

Parkinson's disease patients. The aberrantly activity of LRRK2 has a high clinical relationship with the initiation and progression of Parkinson's disease. It is expected that of the modulation of LRRK2 activity would be beneficial to control both neuronal apoptosis and neurocytic inflammatory responses, which are the most important pathological evidence in Parkinson's disease.

Meanwhile, 40% of the patients who are currently treated with the drugs for Parkinson's disease have experienced motor fluctuation. Furthermore, the rate of patients experiencing motor fluctuation increases by 10% per one year due to the occurrence of drug-resistance after a certain period of time (e.g., 4 to 6 years from onset).

Accordingly, there is a need for developing a novel small molecule drug which capable of oral administration and offer acceptable safety profile.

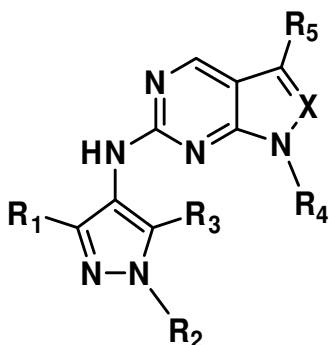
Disclosure

Thus, as the results of the studies, the present inventors have developed and synthesized a novel pyrrolo(pyrazolo)pyrimidine derivative to selectively inhibit LRRK2. It has been confirmed that the derivatives had an excellent inhibitory activity to LRRK2.

Aspects of the invention are defined in the independent claims. Some optional features of the invention are defined in the dependent claims.

Thus, there is disclosed a compound selected from the group consisting of a compound represented by the following Formula 1, and a pharmaceutically acceptable salt, hydrate, solvate, prodrug, and isomer thereof:

[Formula 1]



In the above formula,

X is CH or N;

5 R₁ is hydrogen, halogen, or C₁₋₄ alkyl or C₁₋₄ alkoxy unsubstituted or substituted with one or more halogens;

 R₂ is C₁₋₆ alkyl, C₁₋₃ alkoxy C₁₋₆ alkyl, C₃₋₆ cycloalkyl C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, 4- to 7-membered heterocycloalkyl, or C₆₋₁₀ aryl unsubstituted or substituted with one or more halogens;

10 wherein the 4- to 7-membered heterocycloalkyl may be substituted with C₁₋₄ alkyl, C₁₋₄ alkylcarbonyl unsubstituted or substituted with one or more halogens, C₃₋₆ cycloalkylcarbonyl, 4- to 7-membered heterocycloalkylcarbonyl unsubstituted or substituted with C₁₋₄ alkyl, C₁₋₄ alkylsulfonyl, C₃₋₆ cycloalkylsulfonyl, or oxetanyl, and the heterocycloalkyl contains at least one atom selected from N, O, and S,

15 R₃ is hydrogen, halogen, or C₁₋₄ alkyl;

 R₄ is C₁₋₆ alkyl or C₃₋₆ cycloalkyl unsubstituted or substituted with one or more halogens; and

 R₅ is halogen or C₁₋₄ alkyl unsubstituted or substituted with one or more halogens.

20 Thus, it may be possible to provide a novel compound excellent in the inhibitory effect on the activity of LRRK2. It may also be possible to provide a pharmaceutical composition for preventing or treating a degenerative brain disease, which comprises the compound as an active ingredient.

Advantageous Effects

The pyrrolo(pyrazolo)pyrimidine derivative according to the present disclosure is excellent in the selective inhibitory activity to LRRK2 and is useful as a drug for preventing or treating a degenerative brain disease including Parkinson's disease.

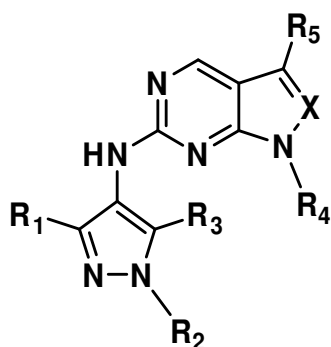
5 Hereinafter, the invention will be described, by way of example only, in detail with reference to embodiments. The embodiments are not limited to what is disclosed below. Rather, they may be modified in various forms as long as the gist of the invention is not altered.

