

normal function, to ameliorate SMA symptoms.

Prior Art Literature

Patent Literature

[0007]

Patent Literature 1: Unexamined Patent Application Publication No. WO2010/148249

Summary ~~of the Invention~~

Problem to be Solved ~~by the Invention~~

[0008]

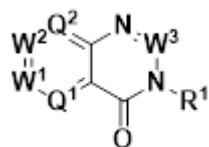
An object of the present ~~invention-disclosure~~ is to provide prophylactic or therapeutic agents for spinal muscular atrophy.

Means for Solving the Problem

[0009]

~~An aspect of the The~~ present ~~invention-disclosure is-provides~~ a compound or a salt thereof, the compound being represented by the formula (I):

[Chemical formula 1]



(I)

wherein:

W¹, W², and W³ are each independently selected from the group consisting of C-R², C-R³, C-R^c, and C-R^d, and are defined by one of the followings (i) to (iv):

- (i) when W³ is C-R², then W¹ is C-R³, W² is C-R^c or N, and R¹ is a hydrogen atom;
- (ii) when W³ is C-R³, then W¹ is C-R², W² is C-R^c or N, and R¹ is a hydrogen atom, C₁₋₈ alkyl, or C₁₋₈ alkoxy;
- (iii) when W¹ is C-R², then W² is C-R^c or N, W³ is C-R^d, and R¹ is an aliphatic heterocycle containing one or more nitrogen atoms, the aliphatic heterocycle being optionally substituted with a non-aromatic substituent; and
- (iv) when W² is C-R², W¹ is C-R^c, W³ is C-R^d, and R¹ is an aliphatic heterocycle containing one or more nitrogen atoms, the aliphatic heterocycle being optionally substituted with a non-aromatic substituent;

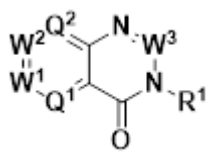
R² is a 6- or more membered aromatic ring optionally substituted with a non-aromatic substituent;

R³ is an aliphatic heterocycle containing one or more nitrogen atoms, the aliphatic heterocycle being optionally substituted with a non-aromatic substituent;

- (c) a nitro group;
 - (d) a C₁₋₆ alkoxy group;
 - (e) a C₁₋₆ alkylamino group; and
 - (f) a C₁₋₆ alkyl(C₁₋₆ alkyl)amino group;
- (V) an amino group optionally substituted with a C₁₋₆ alkyl or C₁₋₁₀ cycloalkyl group optionally substituted with one to five substituents selected from the group consisting of:
- (a) halogen;
 - (b) a cyano group;
 - (c) a nitro group;
 - (d) a C₁₋₆ alkoxy group;
 - (e) a C₁₋₆ alkylamino group; and
 - (f) a C₁₋₆ alkyl(C₁₋₆ alkyl)amino group; and
- (VI) a C₁₋₆ alkyl or C₁₋₁₀ cycloalkyl group optionally substituted with one to five substituents selected from the group consisting of:
- (a) halogen;
 - (b) a cyano group;
 - (c) a nitro group;
 - (d) a C₁₋₆ alkoxy group;
 - (e) a C₁₋₆ alkylamino group; and
 - (f) a C₁₋₆ alkyl(C₁₋₆ alkyl)amino group.

[0010a]

One aspect of the present disclosure provides a compound represented by the formula (I) or a salt thereof:



(I)

wherein:

W³ is C-R², W¹ is C-R³, W² is C-R^c, and R¹ is a hydrogen atom;
R² is pyrazolo[1,5-α]pyrazinyl optionally substituted with one to three R⁴ groups;
R³ is an aliphatic heterocycle selected from the group consisting of azetidiny,

pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, azepanyl, 1,4-diazepanyl, 1,4-oxazepanyl, octahydropyrrolo[3,4-*b*]pyrrolyl, octahydropyrrolo[3,4-*c*]pyrrolyl, octahydropyrrolo[3,2-*b*]pyrrolyl, octahydro-1*H*-pyrrolo[3,2-*b*]pyridinyl, octahydro-5*H*-pyrrolo[3,2-*c*]pyridinyl, octahydro-1*H*-pyrrolo[2,3-*c*]pyridinyl, octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, octahydro-1*H*-pyrrolo[3,4-*c*]pyridinyl, octahydro-1*H*-cyclopentapyrazine, octahydro-1*H*-pyrrolo[1,2-*a*]pyrazinyl, decahydro-2,6-naphthyridinyl, decahydro-2,7-naphthyridinyl, decahydro-1,6-naphthyridinyl, decahydro-1,7-naphthyridinyl, decahydro-quinoxalanyl, octahydro-2*H*-pyrido[1,2-*a*]pyrazinyl, 3-azabicyclo[3.1.0]hexyl, 1-azabicyclo[2.2.1]heptyl, 2-azabicyclo[2.2.1]heptyl, 7-azabicyclo[2.2.1]heptyl, 1-azabicyclo[2.2.2]octyl, 2-azabicyclo[2.2.2]octyl, 1-azabicyclo[3.2.1]octyl, 2-azabicyclo[3.2.1]octyl, 3-azabicyclo[3.2.1]octyl, 6-azabicyclo[3.2.1]octyl, 8-azabicyclo[3.2.1]octyl, 1-azabicyclo[3.2.2]nonyl, 2-azabicyclo[3.2.2]nonyl, 3-azabicyclo[3.2.2]nonyl, 6-azabicyclo[3.2.2]nonyl, 1-azabicyclo[3.3.1]nonyl, 2-azabicyclo[3.3.1]nonyl, 3-azabicyclo[3.3.1]nonyl, 9-azabicyclo[3.3.1]nonyl, 2,5-diazabicyclo[2.2.1]heptyl, 1,4-diazabicyclo[2.2.2]octyl, 2,5-diazabicyclo[2.2.2]octyl, 1,4-diazabicyclo[3.2.1]octyl, 2,6-diazabicyclo[3.2.1]octyl, 3,6-diazabicyclo[3.2.1]octyl, 3,8-diazabicyclo[3.2.1]octyl, 1,4-diazabicyclo[3.2.2]nonyl, 1,5-diazabicyclo[3.2.2]nonyl, 2,6-diazabicyclo[3.2.2]nonyl, 3,6-diazabicyclo[3.2.2]nonyl, 6,8-diazabicyclo[3.2.2]nonyl, 1-azaspiro[3.3]heptyl, 2-azaspiro[3.3]heptyl, 1-azaspiro[3.4]octyl, 2-azaspiro[3.4]octyl, 5-azaspiro[3.4]octyl, 6-azaspiro[3.4]octyl, 1-azaspiro[4.4]nonyl, 2-azaspiro[4.4]nonyl, 1-azaspiro[4.5]decanyl, 2-azaspiro[4.5]decanyl, 6-azaspiro[4.5]decanyl, 7-azaspiro[4.5]decanyl, 8-azaspiro[4.5]decanyl, 1,6-diazaspiro[3.3]heptyl, 2,6-diazaspiro[3.3]heptyl, 1,7-diazaspiro[4.4]nonyl, 2,7-diazaspiro[4.4]nonyl, 1,6-diazaspiro[3.5]nonyl, 1,7-diazaspiro[3.5]nonyl, 2,5-diazaspiro[3.5]nonyl, 2,6-diazaspiro[3.5]nonyl, 2,7-diazaspiro[3.5]nonyl, 5,8-diazaspiro[3.5]nonyl, 1,7-diazaspiro[4.5]decyl, 1,8-diazaspiro[4.5]decyl, 2,6-diazaspiro[4.5]decyl, 2,7-diazaspiro[4.5]decyl, 2,8-diazaspiro[4.5]decyl, and 6,9-diazaspiro[4.5]decyl, the aliphatic heterocycle being optionally substituted with one to three R⁵ groups and optionally containing one to three double bonds, the aliphatic heterocycle optionally containing one to three carbonyl groups, each of the carbonyl groups having a carbon atom in a ring of the aliphatic heterocycle;

R⁴ and R⁵ are selected from the group consisting of:

(I) halogen;

(II) a cyano group;

(III) a nitro group;

—

(IV) a hydroxy group optionally substituted with a C₁₋₆ alkyl or C₁₋₁₀ cycloalkyl group optionally substituted with one to five substituents selected from the group consisting of

- (a) halogen;
- (b) a cyano group;
- (c) a nitro group;
- (d) a C₁₋₆ alkoxy group;
- (e) a C₁₋₆ alkylamino group; and
- (f) a C₁₋₆ alkyl(C₁₋₆ alkyl)amino group;

(V) an amino group optionally substituted with a C₁₋₆ alkyl or C₁₋₁₀ cycloalkyl group optionally substituted with one to five substituents selected from the group consisting of:

