAC -z" 5' (sense SEQ ID NO:79)~~

~~**wherein each " | " represents base pairing;**~~

~~**wherein each of A, C, G and U is independently an unmodified ribonucleotide, a modified ribonucleotide, or an unconventional moiety;**~~

~~**wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or non-nucleotide moieties or a combination thereof covalently attached at the 3' terminus of the strand in which it is present;**~~

~~**wherein z" may be present or absent, but if present is a capping moiety covalently attached at the 5' terminus of the sense strand; or**~~

~~**a pharmaceutically acceptable salt of such nucleic acid molecule.**~~

~~4~~2. The double-stranded nucleic acid molecule of claim ~~3~~1, wherein in the antisense strand a mirror nucleotide or a 2'-5' linked ribonucleotide is present in at least one of positions 5, 6, 7 or 8 (5'>3'), one or more 2'-O-Methyl sugar-modified ribonucleotide is present and Z is a nucleotide moiety or a non-nucleotide moiety ~~is~~ covalently attached at the 3' terminus; and

wherein in the sense strand ~~4 or 5 consecutive 2'-5' linked ribonucleotides are present at the 3' terminal or penultimate positions,~~ Z is a nucleotide or non-nucleotide moiety ~~is~~ covalently attached at the 3' terminus, one or more 2'-O-Methyl sugar-modified ribonucleotide is present, and z" is present~~; or~~

~~a pharmaceutically acceptable salt of such nucleic acid molecule~~.

3. The double-stranded nucleic acid molecule of claim 2, wherein in the sense strand 4 or 5 consecutive 2'-5' linked ribonucleotides are present at the 3' terminal or penultimate positions.

~~5~~4. The double-stranded nucleic acid molecule of claim ~~3~~4~~2~~, wherein in the antisense strand (5'>3') 2'-O-Methyl sugar-modified ribonucleotides are present at positions 1, 3, 11, 14, 15, 17 and 18 (5'>3'); and

wherein in the sense strand (5'>3') a 2'-O-Methyl sugar modified ribonucleotide is present at position 1~~, 2'-5' linked ribonucleotides are present at positions 15, 16, 17, 18 and 19~~; or

a pharmaceutically acceptable salt of such nucleic acid molecule.

5. The double-stranded nucleic acid molecule of claim 4, wherein in the sense strand 2'-5' linked ribonucleotides are present at positions 15, 16, 17, 18 and 19.

6. The double-stranded nucleic acid molecule of claim ~~5~~2, ~~wherein in the antisense strand a 2'-5' linked ribonucleotide is present at position 6; and~~

wherein in the sense strand Z' is a non-nucleotide C3Pi moiety ~~is~~ covalently attached to the 3 terminus~~, and wherein z" is an inverted abasic deoxyribonucleotide~~; or

a pharmaceutically acceptable salt of such nucleic acid molecule.

7. The double-stranded nucleic acid molecule of claim 6, wherein z" is selected from the group consisting of abasic moiety, an inverted abasic moiety, an inverted abasic deoxyribonucleotide, a C6 amino and a mirror nucleotide.

~~7~~8. The double-stranded nucleic acid molecule of claim ~~5~~2, wherein in the antisense strand a 2'-5' linked ribonucleotide

is present at position 6, at position 7 or at positions 6 and 7; or a pharmaceutically acceptable salt of such nucleic acid molecule.

~~8~~9. The double-stranded nucleic acid molecule of claim 3,

wherein in the antisense strand ~~2'-O-Methyl sugar-modified ribonucleotides are present at positions 1, 3, 11, 14, 15, 17 and 18 (5'>3'),~~ a 2'-5' linked ribonucleotide is present at position 6, and Z is a C3Pi-C3OH moiety covalently attached to the 3' terminus; and

wherein in the sense strand ~~a 2'-O-Methyl sugar-modified ribonucleotide is present at position 1 (5'>3'), 2'-5' linked ribonucleotides are present at positions 15, 16, 17, 18 and 19 (5'>3'),~~ Z' is a C3Pi moiety covalently attached at the 3' terminus, and z" is an inverted abasic deoxyribonucleotide capping moiety; or

a pharmaceutically acceptable salt of such nucleic acid molecule.

10. The double-stranded nucleic acid molecule of claim 9, wherein in the antisense strand the 5' terminus is phosphorylated; or a pharmaceutically acceptable salt of such nucleic acid molecule.

~~9~~11. The double-stranded nucleic acid molecule of claim ~~3~~9, wherein in the antisense strand 2'-O-Methyl sugar-modified ribonucleotides are present at positions 1, 3, 11, 14, 15, 17 and 18 (5'>3'), ~~a 2'-5' linked ribonucleotide is present at position 6,~~ Z is a C3Pi-C3OH moiety covalently attached to the 3' terminus~~, and the 5' terminus is phosphorylated~~; and

wherein in the sense strand ~~a 2'-O-Methyl sugar-modified ribonucleotide is present at position 1 (5'>3'),~~ 2'-5' linked ribonucleotides are present at positions 15, 16, 17, 18 and 19 (5'>3'), Z' is a ~~C3Pi~~ capping moiety covalently attached at the ~~3~~ 5' terminus~~, and z" is an inverted abasic deoxyribonucleotide capping moiety~~; or

a pharmaceutically acceptable salt of such nucleic acid molecule.

