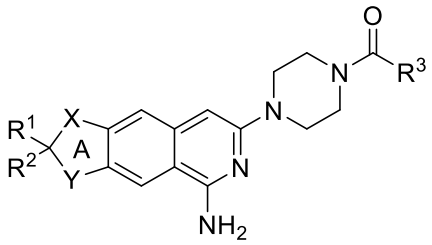
CLAIMS

What is claimed is:

1. An isoquinoline derivative represented by a general structural formula as follows:



, wherein:

ring A represents an optionally substituted five-membered oxygen-containing heterocycle;

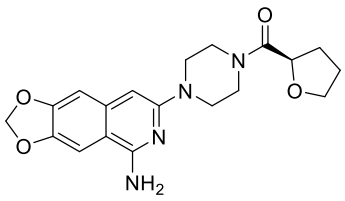
X is O or C, Y is O or C, and at least one of X and Y is O;

R^1 represents hydrogen or methyl;

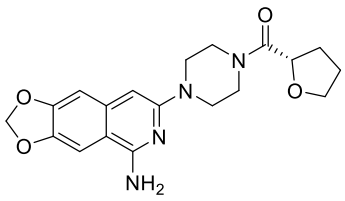
R^2 represents hydrogen or methyl; and

R^3 is five-membered cycloalkyl, or five-membered heterocyclic alkyl containing one heteroatom selected from an oxygen atom or a nitrogen atom,

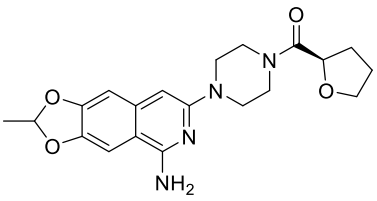
wherein the isoquinoline derivative has any one of the following specific structures:



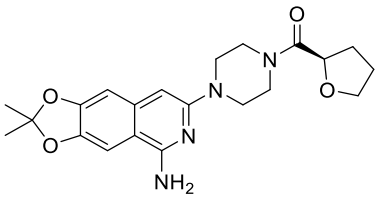
T1



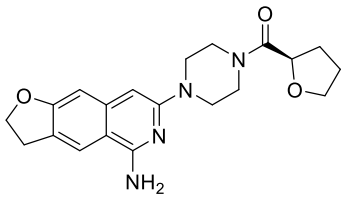
T2



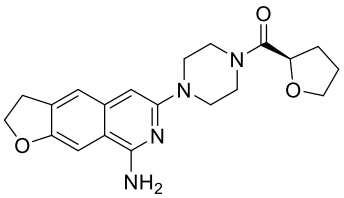
T3



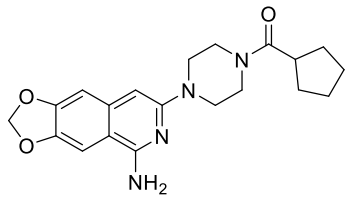
T4



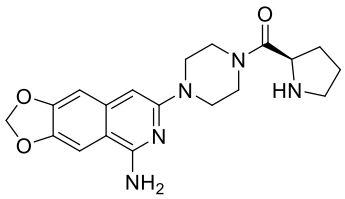
T5



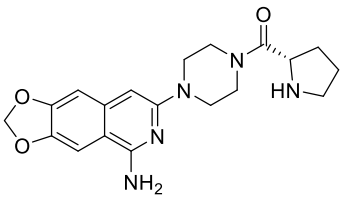
T6



T7



T8



T9 .

2. A pharmaceutically acceptable salt of the isoquinoline derivative according to claim 1, comprising hydrochloride, sulfate, hydrobromide, nitrate, trifluoroacetate, acetate, phosphate, benzenesulfonate, p-toluenesulfonate, methanesulfonate, oxalate, tartrate, fumarate, maleate, succinate, malate, benzoate, citrate, or lactate.