- (a) halogen;
- (b) a cyano group;
- (c) a nitro group;
- (d) a C₁₋₆ alkoxy group;
- (e) a C₁₋₆ alkylamino group; and
- (f) a C₁₋₆ alkyl(C₁₋₆ alkyl)amino group; and

(VI) a C₁₋₆ alkyl or C₁₋₁₀ cycloalkyl group optionally substituted with one to five substituents selected from the group consisting of:

- (a) halogen;
- (b) a cyano group;
- (c) a nitro group;
- (d) a C₁₋₆ alkoxy group;
- (e) a C₁₋₆ alkylamino group; and
- (f) a C₁₋₆ alkyl(C₁₋₆ alkyl)amino group.

Q¹ is selected from C-R^a and N;

Q² is selected from C-R^b and N; and

R^a, R^b and R^c are each independently selected from the group consisting of a hydrogen atom, halogen, C₁₋₈ alkyl, C₁₋₈ alkoxy, and a cyano group.

[0011]

The compound represented by the formula (I) may be
2-(4,6-dimethylpyrazolo[1,5-*a*]pyrazin-2-yl)-6-(4-methylpiperazin-1-yl)quinazolin-4(3*H*)-one.

[0012]

Another aspect of the present ~~invention-disclosure~~ is a medicament including, as an active ingredient, ~~any one of the compounds described above~~ or a salt thereof as described above. This medicament may be a splicing regulator, may be an expression enhancer that enhances

expression of normal SMN mRNA and/or normal SMN protein, or may be a prophylactic or therapeutic agent for spinal muscular atrophy.

[0013]

~~Yet another aspect of the~~The present ~~disclosureinvention is~~provides a splicing regulator, an expression enhancer that enhances expression of normal SMN mRNA and/or normal SMN protein, or a prophylactic or therapeutic agent for spinal muscular atrophy, which includes, as an active ingredient, any one of the compounds described above or a salt thereof. Yet another aspect of the present disclosure is a splicing regulator comprising, as an active ingredient, the compound or a salt thereof as described above. Another aspect of the present disclosure is an expression enhancer that enhances expression of SMN mRNA having a normal function and/or SMN protein having a normal function, the expression enhancer comprising the compound or a salt thereof, as an active ingredient, as described above. A further aspect of the present disclosure is a prophylactic or therapeutic agent for use in the treatment of spinal muscular atrophy, the agent comprising, as an active ingredient, the compound or a salt thereof as described above.

[0014]

~~Yet another aspect of the~~ The present ~~disclosureinvention is~~ provides a method for prophylactic or therapeutic treatment of spinal muscular atrophy, the method including: administering an effective amount of any one of the compounds described above or a salt thereof to a mammal (except for human beings) having spinal muscular atrophy.

[0014a]

Another aspect of the present disclosure is use of the compound or a salt thereof as described above in the manufacture of a medicament for prophylactic or therapeutic treatment of spinal muscular atrophy in a mammal (except for human beings) having spinal muscular atrophy.

[0015]

Still another aspect of the present ~~invention-disclosure~~ is ~~any one of~~ the compounds ~~described above~~ or a salt thereof as described above for use in prophylactic or therapeutic treatment of spinal muscular atrophy.

[0016]

~~Still another aspect of the~~ The present ~~disclosureinvention is~~ provides the use of any one of the compounds described above or a salt thereof for manufacturing a prophylactic or therapeutic agent for spinal muscular atrophy.

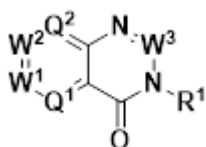
[0016a]

Still another aspect of the present disclosure is use of the compound or a salt thereof as described above in the manufacture a medicament for treatment of spinal muscular atrophy.

