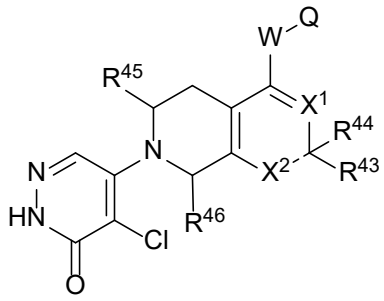
Claims:

1. Use of a TRPC5 inhibitor and a pharmaceutically acceptable carrier in the preparation of a pharmaceutical composition for treating a human subject suffering from a disease or disorder selected from kidney disease, anxiety, depression or cancer, wherein the pharmaceutical composition is to be administered to a human subject selected to have a urinary level of Rac1 above a pre-determined threshold between 100-500 pg/mL;

wherein the TRPC5 inhibitor is a compound of structural formula X:



(X),

or a pharmaceutically acceptable salt thereof, wherein:

"---" is a single bond or a double bond;

X^1 is CH or N;

when "---" is a double bond, X^2 is CH or N;

when "---" is a single bond, X^2 is $N(CH_3)$,

when X^1 is CH, X^2 is N or $N(CH_3)$;

W is -O-, $-N(CH_3)-$, $-N(CH_2CH_2OH)-$, cyclopropan-1,1-diyl, or $-CH(CH_3)-$;

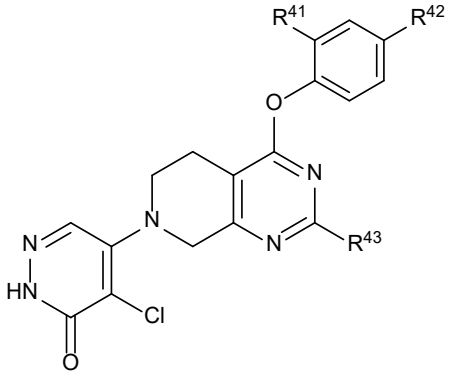
Q is 2-trifluoromethyl-4-fluorophenyl, 2-difluoromethyl-4-fluorophenyl, 2-trifluoromethylphenyl, 2-methyl-4-fluorophenyl, 2-chloro-4-fluorophenyl, 2-chlorophenyl, 1-(benzyl)-4-methylpiperidin-3-yl, 4-trifluoromethylpyridin-3-yl, 2-trifluoromethyl-6-fluorophenyl, 2-trifluoromethyl-3-cyanophenyl, 2-ethyl-3-fluorophenyl, 2-chloro-3-cyanophenyl, 2-trifluoromethyl-5-fluorophenyl, or 2-difluoromethylphenyl;

R^{43} is hydrogen, $-CH_2OH$, $-CH(OH)-CH_2OH$, $-NH_2$, $-CH(OH)CH_3$, $-OCH_3$, or $-NH-(CH_2)_2OH$; and when "---" is a double bond, R^{44} is absent;

and when "---" is a single bond, R^{43} and R^{44} are taken together to form =O; and

each of R^{45} and R^{46} is independently hydrogen or $-CH_3$.

2. The use of claim 1, wherein the TRPC5 inhibitor is a compound of Formula XI:



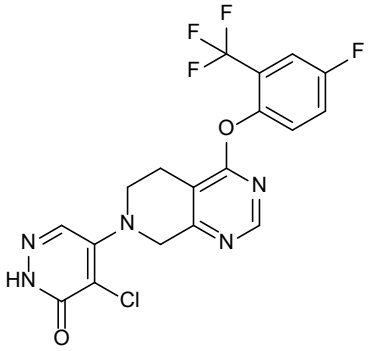
(XI), or a pharmaceutically acceptable salt thereof; wherein:

R^{41} is chloro, $-CF_3$, $-CHF_2$, or $-CH_3$;

R^{42} is hydrogen or fluoro; and

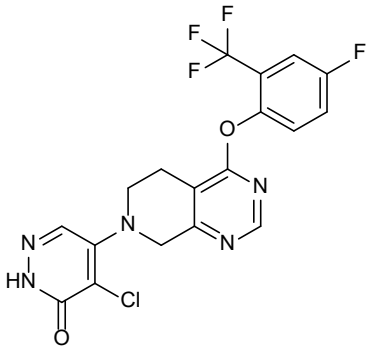
R^{43} is hydrogen, $-NH_2$, $-CH_2OH$, or $CH(OH)-CH_2OH$.

3. The use of claim 2, wherein the TRPC5 inhibitor is:



, or a pharmaceutically acceptable salt thereof.

4. The use of claim 2, wherein the TRPC5 inhibitor is



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5. The use of any one of claims 1-4, wherein the kidney disease is diabetic nephropathy, focal segmental glomerulosclerosis, minimal change disease, membranoproliferative glomerulonephritis (including post-streptococcal glomerulonephritis and bacterial endocarditis-associated glomerulonephritis), membranous nephropathy, other hepatitis C virus-associated glomerulopathies, HIV-associated glomerulopathies, COVID-19-associated acute kidney injury, Alport syndrome, polycystic kidney disease (both autosomal dominant and autosomal recessive), IgA nephropathy, other genetic nephropathies or ciliopathies (e.g., HNF1beta, nephronophthisis, autosomal dominant cystic/tubular kidney disease), lupus nephritis, Goodpasture's syndrome (anti-GBM disease), and another complement- or immune-mediated kidney disease.

6. The use of claim 5, wherein the kidney disease is diabetic nephropathy, or focal segmental glomerulosclerosis.

7. The use of claim 5, wherein the kidney disease is autosomal dominant polycystic kidney disease or autosomal recessive polycystic kidney disease.

8. The use of any one of claims 1-7, wherein the urinary Rac1 level in a subject is measured in a fraction of urine comprising extracellular vesicles.