~~WHAT IS~~ CLAIM~~ED I~~S:

1. Use of a first amount of ornithine phenylacetate and a second amount of ornithine phenylacetate for the manufacture of a medicament for ~~A method of~~ treating or ameliorating hyperammonemia in a patient in need thereof, ~~comprising: administering~~wherein the medicament comprises a first amount of ornithine phenylacetate for administration ~~to the patient~~ during a first period of time~~;~~ and ~~administering a~~ the second amount of ornithine phenylacetate ~~to the patient~~ for administration during a second period of time;

wherein the first amount of ornithine phenylacetate is between about 10 g to about 30 g, and the second amount of ornithine phenylacetate is less than the first amount of ornithine phenylacetate.

2. The ~~method~~ use of claim 1, wherein the first period of time is from about 1 hour to about 10 hours, and a total of the first period of time and the second period of time is from about 18 hours to 36 hours.

~~3. The method use of claim 1 or 2, wherein the second period of time is longer than the first period of time, and a total of the first period of time and the second period of time is from about 18 hours to 36 hours.~~

~~4.~~3.The ~~method~~ use of ~~any one of claims 1 to 3~~claim 1 or 2, wherein the first amount of ornithine phenylacetate is about 20 g, and the first period of time is about 6 hours.

~~5. The method use of any one of claims 1 to 4, wherein the first period of time is about 6 hours.~~

~~6.~~4.The ~~method~~ use of any one of claims 1 to ~~5~~3, wherein the second amount of ornithine phenylacetate is about 15 g, and the second period of time is about 18 hours.

~~7. The method use of any one of claims 1 to 6, wherein the second period of time is about 18 hours.~~

~~8.~~5.The ~~method~~ use of any one of claims 1 to ~~7~~4, wherein the second amount of ornithine phenylacetate is ~~administered~~ for administration immediately after the completion of the administration of the first amount of ornithine phenylacetate.

~~9.~~6.The ~~method~~ use of any one of claims 1 to ~~8~~5, wherein the first amount of ornithine phenylacetate or the second amount of ornithine phenylacetate is ~~administered by~~for intravenous infusion.

~~10. The method use of any one of claims 1 to 9, wherein the second amount of ornithine phenylacetate is adapted to be administered by intravenous infusion.~~

~~11.~~7. The ~~method~~ use of any one of claims 1 to ~~10~~6, ~~further comprising administering a~~wherein the medicament further comprises a third amount of ornithine phenylacetate for

administration during a third period of time immediately following the completion of the administration of the second amount of ornithine phenylacetate~~ during a third period of time~~.

~~12.~~8. The ~~method~~ use of claim 7, wherein the third period of time is from about 2 days to about 10 days, or about 4 days.

~~13. The method use of claim 12, wherein the third period of time is about 4 days.~~

~~14.~~9. The ~~method~~ use of ~~any one of claims~~claim 7 ~~to 13~~or 8, wherein the third amount of ornithine phenylacetate ~~administered~~ for administration per day (24 hours) is the same or less than the second amount of ornithine phenylacetate.

~~15.~~10. The ~~method~~ use of claim 9, wherein the third amount of ornithine phenylacetate ~~administered~~ for administration per day is about 15 g.

~~16.~~11. The ~~method~~ use of any one of claims 7 to 10, wherein the third amount of ornithine phenylacetate is ~~administered by~~for intravenous infusion.

~~17.~~12. The ~~method~~ use of any one of claims 1 to 11, wherein the patient is also receiving standard of care.

~~18.~~13. ~~A method of~~Use of a first amount of ornithine phenylacetate and a second amount of ornithine phenylacetate for the manufacture of a medicament for treating or ameliorating hyperammonemia in a patient in need thereof, the medicament comprises a first amount of ornithine phenylacetate for administration during a first period of time and a second amount of ornithine phenylacetate for administration during a second period of time;~~comprising:~~

wherein the ~~selecting a~~ patient in need of treatment of hyperammonemia ~~who~~ is suffering from impaired renal function and~~, wherein said patient~~ has estimated glomerular filtration rate (eGFR) between 15 mL/min/1.73m^2 and 29 mL/min/1.73m^2; and

~~administering a first amount of ornithine phenylacetate to the patient during a first period of time; and~~

~~administer a second amount of ornithine phenylacetate to the patient during a second period of time;~~

wherein the first amount of ornithine phenylacetate is between about 5 g to about 20 g, and the second amount of ornithine phenylacetate is less than the first amount of ornithine phenylacetate, and wherein the medicament is for intravenous infusion.

~~19.~~14. The ~~method~~ use of claim 13, wherein the first period of time is from about 1 hour to about 10 hours and~~ the second period of time is longer than the first period of time~~ a total of the first period of time and the second period of time is from about 18 hours to 36 hours.

