CLAIMS

~~What is claimed is:~~

1. Use of a compound of Formula I or a pharmaceutically acceptable salt thereof in the manufacture of a medicament ~~A method~~ for determining glomerular filtration rate (GFR) in a patient in need thereof~~,~~ ; ~~said method comprising:~~

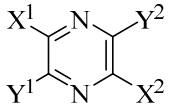
wherein the medicament is intended to be administered subcutaneously or intramuscularly ~~administering~~ to a ~~said~~ patient;

wherein the amount of the compound to be administered to the patient is between about 3 mg to about 250 mg ~~of a compound of Formula I or a pharmaceutically acceptable salt thereof as~~ in a solution at a concentration of ~~an~~ about 60 mg/ml to ~~an~~ about 300 mg/ml ~~solution~~, wherein the administration produces a plasma concentration of the compound that is substantially similar to a plasma concentration produced by intravenous administration of an identical amount of the compound;

wherein ~~measuring~~ a concentration of the compound of Formula I in said patient is intended to be measured, and

~~determining~~ wherein the GFR in said patient is intended to be determined using the concentration of the compound measured; and

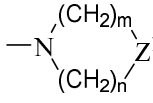
wherein Formula I is



Formula I

each of X^1 and X^2 are independently chosen from -CO(AA), -CN, $-CO_2R^1$, $-CONR^2R^3$, $-COR^4$, $-NO_2$, $-SOR^{35}$, $-SO_2R^6$, $-SO_2OR^7$ and $-PO_3R^8R^9$;

each Y^1 and Y^2 are independently chosen from $-OR^{10}$, $-SR^{11}$, $-NR^{12}R^{13}$, $-N(R^{14})COR^{15}$, -CONH(PS); $-P(R^{16})_2$, $-P(OR^{17})_2$; and


;

Z^1 is a single bond, -$CR^{18}R^{19}$-, -O-, -NR^{20}-, -$NCOR^{21}$-, -S-, -SO-, and -SO_2-; each R^1 to R^{21} are independently chosen from hydrogen, C_1-C_{10} alkyl optionally substituted with hydroxyl and carboxylic acid, C_3-C_6 polyhydroxylated alkyl, C_5-C_{10} aryl, C_5-C_{10} heteroaryl, C_3-C_5 heterocycloalkyl optionally substituted with C(O), -$(CH_2)_aCO_2H$ optionally substituted with C_5-C_{10} heteroaryl, $(CH_2)_aCONR^{30}R^{31}$, -$(CH_2)_aNHSO_3^-$, -$(CH_2)_aNHSO_3H$, -$(CH_2)_aOH$, -$(CH_2)_aOPO_3^=$, -$(CH_2)_aOPO_3H_2$, -$(CH_2)_aOPO_3H^-$, -$(CH_2)_aOR^{22}$, -$(CH_2)_aOSO_3^-$, -$(CH_2)_aOSO_3H$, -$(CH_2)_aPO_3^=$, -$(CH_2)_aPO_3H_2$, -$(CH_2)_aPO_3H^-$, -$(CH_2)_aSO_3^-$, -$(CH_2)_aSO_3H$, -$(CH_2)_dCO(CH_2CH_2O)_cR^{23}$, -$(CH_2)_d(CH_2CH_2O)_cR^{24}$, -$(CHCO_2H)_aCO_2H$, -$CH_2(CHNH_2)_aCH_2NR^{25}R^{26}$, -$CH_2(CHOH)_aCO_2H$, -$CH_2(CHOH)_aR^{27}$, -$CH[(CH_2)_bNH_2]_aCH_2OH$, -$CH[(CH_2)_bNH_2]_aCO_2H$, and -$(CH_2)_aNR^{28}R^{29}$; each R^{22} to R^{31} are independently chosen from hydrogen, C_1-C_{10} alkyl, and C_1-C_5-dicarboxylic acid; R^{35} is chosen from C_1-C_{10} alkyl optionally substituted with hydroxyl and carboxylic acid, C_3-C_6 polyhydroxylated alkyl, C_5-C_{10} aryl, C_5-C_{10} heteroaryl, C_3-C_5 heterocycloalkyl optionally substituted with C(O), -$(CH_2)_aCO_2H$ optionally substituted with C_5-C_{10} heteroaryl, -$(CH_2)_aCONR^{30}R^{31}$, -$(CH_2)_aNHSO_3^-$, -$(CH_2)_aNHSO_3H$, -$(CH_2)_aOH$, -$(CH_2)_aOPO_3^=$, -$(CH_2)_aOPO_3H_2$, -$(CH_2)_aOPO_3H^-$, -$(CH_2)_aOR^{22}$, -$(CH_2)_aOSO_3^-$, -$(CH_2)_aOSO_3H$, -$(CH_2)_aPO_3^=$, -$(CH_2)_aPO_3H_2$, -$(CH_2)_aPO_3H^-$, -$(CH_2)_aSO_3^-$, -$(CH_2)_aSO_3H$, -$(CH_2)_dCO(CH_2CH_2O)_cR^{23}$, -$(CH_2)_d(CH_2CH_2O)_cR^{24}$, -$(CHCO_2H)_aCO_2H$, -$CH_2(CHNH_2)_aCH_2NR^{25}R^{26}$, -$CH_2(CHOH)_aCO_2H$, -$CH_2(CHOH)_aR^{27}$, -$CH[(CH_2)_bNH_2]_aCH_2OH$, -$CH[(CH_2)_bNH_2]_aCO_2H$, and -$(CH_2)_aNR^{28}R^{29}$;

AA is a peptide chain comprising one or more amino acids selected from the group consisting of natural and unnatural amino acids, linked together by peptide or amide bonds and each instance of AA may be the same or different than each other instance;

PS is a sulfated or non-sulfated polysaccharide chain comprising one or more monosaccharide units connected by glycosidic linkages; and

'a' is a number from 1 to 10, 'c' is a number from 1 to 100, and each of 'm' and 'n' are independently a number from 1 to 3.

