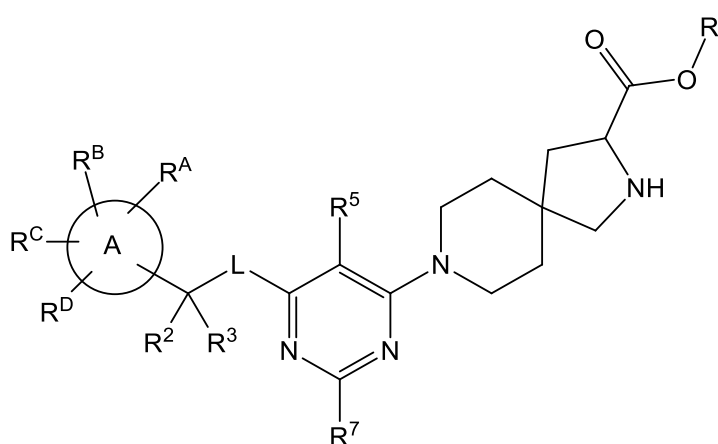


The Claims defining the Invention are as follows:

1. Use of a compound of Formula IIa:



IIa

or a pharmaceutically acceptable salt thereof, wherein:

Ring A is C_{3-10} cycloalkyl, C_{6-10} aryl, or 5 to 10-membered heteroaryl;

L is O or NR^4 ;

R^1 is H, C_{1-10} alkyl, or $-(CR^8R^9)_pOC(O)R^{10}$, wherein said C_{1-10} alkyl, is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from F, Cl, Br, CN, C_{1-4} alkyl, and C_{1-4} haloalkyl;

R^2 and R^3 are selected from H, and C_{1-4} haloalkyl;

wherein one of R^2 and R^3 is H and the other of R^2 and R^3 is a C_{1-4} haloalkyl;

R^4 is H or C_{1-4} alkyl;

R^5 is H;

R^7 is C_{1-4} alkyl or $NR^{13}R^{14}$;

R^8 and R^9 are each independently selected from H and C_{1-4} alkyl;

R^{10} is C_{1-6} alkyl optionally substituted by 1, 2 or 3 substituents independently selected from C_{1-6} haloalkyl, C_{3-10} cycloalkyl, OR^a , and NR^cR^d ;

R^{11} and R^{12} are each independently selected from H and C_{1-6} alkyl;

R^{13} is H or C_{1-4} alkyl;

R^{14} is H, C_{1-4} alkyl, C_{3-7} cycloalkyl, or $C(O)OR^{a1}$;

R^{15} is C_{3-7} cycloalkyl or C_{6-10} aryl;

R^A is H, Cy^1 , halo, C_{1-6} alkyl, C_{2-6} alkenyl, CN, NO_2 , OR^{a2} , SR^{a2} , $C(O)R^{b2}$, $C(O)NR^{c2}R^{d2}$, $C(O)OR^{a2}$, $OC(O)R^{b2}$, $OC(O)NR^{c2}R^{d2}$, $NR^{c2}R^{d2}$, $NR^{c2}C(O)R^{b2}$, $NR^{c2}C(O)OR^{a2}$, $NR^{c2}C(O)NR^{c2}R^{d2}$, $NR^{c2}S(O)R^{b2}$, $NR^{c2}S(O)_2R^{b2}$, $NR^{c2}S(O)_2NR^{c2}R^{d2}$, $S(O)R^{b2}$, $S(O)NR^{c2}R^{d2}$, $S(O)_2R^{b2}$, or $S(O)_2NR^{c2}R^{d2}$, wherein said C_{1-6} alkyl and C_{2-6} alkenyl are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from Cy^1 , halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} haloalkyl, CN, NO_2 , OR^{a2} , SR^{a2} , $C(O)R^{b2}$, $C(O)NR^{c2}R^{d2}$, $C(O)OR^{a2}$, $OC(O)R^{b2}$, $OC(O)NR^{c2}R^{d2}$, $NR^{c2}R^{d2}$, $NR^{c2}C(O)R^{b2}$, $NR^{c2}C(O)OR^{a2}$, $NR^{c2}C(O)NR^{c2}R^{d2}$, $NR^{c2}S(O)R^{b2}$, $NR^{c2}S(O)_2R^{b2}$, $NR^{c2}S(O)_2NR^{c2}R^{d2}$, $S(O)R^{b2}$, $S(O)NR^{c2}R^{d2}$, $S(O)_2R^{b2}$, and $S(O)_2NR^{c2}R^{d2}$;

