Table 18

Group	Number	Administration information						
	Male	Test compound	Administration dosage* (mg/kg)	Administration concentration (mg/mL)	Administration volume (mL/kg)	Collected sample	Mode of administration	Vehicle
G1	3	Compound of the present disclosure	10	1	10	Plasma	Oral administration (Intragastric administration)	0.5% MC
G2	3	Compound of the present disclosure	1	0.2	5	Plasma	Intravenous injection	5% DMA + 5% Solutol + 90% Saline

* Dosage is calculated based on free base.

[126] **Sampling:** before and after the administration, 0.15 mL of blood was taken from the orbits under isoflurane anesthesia and placed in an EDTAK2 centrifuge tube. Centrifugation was performed at 5000 rpm at 4°C for 10 min, and the plasma was collected.

[127] The plasma collection time points for IV&PO groups were 0, 5 min, 15 min, 30 min, 1 h, 2 h, 4 h, 6 h, 8 h, and 24 h.

[128] Before analysis and detection, all samples were stored at -60°C. The samples were analyzed quantitatively by LC-MS/MS.

Table 19 Pharmacokinetic parameters of compounds of the present disclosure in plasma of rats

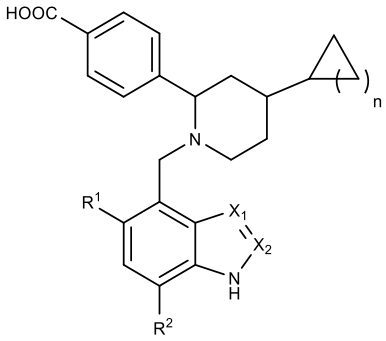
Test compound	Mode of administration*	Cmax (ng.mL-1)	$T_{1/2}$ (h)	Tmax (h)	$AUC_{0\text{-}24\ h}$ (ng/mL·h)	F%
Trifluoroacetate of compound 1	i.g. (10 mg/kg)	1128	3.20	-	9164	72.1
LNP023	i.g. (10 mg/kg)	867	3.39	3.5	9867	49

* Note: i.g. (intragastrically) administration of the compounds

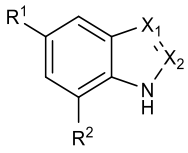
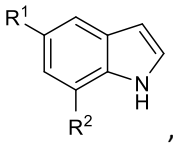
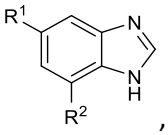
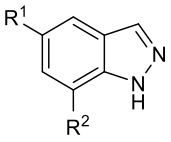
[129] Conclusion: the compounds of the present disclosure had good oral absorption in rats. Compared with LNP023, the trifluoroacetate of compound 1 had a higher maximum plasma concentration and higher oral bioavailability in rats.

Claims

1. A pharmaceutical composition, comprising an active ingredient A and a pharmaceutically acceptable excipient, wherein the active ingredient A is selected from a compound represented by general formula (I) or a stereoisomer, a tautomer, a deuterated form, a solvate, a prodrug, a metabolite, a pharmaceutically acceptable salt or an eutectic crystal thereof,



(I)


is selected from , , or ;

R^1 is selected from $-OCH_3$ or $-OCD_3$;

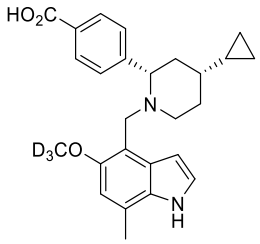
R^2 is selected from $-CH_3$ or $-CD_3$;

n is selected from 1, 2 or 3; and

the content of the active ingredient A is selected from 1.0%-90.0%, preferably 5.0%-75.0%, more preferably 10.0%-50.0%.