3. An isoquinoline derivative formulation, comprising, as an active ingredient:

the isoquinoline derivative according to claim 1; and/or

the pharmaceutically acceptable salt of the isoquinoline derivative according to claim 2,

wherein the formulation is respective pharmaceutical formulations prepared from the isoquinoline derivative or pharmaceutically acceptable salt thereof with a pharmaceutically acceptable excipient, such as water, alcohol, vegetable oil, starch, microcrystalline cellulose, lactose, gelatin, magnesium stearate, sodium alginate, maltodextrin, talc, crospovidone, gum, petrolatum, and the like.

4. A phosphoglycerate kinase activator, wherein the activator is the isoquinoline derivative according to claim 1, the pharmaceutically acceptable salt of the isoquinoline derivative according to claim 2, or the isoquinoline derivative formulation according to claim 3.

5. A medicament for treating or preventing a neurodegenerative disease, wherein the medicament is the isoquinoline derivative according to claim 1, the pharmaceutically acceptable salt of the isoquinoline derivative according to claim 2, or the isoquinoline derivative formulation according to claim 3.

6. A medicament for treating or preventing a metabolic disease, wherein the medicament is the isoquinoline derivative according to claim 1, the pharmaceutically acceptable salt of the isoquinoline derivative according to claim 2, or the isoquinoline derivative formulation according to claim 3.

7. The isoquinoline derivative according to claim 1, the pharmaceutically acceptable salt

of the isoquinoline derivative according to claim 2, or the isoquinoline derivative formulation according to claim 3 for use in therapy of a neurodegenerative disease.

8. The isoquinoline derivative according to claim 1, the pharmaceutically acceptable salt of the isoquinoline derivative according to claim 2, or the isoquinoline derivative formulation according to claim 3 for use in therapy of a metabolic disease.

9. Use of the isoquinoline derivative according to claim 1, the pharmaceutically acceptable salt of the isoquinoline derivative according to claim 2, or the isoquinoline derivative formulation according to claim 3 in manufacture of a medicament for treating or preventing a neurodegenerative disease.

10. Use of the isoquinoline derivative according to claim 1, the pharmaceutically acceptable salt of the isoquinoline derivative according to claim 2, or the isoquinoline derivative formulation according to claim 3 in manufacture of a medicament for treating or preventing a metabolic disease.

11. A method for preparing the isoquinoline derivative according to claim 1, the method comprising one of the following synthetic routes or a combination thereof:

synthetic route A:

adding malonic acid and piperidine to a solution of compound I for reaction, to obtain compound II;

reacting compound II in the presence of a catalyst under a H_2 atmosphere to obtain compound III;

reacting compound III with an oxalyl chloride to generate an acyl chloride, then reacting under catalysis of aluminum trichloride to obtain compound IV;

reacting compound IV with isoamyl nitrite under an acidic condition to obtain compound V;

reacting compound V with phosphorus oxychloride to obtain compound VI;