In this specification, when a part is referred to as "comprising" a component, it
10 means that the component can be further included rather than excluding other components, unless otherwise indicated.

In this specification, examples of halogen include fluorine, chlorine, bromine, and iodine.

One embodiment provides a compound selected from the group consisting of a
15 compound represented by the following Formula 1, and a pharmaceutically acceptable salt, hydrate, solvate, prodrug, and isomer thereof.

[Formula 1]



In the above formula,

20 X is CH or N;

R₁ is hydrogen, halogen, or C₁₋₄ alkyl or C₁₋₄ alkoxy unsubstituted or substituted with one or more halogens;

R₂ is C₁₋₆ alkyl, C₁₋₃ alkoxy C₁₋₆ alkyl, C₃₋₆ cycloalkyl C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, 4- to 7-membered heterocycloalkyl, or C₆₋₁₀ aryl unsubstituted or substituted

as tablets, pills, granules, capsules, powders, aqueous solutions, or suspensions, injection solutions, elixirs, or syrups according to conventional formulation methods in the pharmaceutical field.

In order to prepare capsules, it is advantageous to use lactose and high molecular weight polyethylene glycol. If aqueous suspensions are used, they may contain emulsifiers or agents that facilitate suspension. Such diluents as sucrose, ethanol, polyethylene glycol, propylene glycol, glycerol, chloroform, or mixtures thereof may also be used.

As such, the pharmaceutical composition may be administered non-orally or orally as needed. It may be administered in single or multiple doses once a day. The non-oral dose range is from 0.5 mg/kg to 5 mg/kg per body weight, preferably 1 mg/kg to 4 mg/kg per body weight; of the oral dose range is from 5 mg/kg to 50 mg/kg per body weight, preferably 10 mg/kg to 40 mg/kg per body weight. The dosage for patients may vary depending on body weight, age, sex, health status, diet, administration time, administration method, excretion rate, and severity of the disease for each patient.

According to an embodiment, there is provided a use of the compound for the preparation of a medicament for preventing or treating a degenerative brain disease.

According to an embodiment, there is provided a method of treating a degenerative brain disease, which comprises administering the compound to a patient.

Hereinafter, the present invention will be described, by way of example only, in more detail with reference to the following examples. However, these examples are provided to illustrate the present invention with specific embodiments. It is not intended to limit the scope of the present invention to the those described therein.

Preparation Example 1: Synthesis of Intermediate 1 (2,5-dichloro-7-methyl-7H-pyrrolo[2,3-d]pyrimidine)

acetate and then dried over MgSO_4 . It was filtered under reduced pressure, concentrated, and subjected to column chromatography to obtain 0.83 g of the target compound (yield: 84%).

MS (ESI) m/z 170.0 $[\text{M}+\text{H}]^+$

5 **Step 2: Synthesis of 5-chloro-4-nitro-1-(oxetan-3-yl)-1H-pyrazole**

THF (10 ml) was added to 4-nitro-1-(oxetan-3-yl)-1H-pyrazole (0.83 g, 4.90 mmol). After the temperature was lowered to -78°C , LiHMDS (1 M in THF, 9.81 ml) was added thereto dropwise. After it was stirred for 30 minutes, hexachloroethane (1.39 g, 5.88 mmol) dissolved in THF (5 ml) was added thereto. After it was stirred at -78°C for 1 hour, aqueous NaCl (10 ml) was added thereto to terminate the reaction, followed by extraction with ethyl acetate. It was dried over MgSO_4 , concentrated, and then subjected to column chromatography to obtain 0.42 g of the target compound (yield: 43%).