2. The pharmaceutical composition according to claim 1, wherein the pharmaceutical composition comprises 10-800 mg of the active ingredient A (calculated based on a free base).
3. The pharmaceutical composition according to claim 2, wherein the pharmaceutical composition comprises 10-400 mg of the active ingredient A (calculated based on a free base).
4. The pharmaceutical composition according to claim 3, wherein the pharmaceutical composition comprises 20-400 mg of the active ingredient A (calculated based on a free base).
5. The pharmaceutical composition according to claim 4, wherein the pharmaceutical composition comprises 30-200 mg of the active ingredient A (calculated based on a free base).

6. The pharmaceutical composition according to claim 2, wherein the pharmaceutical composition comprises 30 mg, 50 mg, 100 mg, 200 mg, 300 mg, 400 mg, 500 mg, 600 mg, 700 mg, or 800 mg of the active ingredient A (calculated based on a free base).
7. The pharmaceutical composition according to claim 1, wherein the pharmaceutical composition comprises the active ingredient A and a pharmaceutically acceptable excipient, the active ingredient A being selected from the compound represented by general formula (I) or a stereoisomer, a tautomer, a deuterated form, a solvate, a prodrug, a metabolite, a pharmaceutically acceptable salt or an eutectic crystal thereof, and the structure of the compound represented by general formula (I) being selected from one of the structures shown in Table S-1.
8. The pharmaceutical composition according to claim 1, wherein the structure of the compound represented by general formula (I) is selected from the following structure:



(Compound 1).

9. The pharmaceutical composition according to claim 1, wherein the active ingredient A is selected from compound 1 or succinate of compound 1, and preferably the molar ratio of compound 1 to succinic acid is 1 : 0.75.
10. The pharmaceutical composition according to claim 1, wherein the pharmaceutically acceptable excipient is selected from one or more of a filler, a disintegrant, a binder, a glidant and a lubricant.
11. The pharmaceutical composition according to claim 10, wherein the filler is selected from one or more of microcrystalline cellulose, mannitol, lactose, sucrose, sorbitol, dextran, pregelatinized starch, calcium dihydrogen phosphate and starch.
12. The pharmaceutical composition according to claim 11, wherein the content of the filler is selected from 10.0%-90.0%, preferably 20.0%-80.0%.
13. The pharmaceutical composition according to claim 11, wherein the filler is selected from a combination of microcrystalline cellulose and lactose, the content thereof being selected from10.0%-90.0%, preferably 20.0%-80.0%, and the content ratio of microcrystalline cellulose to lactose being 2 : 1 to 1 : 3, preferably 1 : 1 to 1 : 2.
14. The pharmaceutical composition according to claim 10, wherein the disintegrant is selected from one or more of sodium carboxymethyl starch, low-substituted hydroxypropyl cellulose,

crospovidone, croscarmellose sodium and calcium carboxymethylcellulose, the content thereof being selected from 1.0%-10.0%, preferably 3.0%-8.0%.

15. The pharmaceutical composition according to claim 10, wherein the binder is selected from one or more of povidone, hydroxypropyl cellulose, hypromellose and methylcellulose, the content thereof being selected from 1.0%-10.0%, preferably 2.0%-8.0%.
16. The pharmaceutical composition according to claim 10, further comprising a wetting agent, wherein the wetting agent is selected from one or both of water and ethanol.
17. The pharmaceutical composition according to claim 10, wherein the glidant is selected from one or more of talc, silica, colloidal silicon dioxide, polyethylene glycol and magnesium lauryl sulfate, the content thereof being selected from 0.1%-3.0%.
18. The pharmaceutical composition according to claim 10, wherein the lubricant is selected from one or more of magnesium stearate, calcium stearate, stearic acid and sodium stearyl fumarate, the content thereof being selected from 0.1%-3.0%.
19. The pharmaceutical composition according to claim 10, wherein the pharmaceutically acceptable excipient further comprises one or more of a flavoring agent, an antioxidant, a preservative, an opacifier and a film coating premixer.
20. Use of the pharmaceutical composition according to any one of claims 1-19 in the preparation of a related drug for treating nephropathy.