~~20. The method use of claim 18 or 19, wherein a total of the first period of time and the second period of time is from about 18 hours to 36 hours.~~

~~21.~~15. The ~~method~~ use of ~~any one of claims~~claim 13 ~~to 20~~or 14, wherein the first amount of ornithine phenylacetate is from about 7.5 g to about 15 g, and the first period of time is from about 4 hours to about 6 hours.

~~22. The method use of any one of claims 18 to 21, wherein the first period of time is from about 4 to about 6 hours.~~

~~23.~~16. The ~~method~~ use of any one of claims 13 to ~~22~~15, wherein the second amount of ornithine phenylacetate is from about 7.5 g to about 15 g, and the second period of time is from about 12 hours to about 18 hours.

~~24. The method use of any one of claims 18 to 23, wherein the second period of time is from about 12 hours to about 18 hours.~~

~~25.~~17. The ~~method~~ use of any one of claims 13 to ~~24~~16, wherein the second amount of ornithine phenylacetate is ~~administered~~ for administration immediately after the completion of the administration of the first amount of ornithine phenylacetate.

~~26. The method of any one of claims 18 to 25, wherein the first amount of ornithine phenylacetate is administered by intravenous infusion.~~

~~27. The method of any one of claims 18 to 26, wherein the second amount of ornithine phenylacetate is administered by intravenous infusion.~~

~~28.~~18. The ~~method~~ use of any one of claims 13 to ~~27~~17, ~~further comprising administering~~wherein the medicament further comprises a third amount of ornithine phenylacetate for administration during a third period of time immediately following the completion of the administration of the second amount of ornithine phenylacetate ~~during a third period of time~~.

~~29.~~19. The ~~method~~ use of claim 18, wherein the third period of time is from about 2 days to about 10 days, or from about 3 days to about 4 days.

~~30. The method use of claim 29, wherein the third period of time is from about 3 days to about 4 days.~~

~~31.~~20. The ~~method~~ use of ~~any one of claims~~claim 18 to ~~30~~19, wherein the third amount of ornithine phenylacetate administered per day (24 hours) is the same or less than the second amount of ornithine phenylacetate.

~~32.~~21. The ~~method~~ use of claim 20, wherein the third amount of ornithine phenylacetate ~~administered~~ for administration per day is from about 7.5 g to about 15 g, by intravenous infusion.

~~33. The method of any one of claims 28 to 32, wherein the third amount of ornithine phenylacetate is administered by intravenous infusion.~~

~~34.~~22. The ~~method~~ use of any one of claims 13 to ~~33~~21, wherein the patient is also receiving standard of care.

~~35.~~23. Use of a first amount of ornithine phenylacetate and a second amount of ornithine phenylacetate for the manufacture of a medicament for ~~A method of~~ treating or ameliorating hyperammonemia in a patient in need thereof based on the renal function of the patient, the medicament comprises the first amount of ornithine phenylacetate for administration during a first period of time and the second amount of ornithine phenylacetate for administration during a second period of time;~~, comprising:~~

~~determining the renal function or receiving information on the renal function of a patient who is in need of treatment of hyperammonemia; and~~

~~administering a first amount of ornithine phenylacetate to the patient during a first period of time;~~ wherein the first amount of ornithine phenylacetate is from about 10 g to about 30 g when the patient's estimated creatinine clearance is greater than 35 mL/min/1.73m^2; or

~~administering a first amount of ornithine phenylacetate to the patient during a first period of time;~~ wherein the first amount of ornithine phenylacetate is from about 5 g to about 15 g when the patient's estimated creatinine clearance is equal to or less than 35 mL/min/1.73m^2.

~~36.~~24. Use of a first amount of ornithine phenylacetate and a second amount of ornithine phenylacetate for the manufacture of a medicament for ~~A method of~~ treating or ameliorating hyperammonemia in a patient in need thereof based on ~~, comprising: determining the body weight or body size or receiving information on~~ the body weight or body size of ~~a~~ the patient, the medicament comprises ~~who is in need of treatment of hyperammonemia; administering a~~the first amount of ornithine phenylacetate ~~administered~~for administration ~~to the patient~~ during a first period of time and the second amount of ornithine phenylacetate for administration during a second period of time;

~~monitoring plasma concentration of phenylacetic acid in the patient; and~~

wherein the second ~~adjusting the~~ amount of ornithine phenylacetate adapted for administration ~~administered~~ to the patient is adjustable during a second period of time based on the plasma concentration of phenylacetic acid.