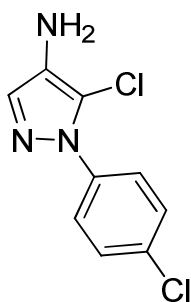
MS (ESI) m/z 204.1 $[\text{M}+\text{H}]^+$

15 **Step 3: Synthesis of Intermediate 18**

EtOH (20 ml) and water (2 ml) were added to 5-chloro-4-nitro-1-(oxetan-3-yl)-1H-pyrazole (0.42 g, 2.06 mmol). Fe (0.34 g, 6.18 mmol) and NH_4Cl (0.33 g, 6.18 mmol) were added thereto, followed by refluxing thereof at 90°C for 3 hours. After the temperature was lowered to room temperature, it was filtered and concentrated under reduced pressure. Ethyl acetate was added thereto, and it was subjected to sonication for 3 minutes. After the insoluble material was filtered out, it was concentrated to obtain 0.34 g of the target compound (yield: 95%).

MS (ESI) m/z 173.9, 176.1 $[\text{M}+\text{H}]^+$

25 **Preparation Example 19: Synthesis of Intermediate 19 (5-chloro-1-(4-chlorophenyl)-1H-pyrazol-4-amine)**



Step 1: Synthesis of 1-(4-chlorophenyl)-4-nitro-1H-pyrazole

4-Nitro-1H-pyrazole (1 g, 8.84 mmol), 4-chlorobenzenboronic acid (2.76 g, 17.68 mmol) and $\text{Cu}(\text{OAc})_2$ (2.40 g, 13.26 mmol) were added to DCM (40 ml). Pyridine (2.85 ml, 35.37 mmol) was added thereto, followed by stirring thereof at room temperature for 20 hours. Upon termination of the reaction, it was filtered and extracted with DCM and water. The organic layer was dried over MgSO_4 and filtered. It was concentrated under reduced pressure and subjected to column chromatography to obtain 0.88 g of the target compound (yield: 44%).

Step 2: Synthesis of 5-chloro-1-(4-chlorophenyl)-4-nitro-1H-pyrazole

THF (6 ml) was added to 1-(4-chlorophenyl)-4-nitro-1H-pyrazole (0.64 g, 2.86 mmol). After the temperature was lowered to -78°C , LiHMDS (1 M in THF, 5.7 ml) was added thereto dropwise. After it was stirred for 30 minutes, hexachloroethane (0.81 g, 3.43 mmol) dissolved in THF (3 ml) was added thereto. After it was stirred at -78°C for 1 hour, aqueous NaCl (10 ml) was added thereto to terminate the reaction. It was extracted with ethyl acetate, dried over MgSO_4 , and concentrated. It was subjected to column chromatography to obtain 0.20 g of the target compound (yield: 27%).

MS (ESI) m/z 258.2, 260.0 $[\text{M}+\text{H}]^+$

Step 3: Synthesis of Intermediate 19

EtOH (15 ml) and water (1.5 ml) were added to 5-chloro-1-(4-chlorophenyl)-4-nitro-1H-pyrazole (0.20 g, 0.77 mmol). Fe (0.12 g, 2.32 mmol) and NH_4Cl (0.12 g, 2.32 mmol) were added thereto, followed by refluxing thereof at 90°C for 3 hours. After the temperature was lowered to room temperature, it was filtered and concentrated under

was added thereto, followed by stirring thereof at room temperature for 1 hour. Intermediate 41 (3-chloro-1-(4-fluorophenyl)-1H-pyrazol-4-amine, 76.2 mg, 0.34 mmol) was added thereto, which was stirred at 120°C for 16 hours. The temperature was then lowered to room temperature. Upon termination of the reaction, it was
 5 extracted with saturated NaHCO₃ and ethyl acetate, dried over MgSO₄, filtered, and concentrated under reduced pressure. It was subjected to column chromatography (MC:MeOH = 40:1) to obtain 21 mg of the target compound (yield: 13%).

MS (ESI) m/z 392.0, 394.0 [M+H]⁺

Method 2:

10 A suction flask was charged with Intermediate 8 (3-chloro-1-ethyl-6-(methylsulfonyl)-1H-pyrazolo[3,4-d]pyrimidine, 82.4 mg, 0.34 mmol), Intermediate 41 (3-chloro-1-(4-fluorophenyl)-1H-pyrazol-4-amine, 104.5 mg, 0.49 mmol), and p-toluenesulfonic acid (PTSA, 72.2 mg, 0.38 mmol). NMP (1 ml) was added thereto, followed by stirring thereof at 110°C for 16 hours. The temperature was lowered to
 15 room temperature, and it was neutralized with saturated NaHCO₃ to precipitate a brown solid. The solid obtained by filtration was subjected to column chromatography with ethyl acetate to obtain 76.7 mg of the target compound (yield: 51%).