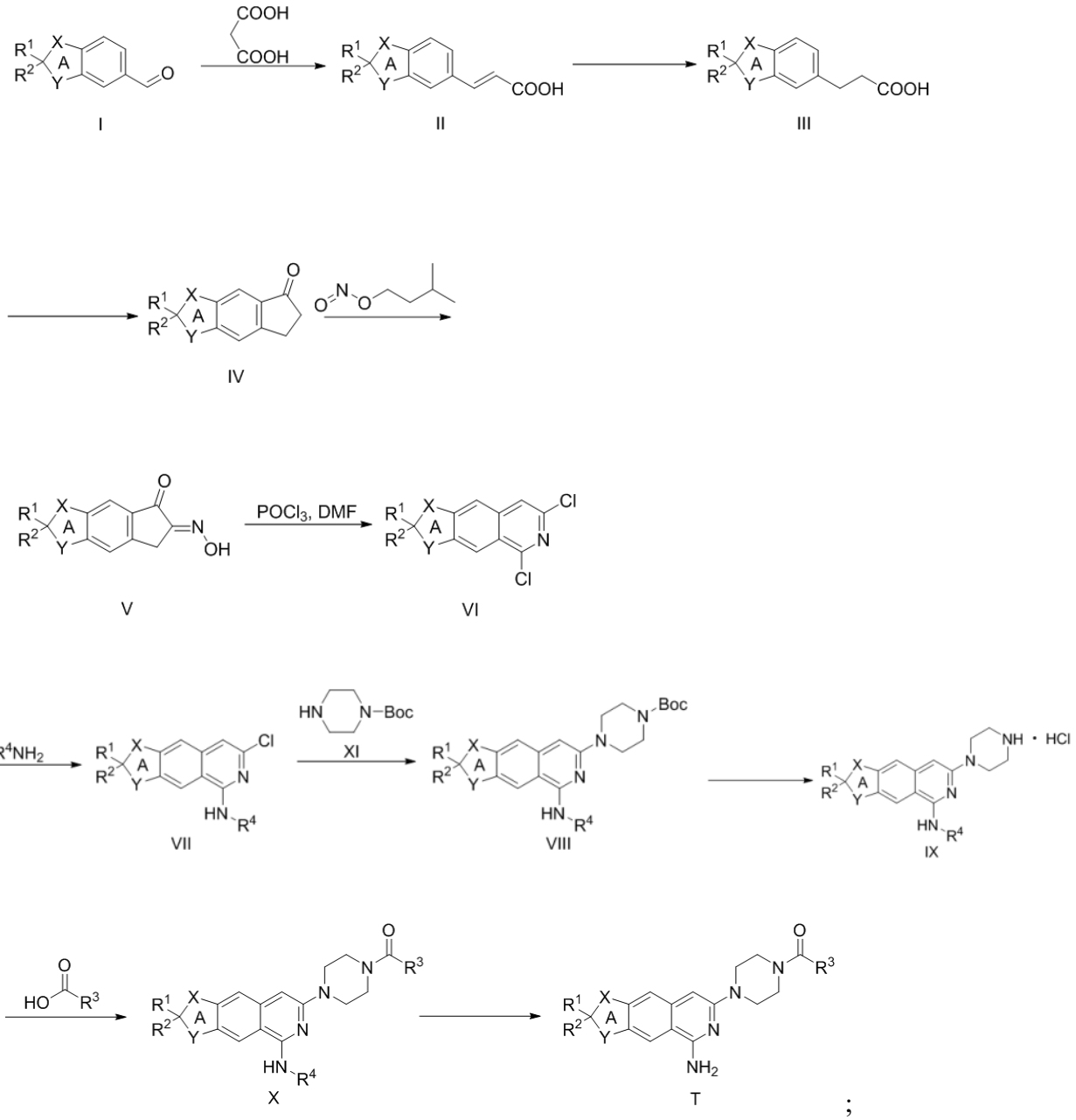
reacting compound VI with an amino protecting reagent in N-methylpyrrolidone to obtain compound VII;

reacting compound VII, compound XI, dioxane, $Pd_2(dba)_3$, RuPhos, and cesium carbonate together to obtain compound VIII;

deprotecting compound VIII to remove a Boc protecting group to obtain compound IX;

reacting compound IX with R^3-COOH to obtain compound X; and

reacting compound X with trifluoroacetic acid to remove an amino protecting group to obtain isoquinoline derivative compound T, the reaction route A being as follows:



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synthetic route B:

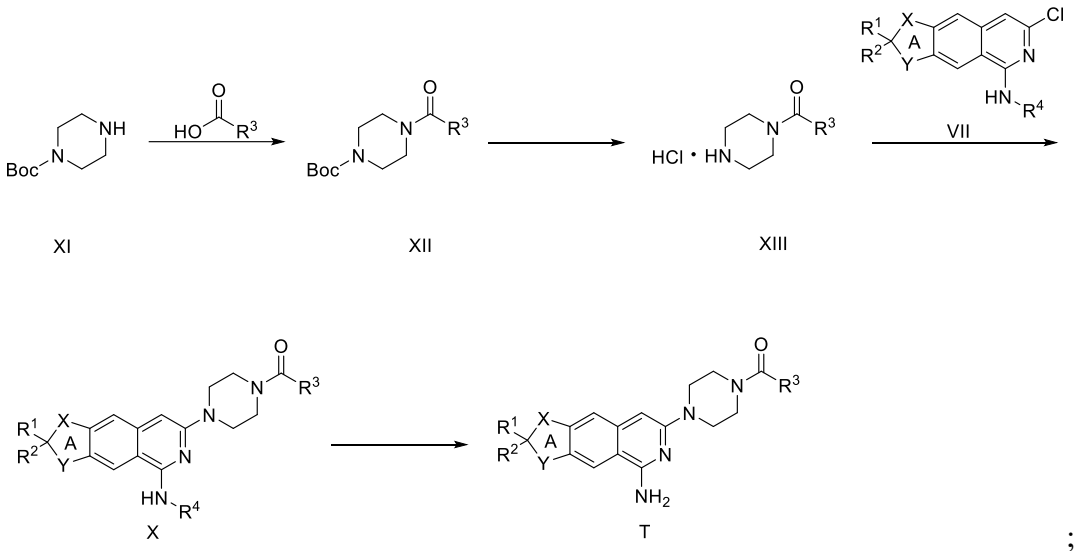
reacting compound XI with R^3-COOH, O-(7-azabenzotriazol-1-yl)-N,N,N',N'-