[0017]

~~Still another aspect of the~~ The present ~~disclosureinvention is~~ provides a method of examining whether a compound or a salt thereof, the compound being represented by the formula (I):

[Chemical formula 1]



(I)

wherein:

W¹, W², and W³ are each independently selected from the group consisting of C-R², C-R³, C-R^c, and C-R^d, and are defined by one of the following (i) through (iv):

- (i) when W³ is C-R², then W¹ is C-R³, W² is C-R^c or N, and R¹ is a hydrogen atom;
- (ii) when W³ is C-R³, then W¹ is C-R², W² is C-R^c or N, and R¹ is a hydrogen atom,

C₁₋₈ alkyl, or C₁₋₈ alkoxy;

(iii) when W¹ is C-R², then W² is C-R^c or N, W³ is C-R^d, and R¹ is an aliphatic heterocycle containing one or more nitrogen atoms, the aliphatic heterocycle being optionally substituted with a non-aromatic substituent; and

(iv) when W² is C-R², W¹ is C-R^c, W³ is C-R^d, and R¹ is an aliphatic heterocycle containing one or more nitrogen atoms, the aliphatic heterocycle being optionally substituted with a non-aromatic substituent;

R² is a 6- or more membered aromatic ring optionally substituted with a non-aromatic substituent;

R³ is an aliphatic heterocycle containing one or more nitrogen atoms, the aliphatic heterocycle being optionally substituted with a non-aromatic substituent;

Q¹ is selected from C-R^a and N;

Q² is selected from C-R^b and N; and

R^a, R^b, R^c, and R^d are each independently selected from the group consisting of a hydrogen atom, halogen, C₁₋₈ alkyl, C₁₋₈ alkoxy, and a cyano group, enhances expression of normal SMN mRNA and/or normal SMN protein. This method may include the steps of: bringing a cell into contact with the compound or a salt thereof, the cell including an *SMN* gene with thymine at nucleotide position 6 in exon 7; and examining whether an expression level, in the cell, of SMN mRNA including exon 7 or SMN protein including an amino acid sequence encoded by exon 7 is elevated by the compound or a salt thereof. The expression may be examined using PCR or Western blotting.

[0017a]

A still further aspect of the present disclosure is a method of examining whether the compound or a salt thereof as described above enhances expression of SMN mRNA having a normal function and/or SMN protein having a normal function the method comprising the steps of: bringing a cell in culture into contact with the compound or a salt thereof, the cell comprising an SMN gene with a nucleotide at position 6 in exon 7 mutated from C to T; and examining whether an expression level of SMN mRNA comprising exon 7 in the cell or SMN protein comprising an amino acid sequence encoded by exon 7 is enhanced by the compound or a salt thereof.

==Cross-Reference with Related Literature==

The present application claims priority based on Japanese Patent Application 2018-122551 filed on June 27, 2008; the basic application is hereby incorporated in the present specification by reference.

Brief description of the drawings

[0018]

Fig. 1 is a representation of nucleotide sequences of oligo DNA standards used in a Working Example of the present invention.

Fig. 2 is a representation of nucleotide sequences of primers and probes for PCR used in a Working Example of the present invention. (A) primers and a probe for PCR used for detecting FL-SMN containing exons 7 and 8 of SMN in succession; and (B) primers and a probe for PCR used for detecting Delta7 of SMN with exon 7 skipped.

Fig. 3 is a diagrammatic representation showing the principle of a qPCR system that specifically detects cDNA for FL-SMN with exon 7 and Delta7 without exon 7 in a Working

Example of the present invention. (A) the structure of the *SMN2* gene on the genome; (B) a mechanism of detecting FL-SMN cDNA; (C) a calibration curve generated using the FL-SMN oligo DNA standard; (D) a mechanism of detecting Delta7 cDNA, and (E) a calibration curve generated using the Delta7 oligo DNA standard.

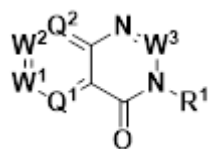
Fig. 4 shows a calibration curve generated using the GAPDH oligo DNA standard in a Working Example of the present invention.

Fig. 5-1 is a representation showing dose-dependent change in amounts of FL-SMN mRNA and Delta7 mRNA and increase of SMN protein for representative compounds in a Working Example of the present invention. The y-axis represents the percentages of the

CLAIMS

1. A compound represented by the formula (I) or a salt thereof:

~~[Chemical formula 1]~~



(I)

wherein:

~~W¹, W², and W³ are each independently selected from the group consisting of C-R², C-R³, C-R^e, and C-R^d, and are defined by one of the followings (i) to (iv):~~

~~(i) when W³ is C-R², then W¹ is C-R³, W² is C-R^e or N, and R¹ is a hydrogen atom;~~

~~(ii) when W³ is C-R³, then W¹ is C-R², W² is C-R^e or N, and R¹ is a hydrogen atom, R² is~~

~~pyrazolo[1,5- α]pyrazinyl optionally substituted with one to three R⁴ groups;~~