Examples 45 to 62: Preparation of Compounds 45 to 62

Compounds 45 to 62 were prepared by a procedure and a method similar to those
 20 of Example 44, except that the type of each intermediate was changed as shown in Table 4 below. The physicochemical properties of each compound are shown in Table 5 below.

[Table 4]

No.	Intermediate	
Example 45	Intermediate 8	Intermediate 29
Example 46	Intermediate 10	Intermediate 47
Example 47	Intermediate 8	Intermediate 49
Example 48	Intermediate 8	Intermediate 50
Example 49	Intermediate 9	Intermediate 47
Example 50	Intermediate 9	Intermediate 29
Example 51	Intermediate 8	Intermediate 56

Test method

After the compound was dissolved in 100% DMSO at 10 mM, it was serially diluted to the range of 1 μ M to 10 μ M using biochemical LRRK2 assay buffer (50 mM HEPES (4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid) pH 7.5, 10 mM MgCl₂, 1 mM EGTA (1,2-bis(o-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid), 2 mM DTT (dithiothreitol), and 0.01% Tween-20 (Aldrich)). Purified LRRK2 (CARNA BIOSCIENCES) was added to a black U-bottom 96-well microtiter plate containing 6 μ l of the serially diluted compound, followed by incubation at room temperature for 30 minutes. For the kinase reaction, ATP and a substrate solution specific urea-polypeptide (UlightTM-poly TK, PerkinElmer) were added. The reaction was carried out at room temperature for 1 hour, and it was detected with an detection solution (brand name: LANCE) containing EDTA. A LANCE detection solution containing europium-labeled antibody (LRRK2 specific PT66) was added, followed by incubation at room temperature for 50 minutes, to terminate the kinase experiment. The phosphorylated substrate was detected by 665 nm emission measurement. IC₅₀ values were calculated by a non-linear regression analysis using a Prism program (PrismTM software) with reference to the absence of a kinase inhibitor. The results are shown in Table 6 below.

As a comparative assay, a compound LRR2-IN-1, that known to be a reference compound for LRRK2 inhibitor, have also tested an inhibitory activity.

[Table 6]

Compound No.	IC ₅₀ (nM)	Compound No.	IC ₅₀ (nM)
LRRK2-IN-1	8.20	43	5.83
25	6.67	46	7.91
28	6.50	47	6.48
30	2.02	51	4.75
31	4.66	52	5.60
32	2.50	55	4.49
33	6.07	57	7.22
35	6.66	58	5.92
42	5.11	59	3.94

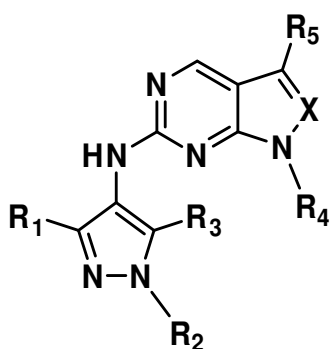
As shown in Table 6 above, the compounds of the present disclosure had an

Claims

[Claim 1]

A compound selected from the group consisting of a compound represented by the following Formula 1, and a pharmaceutically acceptable salt, hydrate, solvate, prodrug, and isomer thereof:

[Formula 1]



in the above formula,

X is CH or N;

R₁ is hydrogen, halogen, or C₁₋₄ alkyl or C₁₋₄ alkoxy unsubstituted or substituted with one or more halogens;