tetramethyluronium hexafluorophosphate, and N,N-diisopropylethylamine in a solvent to obtain compound XII;

deprotecting compound XII to remove a Boc protecting group to obtain compound XIII;

reacting compound XIII with compound VII obtained according to synthetic route A, dioxane, $Pd_2(dba)_3$, RuPhos, and cesium carbonate together to obtain compound X; and

reacting compound X with trifluoroacetic acid to remove an amino protecting group to obtain isoquinoline derivative compound T; the reaction route B being as follows:



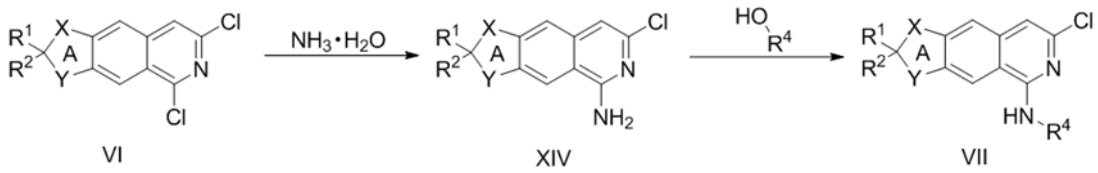
; and

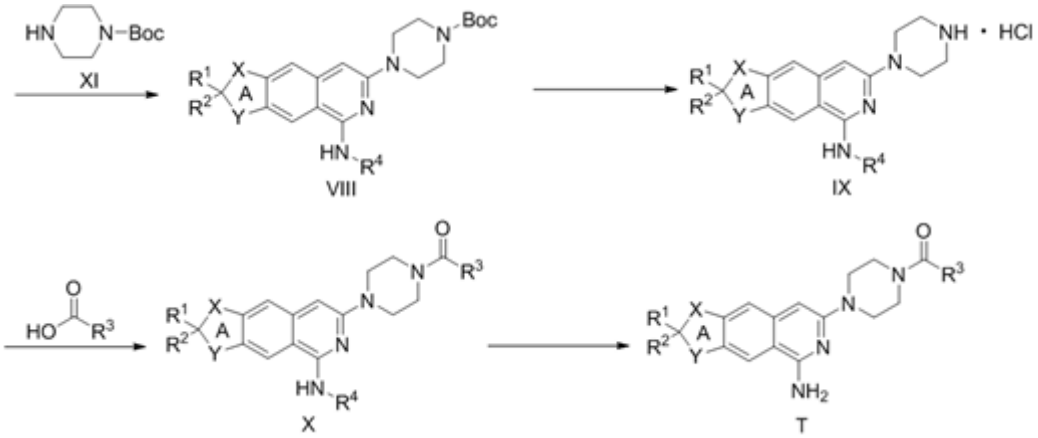
synthetic route C:

reacting compound VI obtained according to synthetic route A with ammonia water to obtain compound XIV;

reacting compound XIV with an amino protecting reagent to obtain compound VII; and

treating compound VII according to a method of synthetic route A to obtain isoquinoline derivative Compound T; the reaction route C being as follows:





,

wherein R^4 of compounds involved in synthetic route A, synthetic route B, and synthetic route C is an amino protecting group.