~~C₁₋₈-alkyl, or C₁₋₈-alkoxy;~~

~~(iii) when W¹ is C-R², then W² is C-R^e or N, W³ is C-R^d, and R¹ is an aliphatic heterocycle containing one or more nitrogen atoms, the aliphatic heterocycle being optionally substituted with a non-aromatic substituent; and~~

~~(iv) when W² is C-R², W¹ is C-R^e, W³ is C-R^d, and R¹ is an aliphatic heterocycle containing one or more nitrogen atoms, the aliphatic heterocycle being optionally substituted with a non-aromatic substituent;~~

~~———— R² is a 6 or more membered aromatic ring optionally substituted with a non-aromatic substituent;~~

~~———— R³ is an aliphatic heterocycle containing one or more nitrogen atoms, the aliphatic heterocycle being optionally substituted with a non-aromatic substituent;~~

~~———— Q¹ is selected from C-R^a and N;~~

~~———— Q² is selected from C-R^b and N; and~~

~~———— R^a, R^b, R^c, and R^d are each independently selected from the group consisting of a hydrogen atom, halogen, C₁₋₈-alkyl, C₁₋₈-alkoxy, and a cyano group.~~

2. ——— The compound or a salt thereof according to Claim 1, wherein

———— R² is an 8 to 10 membered nitrogen-containing aromatic heterocyclic group containing two or more heteroatoms, the 8 to 10 membered nitrogen-containing aromatic heterocyclic group being optionally substituted with a non-aromatic substituent; and

———— R³ is a 3 to 14 membered non-aromatic heterocyclic group containing one or more nitrogen

atoms, the 3- to 14-membered non-aromatic heterocyclic group being optionally substituted with a non-aromatic substituent.

3. — The compound or a salt thereof according to Claim 1 or 2, wherein

— R^2 is an aromatic heterocycle selected from the group consisting of indazolyl, benzimidazolyl, pyrrolo[1,2-*a*]pyrazinyl, pyrrolo[1,2-*b*]pyridazinyl, pyrrolo[1,2-*c*]pyrimidinyl, pyrrolo[1,2-*b*]pyrimidinyl, imidazo[1,2-*a*]pyridinyl, pyrazolo[1,5-*a*]pyridinyl, imidazo[1,5-*a*]pyridinyl, pyrrolo[3,2-*b*]pyridinyl, pyrrolo[3,2-*c*]pyridinyl, pyrrolo[2,3-*c*]pyridinyl, pyrrolo[2,3-*b*]pyridinyl, 1,3-benzoxazolyl, 1,2-benzisoxazolyl, 2,1-benzisoxazolyl, furo[3,2-*b*]pyridinyl, furo[3,2-*c*]pyridinyl, furo[2,3-*c*]pyridinyl, furo[2,3-*b*]pyridinyl, pyrazolo[3,4-*b*]pyridinyl, 1*H*-pyrazolo[3,4-*b*]pyridinyl, pyrazolo[3,4-*c*]pyridinyl, 1*H*-pyrazolo[3,4-*c*]pyridinyl, pyrazolo[4,3-*c*]pyridinyl, pyrazolo[4,3-*b*]pyridinyl, pyrazolo[1,5-*a*]pyrazinyl, pyrazolo[1,5-*a*]pyrimidinyl, pyrazolo[1,5-*c*]pyrimidinyl, pyrazolo[1,5-*b*]pyridazinyl, imidazo[4,5-*b*]pyridinyl, imidazo[4,5-*c*]pyridinyl, imidazo[1,2-*a*]pyrimidinyl, imidazo[1,2-*a*]pyrazinyl, imidazo[1,2-*c*]pyrimidinyl, imidazo[1,2-*b*]pyridazinyl, imidazo[1,5-*a*]pyrimidinyl, imidazo[1,5-*a*]pyrazinyl, imidazo[1,5-*c*]pyrimidinyl, imidazo[1,5-*b*]pyridazinyl, pyrrolo[3,2-*c*]pyridazinyl, pyrrolo[3,2-*d*]pyrimidinyl, pyrrolo[2,3-*b*]pyrazinyl, pyrrolo[2,3-*d*]pyridazinyl, pyrrolo[2,3-*d*]pyrimidinyl, pyrrolo[2,3-*c*]pyridazinyl, oxazolo[5,4-*b*]pyridinyl, oxazolo[5,4-*c*]pyridinyl, oxazolo[4,5-*c*]pyridinyl, oxazolo[4,5-*b*]pyridinyl, [1,2,4]triazolo[1,5-*a*]pyridinyl, [1,2,4]triazolo[4,3-*a*]pyridinyl, purinyl, pyrazolo[3,4-*d*]pyrimidyl, pyrazolo[4,3-*d*]pyrimidyl, isoxazolo[5,4-*d*]pyrimidinyl, isoxazolo[4,5-*d*]pyrimidinyl, oxazolo[4,5-*d*]pyrimidinyl, and oxazolo[5,4-*d*]pyrimidinyl, the aromatic heterocycle being optionally substituted with one to three R^4 -groups;