R₂ is C₁₋₆ alkyl, C₁₋₃ alkoxy C₁₋₆ alkyl, C₃₋₆ cycloalkyl C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, 4- to 7-membered heterocycloalkyl, or C₆₋₁₀ aryl unsubstituted or substituted with one or more halogens;

wherein the 4- to 7-membered heterocycloalkyl may be substituted with C₁₋₄ alkyl, C₁₋₄ alkylcarbonyl unsubstituted or substituted with one or more halogens, C₃₋₆ cycloalkylcarbonyl, 4- to 7-membered heterocycloalkylcarbonyl unsubstituted or substituted with C₁₋₄ alkyl, C₁₋₄ alkylsulfonyl, C₃₋₆ cycloalkylsulfonyl, or oxetanyl, and

the heterocycloalkyl contains at least one atom selected from N, O, and S,

R₃ is hydrogen, halogen, or C₁₋₄ alkyl;

R₄ is C₁₋₆ alkyl or C₃₋₆ cycloalkyl unsubstituted or substituted with one or more halogens; and

R₅ is halogen, or C₁₋₄ alkyl unsubstituted or substituted with one or more

halogens.

[Claim 2]

The compound of claim 1, wherein R₁ is hydrogen, halogen, trifluoro C₁₋₄ alkyl, C₁₋₄ alkyl, or C₁₋₄ alkoxy.

[Claim 3]

The compound of claim 1, wherein R₄ is trifluoro C₁₋₄ alkyl, C₁₋₄ alkyl, or C₃₋₆ cycloalkyl.

[Claim 4]

The compound of claim 1, wherein R₅ is halogen, trifluoro C₁₋₄ alkyl, or C₁₋₄ alkyl.

[Claim 5]

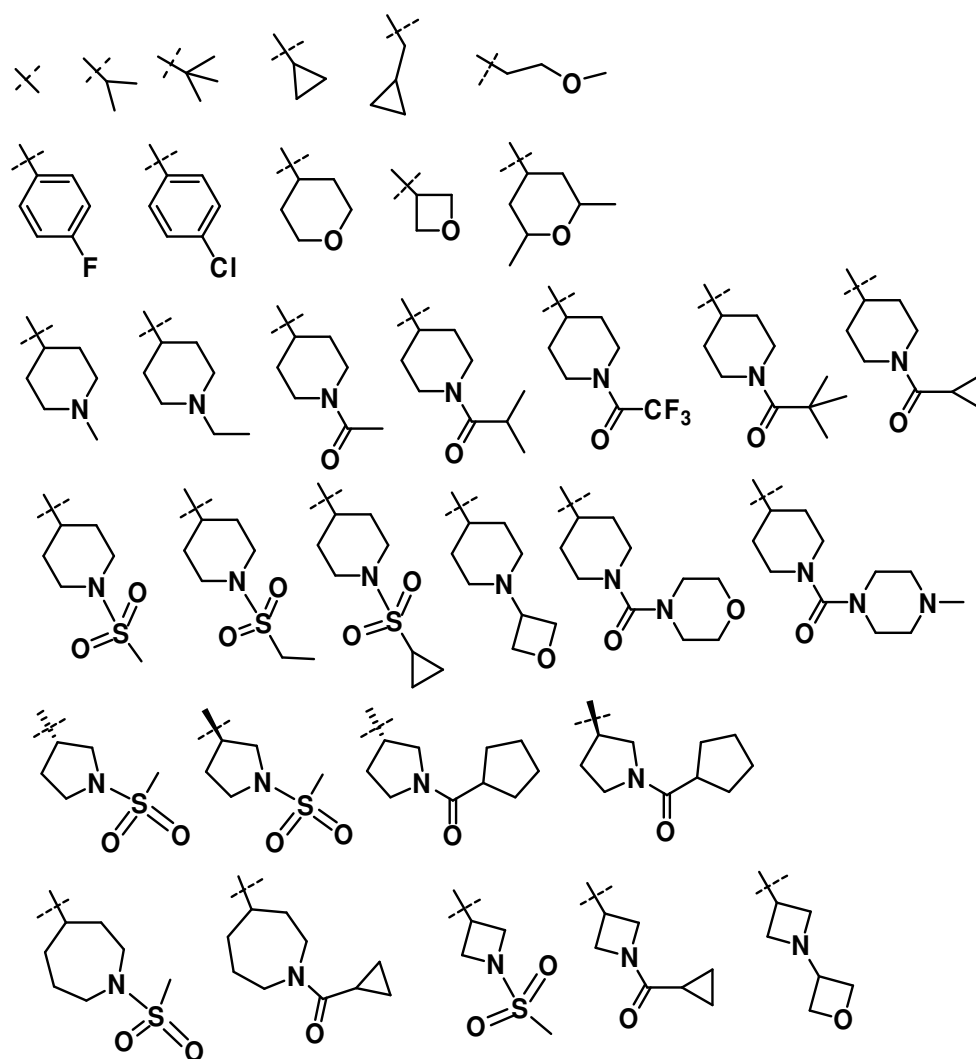
The compound of claim 1, wherein R₂ is C₁₋₄ alkyl, C₁₋₃ alkoxy C₁₋₄ alkyl, C₃₋₆ cycloalkyl C₁₋₄ alkyl, C₁₋₄ alkoxy, C₃₋₆ cycloalkyl, 4- to 7-membered heterocycloalkyl, or C₆₋₁₀ aryl substituted with F or Cl,