~~37.~~25. Use of a first amount of ornithine phenylacetate and a second amount of ornithine phenylacetate for the manufacture of a medicament for ~~A method of~~ treating or ameliorating

hyperammonemia in a patient in need thereof~~, comprising:determining~~ based on the degree of hepatic impairment ~~or receiving information on the degree of hepatic impairment~~ of the~~a~~ patient, the medicament comprises ~~who is in need of treatment of hyperammonemia; andadministering a~~ the first amount of ornithine phenylacetate ~~administered~~ for administration ~~to the patient~~ during a first period of time and the second amount of ornithine phenylacetate for administration during a second period of time;

~~monitoring plasma concentration of phenylacetic acid in the patient; and~~

~~adjusting the~~wherein the second amount of ornithine phenylacetate ~~administered to the patient~~for administration during ~~a~~ the second period of time is adjustable based on the plasma concentration of phenylacetic acid.

~~38. The method of any one of claims 1 to 37, further comprising measuring a serum ammonia level of the patient prior to administering the first amount of ornithine phenylacetate to the patient.~~

~~39.~~26. The ~~method~~ use of ~~claim 38~~any one of claims 1 to ~~37~~25, wherein the patient's serum ammonia level ~~of the patient~~ is ≥ 21 μmol/L.

~~40. A method of treating or ameliorating hyperammonemia in a patient in need thereof, comprising:~~

~~identifying or selecting a patient having or at risk of having an acute or chronic liver disease or condition;~~

~~measuring a serum ammonia level or receiving information on the serum ammonia level of the patient; and~~

~~administering a first amount of ornithine phenylacetate to the patient when the patient's serum ammonia level is ≥ 21 μmol/L.~~

~~41.~~27. The ~~method~~ use of any one of claims 1 to 26~~40~~, wherein the patient has cirrhosis.

~~42.~~28. The ~~method~~ use of any one of claims 1 to 27~~41~~, wherein the patient is at risk of hepatic encephalopathy or has had at least one episode of hepatic encephalopathy, or is hospitalized due to one or more hepatic encephalopathy episodes.

~~43. The method use of any one of claims 1 to 42~~41, ~~wherein the patient is hospitalized due to one or more hepatic encephalopathy episodes.~~

~~44.~~29. The ~~method~~ use of any one of claims 1 to 28~~43~~, wherein the patient has received at least 4 hours to 6 hours of standard of care prior to the administration of the first amount of ornithine phenylacetate.

~~45.~~30. The ~~method~~ use of any one of claims 1 to 29~~44~~, wherein ornithine phenylacetate is ~~administered~~ for administration as an aqueous solution comprising about 200 mg/mL to about 400 mg/mL ornithine phenylacetate, or about 300 mg/mL ornithine phenylacetate.

~~46. The method of claim 45, wherein the aqueous solution comprises about 300 mg/mL ornithine phenylacetate.~~

~~47.~~31. The ~~method~~ use of claim ~~45 or 46~~30, wherein the aqueous solution of ornithine phenylacetate has a pH of at least about 5, or a pH range of about 5.4 to about 6.5.

~~48. The method of claim 47, wherein the aqueous solution of ornithine phenylacetate has a pH range of about 5.4 to about 6.5.~~

~~49.~~32. A pharmaceutical formulation comprising an aqueous solution of about 200 mg/mL to 400 mg/mL of ornithine phenylacetate and at least one pH adjusting agent, wherein the aqueous solution has a pH of at least about 5.

~~50.~~33. The pharmaceutical formulation of claim ~~49~~32, wherein the pH of the aqueous solution has a pH range of about 5.4 to about 6.5.

~~51.~~34. The pharmaceutical formulation of claim ~~49–~~32 or ~~50~~33, wherein the pH adjusting agent is HCl or citric acid, or a combination thereof.

~~52. The pharmaceutical formulation of any one of claims 49 to 51, wherein the pharmaceutical formulation is stored at a temperature ranging from about 2°C to about 8°C.~~

~~53. The pharmaceutical formulation of any one of claims 49 to 52, wherein the aqueous solution comprises about 300 mg/mL of L-ornithine phenylacetate.~~

~~54.~~35. The pharmaceutical formulation of ~~any one of claims~~claim ~~49~~ 32 ~~to 53~~or 34, wherein formulation comprises less than 1% ornithine phenylacetate precipitate.

~~55.~~36. The pharmaceutical formulation of any one of claims ~~49~~ 32 to 35~~54~~, wherein the formulation comprises less than about 0.1% by weight of 3-amino-2-piperidone for up to 6 months at a storage temperature ranging from about 2°C to about 8°C.

~~56. The pharmaceutical formulation of claim 55, wherein 3-amino-2-piperidone is about 0.05% by weight or below at about 5 °C for up to six months.~~