— R^3 is an aliphatic heterocycle selected from the group consisting of azetidiny, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, azepanyl, 1,4-diazepanyl, 1,4-oxazepanyl, octahydropyrrolo[3,4-*b*]pyrrolyl, octahydropyrrolo[3,4-*c*]pyrrolyl, octahydropyrrolo[3,2-*b*]pyrrolyl, octahydro-1*H*-pyrrolo[3,2-*b*]pyridinyl, octahydro-5*H*-pyrrolo[3,2-*c*]pyridinyl, octahydro-1*H*-pyrrolo[2,3-*c*]pyridinyl, octahydro-6*H*-pyrrolo[3,4-*b*]pyridinyl, octahydro-1*H*-pyrrolo[3,4-*c*]pyridinyl, octahydro-1*H*-cyclopentapyrazine, octahydro-1*H*-pyrrolo[1,2-*a*]pyrazinyl, decahydro-2,6-naphthyridinyl, decahydro-2,7-naphthyridinyl, decahydro-1,6-naphthyridinyl, decahydro-1,7-naphthyridinyl, decahydro-quinoxaliny, octahydro-2*H*-pyrido[1,2-*a*]pyrazinyl, 3-azabicyclo[3.1.0]hexyl, 1-azabicyclo[2.2.1]heptyl, 2-azabicyclo[2.2.1]heptyl, 7-azabicyclo[2.2.1]heptyl, 1-azabicyclo[2.2.2]octyl, 2-azabicyclo[2.2.2]octyl, 1-azabicyclo[3.2.1]octyl, 2-azabicyclo[3.2.1]octyl, 3-azabicyclo[3.2.1]octyl, 6-azabicyclo[3.2.1]octyl, 8-azabicyclo[3.2.1]octyl, 1-azabicyclo[3.2.2]nonyl, 2-azabicyclo[3.2.2]nonyl, 3-azabicyclo[3.2.2]nonyl, 6-azabicyclo[3.2.2]nonyl, 1-azabicyclo[3.3.1]nonyl, 2-azabicyclo[3.3.1]nonyl, 3-azabicyclo[3.3.1]nonyl, 9-azabicyclo[3.3.1]nonyl, 2,5-diazabicyclo[2.2.1]heptyl, 1,4-diazabicyclo[2.2.2]octyl, 2,5-diazabicyclo[2.2.2]octyl, 1,4-diazabicyclo[3.2.1]octyl, 2,6-diazabicyclo[3.2.1]octyl, 3,6-diazabicyclo[3.2.1]octyl, 3,8-diazabicyclo[3.2.1]octyl, 1,4-diazabicyclo[3.2.2]nonyl,

1,5-diazabicyclo[3.2.2]nonyl, 2,6-diazabicyclo[3.2.2]nonyl, 3,6-diazabicyclo[3.2.2]nonyl, 6,8-diazabicyclo[3.2.2]nonyl, 1-azaspiro[3.3]heptyl, 2-azaspiro[3.3]heptyl, 1-azaspiro[3.4]octyl, 2-azaspiro[3.4]octyl, 5-azaspiro[3.4]octyl, 6-azaspiro[3.4]octyl, 1-azaspiro[4.4]nonyl, 2-azaspiro[4.4]nonyl, 1-azaspiro[4.5]decanyl, 2-azaspiro[4.5]decanyl, 6-azaspiro[4.5]decanyl, 7-azaspiro[4.5]decanyl, 8-azaspiro[4.5]decanyl, 1,6-diazaspiro[3.3]heptyl, 2,6-diazaspiro[3.3]heptyl, 1,7-diazaspiro[4.4]nonyl, 2,7-diazaspiro[4.4]nonyl, 1,6-diazaspiro[3.5]nonyl, 1,7-diazaspiro[3.5]nonyl, 2,5-diazaspiro[3.5]nonyl, 2,6-diazaspiro[3.5]nonyl, 2,7-diazaspiro[3.5]nonyl, 5,8-diazaspiro[3.5]nonyl, 1,7-diazaspiro[4.5]decyl, 1,8-diazaspiro[4.5]decyl, 2,6-diazaspiro[4.5]decyl, 2,7-diazaspiro[4.5]decyl, 2,8-diazaspiro[4.5]decyl, and 6,9-diazaspiro[4.5]decyl, the aliphatic heterocycle being optionally substituted with one to three R⁵ groups and optionally containing one to three double bonds, the aliphatic heterocycle optionally containing one to three carbonyl groups, each of the carbonyl groups having a carbon atom in a ring of the aliphatic heterocycle;