wherein the 4- to 7-membered heterocycloalkyl may be substituted with C₁₋₄ alkyl, trifluoro C₁₋₄ alkylcarbonyl, C₁₋₄ alkylcarbonyl, C₃₋₆ cycloalkylcarbonyl, 4- to 7-membered heterocycloalkylcarbonyl unsubstituted or substituted with C₁₋₄ alkyl, C₁₋₄ alkylsulfonyl, C₃₋₆ cycloalkylsulfonyl, or oxetanyl, and

the heterocycloalkyl contains at least one atom selected from N and O.

[Claim 6]

The compound of claim 5, wherein R₂ is selected from the following substituents:



in the above substituents, , , and  refer to the sites to be bonded.

[Claim 7]

The compound of claim 1, wherein the compound represented by Formula 1 is selected from the group consisting of the following compounds:

- 1) N-(5-chloro-1-methyl-1H-pyrazol-4-yl)-7-methyl-5-(trifluoromethyl)-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 2) 5-chloro-N-(1-isopropyl-3-methoxy-1H-pyrazol-4-yl)-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 3) 5-chloro-N-(3-chloro-1-isopropyl-1H-pyrazol-4-yl)-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,

- 4) 5-chloro-7-methyl-N-(1-(tetrahydro-2H-pyran-4-yl)-3-(trifluoromethyl)-1H-pyrazol-4-yl)-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 5) 5-chloro-N-(5-chloro-1-methyl-1H-pyrazol-4-yl)-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 6) 5-chloro-N-(5-chloro-1-methyl-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 7) 5-chloro-N-(3-chloro-1-isopropyl-1H-pyrazol-4-yl)-7-isopropyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 8) 5-chloro-N-(3-chloro-1-isopropyl-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 9) 5-chloro-N-(1-isopropyl-3-(trifluoromethyl)-1H-pyrazol-4-yl)-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 10) 5-chloro-N-(1-(2-methoxyethyl)-3-(trifluoromethyl)-1H-pyrazol-4-yl)-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 11) N-(1-butyl-3-(trifluoromethyl)-1H-pyrazol-4-yl)-5-chloro-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 12) 5-chloro-N-(3-chloro-1-(2-methoxyethyl)-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 13) 5-chloro-N-(3-chloro-1-(cyclopropylmethyl)-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 14) 5-chloro-N-(3-chloro-1-cyclopropyl-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 15) 5-chloro-N-(3-chloro-1-cyclopropyl-1H-pyrazol-4-yl)-7-cyclopropyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 16) 5-chloro-N-(5-chloro-1-(oxetan-3-yl)-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 17) 5-chloro-N-(3-chloro-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 18) 5-chloro-N-(3-chloro-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 19) 5-chloro-N-(3-chloro-1-(2,6-dimethyltetrahydro-2H-pyran-4-yl)-1H-

pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,

20) 5-chloro-N-(3-chloro-1-(1-ethylpiperidin-4-yl)-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,

21) 5-chloro-N-(3-chloro-1-(4-fluorophenyl)-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,

22) 5-chloro-N-(5-chloro-1-(4-chlorophenyl)-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,