10. The double-stranded nucleic acid molecule of claim 3, wherein in the antisense strand 2'-O-Methyl sugar-modified ribonucleotides are present at positions 1, 3, 11, 14, 15, 17 and 18 (5'>3'); a 2'-5' linked ribonucleotide is present at position 6; Z is a C3Pi-C3OH moiety covalently attached to the 3' terminus, and the 5' terminus is phosphorylated; and

wherein in the sense strand a 2'-O-Methyl sugar-modified ribonucleotide is present at position 1 (5'>3'), 2'-5' linked ribonucleotides are present at positions 15, 16, 17, 18 and 19 (5'>3'), and z" is a capping moiety covalently attached at the 5' terminus; or

a pharmaceutically acceptable salt of such nucleic acid molecule.

11. The double-stranded nucleic acid molecule of claim 1 described as RHOA_48u, wherein the antisense strand comprises the sequence 5' AGUAGCAAGAUGACUUCUG 3' (SEQ ID NO: 114) and wherein the sense strand comprises the sequence 5' CAGAAGUCAUCUUGCUACU 3' (SEQ ID NO: 80), or a pharmaceutically acceptable salt of such nucleic acid molecule.

12. The double-stranded nucleic acid of claim 11, having the structure:

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5'    AGUAGCAAGAUGACUUCUG -Z  3' (antisense SEQ ID NO:114)
      ||||||||||||||||||
3' Z'-UCAUCGUUCUACUGAAGAC -z" 5' (sense SEQ ID NO:80)
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wherein each "|" represents base pairing;

wherein each of A, C, G and U is independently an unmodified ribonucleotide, a modified ribonucleotide, or an unconventional moiety;

wherein each of Z and Z' is independently present or absent, but if present is independently 1-5 consecutive nucleotides or non-nucleotide moieties or a combination thereof covalently attached at the 3' terminus of the strand in which it is present;

~~wherein z" may be present or absent, but if present is a capping moiety covalently attached at the 5' terminus of the sense strand; or~~

~~a pharmaceutically acceptable salt of such nucleic acid molecule.~~

~~13~~12. The double-stranded nucleic acid molecule of claim ~~12~~1, wherein in the antisense strand one or more 2'-O-Methyl sugar modified ribonucleotide ~~is present~~, a mirror nucleotide or a 2'-5' linked ribonucleotide is present in at least one of positions 5, 6, 7 or 8 (5'>3'), and a nucleotide moiety or a non-nucleotide moiety is covalently attached at the 3' terminus; and wherein in the sense strand 4 or 5 consecutive 2'-5' linked ribonucleotides are present at the 3' terminal or penultimate positions, a nucleotide or non-nucleotide moiety is covalently attached at the 3' terminus, and z" is present; or
a pharmaceutically acceptable salt of such nucleic acid molecule.

~~14~~13. A pharmaceutical composition comprising the nucleic acid molecule or a pharmaceutically acceptable salt of such nucleic acid molecule of claims 1-~~13~~12; and a pharmaceutically acceptable carrier.

~~15~~14. A pharmaceutical composition comprising the nucleic acid molecule or a pharmaceutically acceptable salt of such nucleic acid molecule of any one of claims 1-~~13~~12, in an amount effective to down-regulate expression of a RHOA gene; and a pharmaceutically acceptable carrier.

~~16~~15. Use of the nucleic acid molecule or a pharmaceutically acceptable salt of such nucleic acid molecule of any one of claims 1-~~13~~12, in the manufacture of a medicament for treating

an individual at risk of or suffering from an injury, a disease or a disorder associated with RHOA expression.

~~17~~16. The use of claim ~~16~~15, wherein the injury, the disease or the disorder associated with RHOA expression is an injury, a disease or a disorder of the central nervous system (CNS).

~~18~~17. The use of claim ~~17~~16, wherein the injury, the disease or the disorder of the CNS comprises neuronal degeneration.

~~19~~18. Use of the nucleic acid molecule or a pharmaceutically acceptable salt of such nucleic acid molecule of any one of claims 1-~~13~~12, in the manufacture of a medicament for effecting neuroprotection or neural regeneration to a neuron damaged, or at risk of damage, by an injury, a disease, or a disorder in a central nervous system (CNS).

~~20~~19. The use of claim ~~16~~15, wherein the injury, the disease, or the disorder is selected from the group consisting of a neurological injury, a neurodegenerative disease, a neurodegenerative disorder, a cardiovascular event, a brain damage caused by a cardiovascular event, cardiac arrest, cardiac surgery, a cerebrovascular disorder, a cerebrovascular disease; a dementia, a Lewy body dementia, a vascular dementia, a dementia caused by Parkinson's disease, a hearing disorder, hearing loss, hearing loss associated with neuronal degeneration, a traumatic injury, a traumatic brain injury (TBI), a spinal cord injury, a brain ischemia, a stroke, cerebral damage produced by thromboembolic (thrombotic) stroke, a cranium-brain traumatic injury, Alzheimer's disease, Parkinson's disease, Creutzfeld-Jacob disease (CJD), facial nerve (Bell's) palsy, multiple sclerosis, glaucoma, Huntington's chorea, amyotrophic lateral sclerosis, HIV infection, Meniere's disease, glaucoma, primary open-angle glaucoma (POAG), macular degeneration, age-related macular degeneration (AMD), wet age-related macular degeneration (wet AMD) neurodegeneration of the optic nerve, Anterior Ischemic

Optic Neuropathy (AION), Nonarteritic Anterior Ischemic Optic Neuropathy (NAION), Arteritic Anterior Ischemic Optic Neuropathy (AAION), neuropathic pain (NP), allodynia, cancer, tumor growth; and a proliferative disease.

~~21~~20. The use of claim ~~20~~19, wherein the injury is a spinal cord injury.

~~22~~21. The use of claim ~~20~~19, wherein the disorder is neuropathic pain (NP) or allodynia.