R⁴ and R⁵ are selected from the group consisting of:

- (I) halogen;
- (II) a cyano group;
- (III) a nitro group;
- (IV) a hydroxy group optionally substituted with a C₁₋₆ alkyl or C₁₋₁₀ cycloalkyl group optionally substituted with one to five substituents selected from the group consisting of:
 - (a) halogen;
 - (b) a cyano group;
 - (c) a nitro group;
 - (d) a C₁₋₆ alkoxy group;
 - (e) a C₁₋₆ alkylamino group; and
 - (f) a C₁₋₆ alkyl(C₁₋₆ alkyl)amino group;
- (V) an amino group optionally substituted with a C₁₋₆ alkyl or C₁₋₁₀ cycloalkyl group optionally substituted with one to five substituents selected from the group consisting of:
 - (a) halogen;
 - (b) a cyano group;
 - (c) a nitro group;
 - (d) a C₁₋₆ alkoxy group;
 - (e) a C₁₋₆ alkylamino group; and
 - (f) a C₁₋₆ alkyl(C₁₋₆ alkyl)amino group; and
- (VI) a C₁₋₆ alkyl or C₁₋₁₀ cycloalkyl group optionally substituted with one to five substituents selected from the group consisting of:
 - (a) halogen;
 - (b) a cyano group;
 - (c) a nitro group;
 - (d) a C₁₋₆ alkoxy group;

- (e) a C₁₋₆ alkylamino group; and
(f) a C₁₋₆ alkyl(C₁₋₆ alkyl)amino group.

Q¹ is selected from C-R^a and N;

Q² is selected from C-R^b and N; and

R^a, R^b and R^c are each independently selected from the group consisting of a hydrogen atom, halogen, C₁₋₈ alkyl, C₁₋₈ alkoxy, and a cyano group.

2. The compound or a salt thereof according to Claim 1, wherein Q¹ is C-R^a and Q² is C-R^b.

4. The compound or a salt thereof according to Claim 1 or 2, wherein W² is C-R², W¹ is C-R^c or N, W³ is C-R^d, and R¹ is an aliphatic heterocycle containing one or more nitrogen atoms, the aliphatic heterocycle being optionally substituted with a non-aromatic substituent.

5. The compound or a salt thereof according to Claim 1 or 2, wherein W³ is C-R³, W¹ is C-R², W² is C-R^e or N, and R¹ is a hydrogen atom.

6. The compound or a salt thereof according to Claim 1 or 2, wherein W³ is C-R², W¹ is C-R³, W² is C-R^e or N, and R¹ is a hydrogen atom.

73. The compound or a salt thereof according to Claim 1 or 2, wherein the compound is (S)-6-(2,4-dimethylpiperazin-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)quinazolin-4(3H)-one.

84. The compound or the salt thereof according to Claim 1 or 2, wherein the compound is (R)-6-(2,4-dimethylpiperazin-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)quinazolin-4(3H)-one.

95. The compound or the salt thereof according to Claim 1 or 2, wherein the compound is 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-6-(4-methylpiperazin-1-yl)quinazolin-4(3H)-one.

106. The compound or the salt thereof according to Claim 1 or 2, wherein the compound is 6-(4-cyclopropylpiperazin-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)quinazolin-4(3H)-one.

7. The compound or a salt thereof according to Claim 1 or Claim 2, wherein R³ is an aliphatic heterocycle selected from the group consisting of piperidinyl, piperazinyl, morpholinyl, octahydro-1H-pyrrolo[1,2-a]pyrazinyl, and octahydro-2H-pyrido[1,2-a]pyrazinyl.