23) 1-(4-(5-chloro-4-(5-chloro-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)ethanone,

24) (4-(3-chloro-4-(5-chloro-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)(cyclopropyl)methanone,

25) 5-chloro-N-(3-chloro-1-(1-(methylsulfonyl)piperidin-4-yl)-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,

26) 1-(4-(3-chloro-4-(5-chloro-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)-2-methylpropane-1-one,

27) 5-chloro-N-(5-chloro-1-(1-(oxetan-3-yl)piperidin-4-yl)-1H-pyrazol-4-yl)-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,

28) 5-chloro-N-(5-chloro-1-(1-(oxetan-3-yl)piperidin-4-yl)-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,

29) 5-chloro-N-(5-chloro-1-(1-(oxetan-3-yl)piperidin-4-yl)-1H-pyrazol-4-yl)-7-cyclopropyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,

30) 5-chloro-N-(3-chloro-1-(1-(methylsulfonyl)piperidin-4-yl)-1H-pyrazol-4-yl)-7-cyclopropyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,

31) (4-(3-chloro-4-(5-chloro-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)(morpholino)methanone,

32) (4-(3-chloro-4-(5-chloro-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)(4-methylpiperazin-1-yl)methanone,

33) 1-(4-(3-chloro-4-(5-chloro-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)-2,2-dimethylpropane-1-one,

34) 5-chloro-N-(3,5-dimethyl-1-(1-(methylsulfonyl)piperidin-4-yl)-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,

- 35) 5-chloro-N-(3-chloro-1-(1-(cyclopropylsulfonyl)piperidin-4-yl)-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 36) (R)-5-chloro-N-(3-chloro-1-(1-(methylsulfonyl)pyrrolidin-3-yl)-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 37) (S)-5-chloro-N-(3-chloro-1-(1-(methylsulfonyl)pyrrolidin-3-yl)-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 38) (R)-(3-(3-chloro-4-(5-chloro-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-ylamino)-1H-pyrazol-1-yl)pyrrolidin-1-yl)(cyclopentyl)methanone,
- 39) (S)-(3-(3-chloro-4-(5-chloro-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-ylamino)-1H-pyrazol-1-yl)pyrrolidin-1-yl)(cyclopentyl)methanone,
- 40) 5-chloro-N-(3-chloro-1-(1-(methylsulfonyl)azetidin-3-yl)-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 41) (3-(3-chloro-4-(5-chloro-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-ylamino)-1H-pyrazol-1-yl)azetidin-1-yl)(cyclopropyl)methanone,
- 42) 5-chloro-N-(3-chloro-1-(1-(methylsulfonyl)azepan-4-yl)-1H-pyrazol-4-yl)-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-amine,
- 43) (4-(3-chloro-4-(5-chloro-7-ethyl-7H-pyrrolo[2,3-d]pyrimidin-2-ylamino)-1H-pyrazol-1-yl)azepan-1-yl)(cyclopropyl)methanone,
- 44) 3-chloro-N-(3-chloro-1-(4-fluorophenyl)-1H-pyrazol-4-yl)-1-ethyl-1H-pyrazolo[3,4-d]pyrimidin-6-amine,
- 45) 3-chloro-N-(5-chloro-1-(1-(oxetan-3-yl)piperidin-4-yl)-1H-pyrazol-4-yl)-1-ethyl-1H-pyrazolo[3,4-d]pyrimidin-6-amine,
- 46) 3-chloro-N-(3-chloro-1-(1-(methylsulfonyl)piperidin-4-yl)-1H-pyrazol-4-yl)-1-cyclopropyl-1H-pyrazolo[3,4-d]pyrimidin-6-amine,
- 47) 3-chloro-N-(3-chloro-1-(1-(cyclopropylsulfonyl)piperidin-4-yl)-1H-pyrazol-4-yl)-1-ethyl-1H-pyrazolo[3,4-d]pyrimidin-6-amine,
- 48) 1-(4-(3-chloro-4-(3-chloro-1-ethyl-1H-pyrazolo[3,4-d]pyrimidin-6-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)-2,2,2-trifluoroethanone,
- 49) 3-chloro-N-(3-chloro-1-(1-(methylsulfonyl)piperidin-4-yl)-1H-pyrazol-4-yl)-1-(2,2,2-trifluoroethyl)-1H-pyrazolo[3,4-d]pyrimidin-6-amine,
- 50) 3-chloro-N-(5-chloro-1-(1-(oxetan-3-yl)piperidin-4-yl)-1H-pyrazol-4-yl)-