2. The ~~method~~ use of claim 1, wherein the concentration of ~~a~~ the compound ~~of Formula I~~ in said patient is intended to be measured over a measurement time window.

3. The ~~method~~ use of claim 1, wherein about 10 mg to about 150 mg of the compound ~~of the compound of Formula I~~ is intended to be subcutaneously or intramuscularly administered to ~~a~~ the patient.

4. The ~~method~~ use of claim 1, wherein the compound ~~of Formula I~~ is intended to be administered ~~subcutaneously or intramuscularly administered~~ to ~~a~~ the patient ~~as an~~ in the solution at a concentration of about 60 mg/ml to ~~an~~ about 150 mg/ml ~~solution~~.

5. The ~~method~~ use of claim 1 or claim 2, wherein the ~~solution~~ medicament further comprises at least one pharmaceutically acceptable excipient selected from the group consisting of antibacterial agents, antioxidants, buffering agents, osmolarity adjusting agents, pH adjusting agents, preservatives, solvents, stabilizing agents, surfactants, tonicity modifying agents, viscosity adjusting agents, and combinations thereof.

6. The ~~method~~ use of claim 5, wherein one of the at least one pharmaceutically acceptable excipient is phosphate buffered saline.

7. The ~~method~~ use of any one of the preceding claims, wherein said patient has a GFR of below 90 as determined in a previous measurement.

8. The ~~method~~ use of claim 1, wherein the ~~solution~~ medicament is packaged in a pre-filled syringe.

9. The ~~method~~ use of claim 8, wherein the medicament~~solution~~ is intended to be ~~subcutaneously or intramuscularly~~ administered to said patient by an auto-injector.

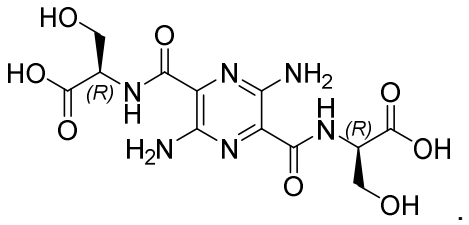
10. The ~~method~~ use of any one of the preceding claims, wherein a sensor is attached to at least one body site of said patient to detect transdermal fluorescence.

11. The ~~method~~ use of claim 10, wherein determining the GFR in said patient using the concentration of the compound measured comprises quantifying and displaying on a mobile computing device the transdermal fluorescence detected by the sensor.

12. The ~~method~~ use of claim 1, wherein both X^1 and X^2 are –CO(AA).

13. The ~~method~~ use of claim 12, wherein each instance of AA is a single D-α-amino acid.

14. The ~~method~~ use of any one of claims 1 to 8, wherein the compound of Formula I is



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15. The ~~method~~ use of any one of the preceding claims, wherein the pharmaceutically acceptable salt is a cationic or anionic salt.

16. The ~~method~~ use of claim 15, wherein the pharmaceutically acceptable salt is a selected from the group consisting of a sodium salt, a choline salt and a meglumine salt.

17. A kit for GFR assessment, the kit comprising:

about 3 mg to about 250 mg of a compound of Formula I or a pharmaceutically acceptable salt thereof as an about 60 mg/ml to an about 300 mg/ml solution,

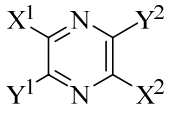
an injector device configured to subcutaneously or intramuscularly administer the solution into the body of a patient;

a sensor configured to attach to the body of the patient and detect transdermal fluorescence;

a mobile computing device wirelessly communicatively coupled to the sensor and programmed to receive data from the sensor and calculate the GFR of the patient based on the data; and

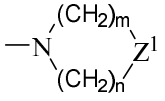
written instructions describing how to use the components of the kit in order to assess the GFR of the patient;

wherein Formula I is



Formula I

each of X^1 and X^2 is independently $–CO_2R^1$, $–CONR^1R^2$, –CO(AA) or –CONH(PS);

each of Y^1 and Y^2 is independently selected from the group consisting of $–NR^1R^2$ and ;

Z^1 is a single bond, $–CR^1R^2–$, –O–, $–NR^1–$, $–NCOR^1–$, –S–, –SO–, or $–SO_2–$;

each of R^1 to R^2 are independently selected from the group consisting of H, $–CH_2(CHOH)_aH$, $–CH_2(CHOH)_aCH_3$, $–CH_2(CHOH)_aCO_2H$, $–(CHCO_2H)_aCO_2H$, $–(CH_2CH_2O)_cH$, $–(CH_2CH_2O)_cCH_3$, $–(CH_2)_aSO_3H$, $–(CH_2)_aSO_3^-$, $–(CH_2)_aSO_2H$, $–(CH_2)_aSO_2^-$, $–(CH_2)_aNHSO_3H$, $–(CH_2)_aNHSO_3^-$, $–(CH_2)_aNHSO_2H$, $–(CH_2)_aNHSO_2^-$,$–(CH_2)_aPO_4H_3$, $–(CH_2)_aPO_4H_2^-$, $–(CH_2)_aPO_4H^{2-}$, $–(CH_2)_aPO_4^{3-}$, $–(CH_2)_aPO_3H_2$, $–(CH_2)_aPO_3H^-$, and $–(CH_2)_aPO_3^{2-}$;

AA is a peptide chain comprising one or more amino acids selected from the group consisting of natural and unnatural amino acids, linked together by peptide or amide bonds and each instance of AA may be the same or different than each other instance;

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