8. The compound or a salt thereof according to any one of Claims 1, 2 or 7, wherein R⁴ and R⁵ are independently selected from the group consisting of:

(I) halogen;

(II) a hydroxy group optionally substituted with a C₁₋₆ alkyl or C₃₋₁₀ cycloalkyl group;

and

(III) a C₁₋₆ alkyl or C₃₋₁₀ cycloalkyl group optionally substituted with a C₁₋₆ alkoxy group.

9. The compound or a salt thereof according to Claim 1, wherein the compound or salt thereof is 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-6-(piperazin-1-yl)quinazolin-4(3H)-one.

10. The compound or a salt thereof according to Claim 1, wherein the compound or salt thereof is (S)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-6-(hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)quinazolin-

4(3H)-one.

11. The compound or a salt thereof according to Claim 1, wherein the compound or salt thereof is 2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-6-(4,7-diazaspiro[2.5]octan-7-yl)quinazolin-4(3H)-one.

12. The compound or a salt thereof according to Claim 1, wherein the compound or salt thereof is (R)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)-6-(hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)quinazolin-4(3H)-one.

13. The compound or a salt thereof according to Claim 1, wherein the compound or salt thereof is 6-(3,3-Dimethylpiperazin-1-yl)-2-(4,6-dimethylpyrazolo[1,5-a]pyrazin-2-yl)quinazolin-4(3H)-one.

~~11~~14. A medicament comprising, as an active ingredient, the compound or a salt thereof according to any one of Claims 1 to ~~10~~13.

15. ~~12~~The medicament according to Claim ~~11~~14, wherein the medicament is a splicing regulator, or an expression enhancer that enhances expression of SMN mRNA having a normal function and/or SMN protein having a normal function.

~~13~~16. The medicament according to Claim ~~11~~14, wherein the medicament is a prophylactic or therapeutic agent for spinal muscular atrophy.

~~14~~17. A splicing regulator comprising, as an active ingredient, the compound or a salt thereof according to any one of Claims 1 to ~~10~~13.

~~15~~18. An expression enhancer that enhances expression of SMN mRNA having a normal function and/or SMN protein having a normal function, the expression enhancer comprising the compound or a salt thereof, as an active ingredient, according to any one of Claims 1 to ~~10~~13.

~~16~~19. A prophylactic or therapeutic agent for use in the treatment of spinal muscular atrophy, the agent comprising, as an active ingredient, the compound or a salt thereof according to any one of Claims 1 to ~~10~~13.

~~17~~20. Use of the compound or a salt thereof according to any one of Claims 1 to 13 in the manufacture of a medicament ~~A method~~ for prophylactic or therapeutic treatment of spinal muscular atrophy ~~in, the method comprising administering an effective amount of the compound or a salt thereof according to any one of Claims 1 to 10 to~~ a mammal (except for human beings) having spinal muscular atrophy.

~~18~~21. The compound or a salt thereof according to any one of Claims 1 to ~~10~~13 for use in prophylactic or therapeutic treatment of spinal muscular atrophy.

~~19~~22. ~~Use of the compound or a salt thereof according to any one of Claims 1 to 10-13 for manufacturing in the manufacture of a medicament for treatment of a prophylactic or therapeutic agent for~~ spinal muscular atrophy.

~~20~~23. A method of examining whether the compound or a salt thereof according to Claim 1 enhances expression of SMN mRNA having a normal function and/or SMN protein having a normal function: the method comprising the steps of:

bringing a cell in culture into contact with the compound or a salt thereof, the cell comprising an

SMN gene with a nucleotide at position 6 in exon 7 mutated from C to T; and

examining whether an expression level of SMN mRNA comprising exon 7 in the cell or SMN protein comprising an amino acid sequence encoded by exon 7 is enhanced by the compound or a salt thereof.

21. ~~The method according to Claim 20, comprising the steps of:~~

~~—bringing a cell into contact with the compound or a salt thereof, the cell comprising an SMN gene with a nucleotide at position 6 in exon 7 mutated from C to T; and~~

~~—examining whether an expression level of SMN mRNA comprising exon 7 in the cell or SMN protein comprising an amino acid sequence encoded by exon 7 is enhanced by the compound or a salt thereof.~~

2224. The method according to Claim ~~21~~ 23, wherein the expression is examined using PCR or Western blotting.