- 1-(2,2,2-trifluoroethyl)-1H-pyrazolo[3,4-d]pyrimidin-6-amine,
- 51) 3-chloro-N-(3-chloro-1-(1-(methylsulfonyl)azepan-4-yl)-1H-pyrazol-4-yl)-1-ethyl-1H-pyrazolo[3,4-d]pyrimidin-6-amine,
- 52) (4-(3-chloro-4-(3-chloro-1-ethyl-1H-pyrazolo[3,4-d]pyrimidin-6-ylamino)-1H-pyrazol-1-yl)azepan-1-yl)(cyclopropyl)methanone,
- 53) 1-(4-(3-chloro-4-(3-chloro-1-ethyl-1H-pyrazolo[3,4-d]pyrimidin-6-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)-2,2-dimethylpropane-1-one,
- 54) (4-(3-chloro-4-(3-chloro-1-ethyl-1H-pyrazolo[3,4-d]pyrimidin-6-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)(morpholino)methanone,
- 55) 3-chloro-N-(3-chloro-1-(1-(methylsulfonyl)piperidin-4-yl)-1H-pyrazol-4-yl)-1-ethyl-1H-pyrazolo[3,4-d]pyrimidin-6-amine,
- 56) (4-(3-chloro-4-(3-chloro-1-ethyl-1H-pyrazolo[3,4-d]pyrimidin-6-ylamino)-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)(cyclopropyl)methanone,
- 57) (4-(3-chloro-4-(3-chloro-1-ethyl-1H-pyrazolo[3,4-d]pyrimidin-6-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)(cyclopropyl)methanone,
- 58) 1-(4-(3-chloro-4-(3-chloro-1-ethyl-1H-pyrazolo[3,4-d]pyrimidin-6-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)ethanone,
- 59) 3-chloro-N-(3-chloro-1-(1-(ethylsulfonyl)piperidin-4-yl)-1H-pyrazol-4-yl)-1-ethyl-1H-pyrazolo[3,4-d]pyrimidin-6-amine,
- 60) (3-(3-chloro-4-(3-chloro-1-ethyl-1H-pyrazolo[3,4-d]pyrimidin-6-ylamino)-1H-pyrazol-1-yl)azetidin-1-yl)(cyclopropyl)methanone,
- 61) 3-chloro-N-(5-chloro-1-(1-(oxetan-3-yl)azetidin-3-yl)-1H-pyrazol-4-yl)-1-ethyl-1H-pyrazolo[3,4-d]pyrimidin-6-amine,
- 62) 3-chloro-N-(5-chloro-1-(1-(methylsulfonyl)piperidin-4-yl)-1H-pyrazol-4-yl)-1-ethyl-1H-pyrazolo[3,4-d]pyrimidin-6-amine.

[Claim 8]

The compound of claim 1, wherein the pharmaceutically acceptable salt is one or more selected from the group consisting of hydrochloride, hydrobromide, hydroiodide, sulfate, nitrate, methanesulfonate, ethanesulfonate, benzenesulfonate, and toluenesulfonate.

[Claim 9]

A pharmaceutical composition for use in the prevention or treatment of a degenerative brain disease, the pharmaceutical composition comprising the compound of any one of claims 1 to 8 as an active ingredient.

[Claim 10]

The pharmaceutical composition of claim 9, wherein the degenerative brain disease is Parkinson's disease.

[Claim 11]

The pharmaceutical composition of claim 9, which has an inhibitory activity selective to LRRK2(leucine-rich repeat kinase 2).

[Claim 12]

A use of the compound of any one of claims 1 to 8 for the preparation of a medicament for preventing or treating a degenerative brain disease.