R^B is H, Cy^2 , halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} haloalkyl, CN, NO_2 , OR^{a3} , SR^{a3} , $C(O)R^{b3}$, $C(O)NR^{c3}R^{d3}$, $C(O)OR^{a3}$, $OC(O)R^{b3}$, $NR^{c3}R^{d3}$, $NR^{c3}C(O)R^{b3}$, $NR^{c3}C(O)OR^{a3}$, $NR^{c3}C(O)NR^{c3}R^{d3}$, $NR^{c3}S(O)R^{b3}$, $NR^{c3}S(O)_2R^{b3}$, $NR^{c3}S(O)_2NR^{c3}R^{d3}$, $S(O)NR^{c3}R^{d3}$, $S(O)_2R^{b3}$, or $S(O)_2NR^{c3}R^{d3}$, wherein said C_{1-6} alkyl and C_{2-6} alkenyl are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from Cy^2 , halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} haloalkyl, CN, NO_2 , OR^{a3} , SR^{a3} , $C(O)R^{b3}$, $C(O)NR^{c3}R^{d3}$, $C(O)OR^{a3}$, $OC(O)R^{b3}$, $OC(O)NR^{c3}R^{d3}$, $NR^{c3}R^{d3}$, $NR^{c3}C(O)R^{b3}$, $NR^{c3}C(O)OR^{a3}$, $NR^{c3}C(O)NR^{c3}R^{d3}$, $NR^{c3}S(O)R^{b3}$, $NR^{c3}S(O)_2R^{b3}$, $NR^{c3}S(O)_2NR^{c3}R^{d3}$, $S(O)R^{b3}$, $S(O)NR^{c3}R^{d3}$, $S(O)_2R^{b3}$, and $S(O)_2NR^{c3}R^{d3}$;

R^C and R^D are independently selected from H, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} haloalkyl, CN, NO_2 , OR^{a4} , SR^{a4} , $C(O)R^{b4}$, $C(O)NR^{c4}R^{d4}$, $C(O)OR^{a4}$, $OC(O)R^{b4}$, $NR^{c4}R^{d4}$, $NR^{c4}C(O)R^{b4}$, $NR^{c4}C(O)OR^{a4}$, $NR^{c4}C(O)NR^{c4}R^{d4}$, $NR^{c4}S(O)R^{b4}$, $NR^{c4}S(O)_2R^{b4}$, $NR^{c4}S(O)_2NR^{c4}R^{d4}$, $S(O)NR^{c4}R^{d4}$, $S(O)_2R^{b4}$, and $S(O)_2NR^{c4}R^{d4}$; wherein said C_{1-6} alkyl and C_{2-6} alkenyl are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from C_{6-10} aryl, C_{3-10} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} haloalkyl, CN, NO_2 , OR^{a4} , SR^{a4} , $C(O)R^{b4}$, $C(O)NR^{c4}R^{d4}$, $C(O)OR^{a4}$, $OC(O)R^{b4}$, $OC(O)NR^{c4}R^{d4}$, $NR^{c4}R^{d4}$, $NR^{c4}C(O)R^{b4}$, $NR^{c4}C(O)OR^{a4}$, $NR^{c4}C(O)NR^{c4}R^{d4}$, $NR^{c4}S(O)R^{b4}$, $NR^{c4}S(O)_2R^{b4}$, $NR^{c4}S(O)_2NR^{c4}R^{d4}$, $S(O)R^{b4}$, $S(O)NR^{c4}R^{d4}$, $S(O)_2R^{b4}$, and $S(O)_2NR^{c4}R^{d4}$;

Cy^1 and Cy^2 are each independently selected from C_{6-10} aryl, C_{3-10} cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, each of which is optionally substituted by 1, 2, 3, 4, or 5 substituents independently selected from R^{Cy} ;

each R^{Cy} is independently selected from halo, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{6-10} aryl, C_{3-10} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, CN, OR^{a5} , $C(O)R^{b5}$, $C(O)NR^{c5}R^{d5}$, $C(O)OR^{a5}$, $OC(O)R^{b5}$, $OC(O)NR^{c5}R^{d5}$, $NR^{c5}R^{d5}$, $NR^{c5}C(O)R^{b5}$, $NR^{c5}C(O)OR^{a5}$, $NR^{c5}C(O)NR^{c5}R^{d5}$, $NR^{c5}S(O)R^{b5}$, $NR^{c5}S(O)_2R^{b5}$, $NR^{c5}S(O)_2NR^{c5}R^{d5}$, $S(O)NR^{c5}R^{d5}$, $S(O)_2R^{b5}$, and $S(O)_2NR^{c5}R^{d5}$, wherein said C_{1-6} alkyl, C_{2-6} alkenyl, C_{6-10} aryl, C_{3-10} cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halo, C_{1-6} alkyl, CN, NO_2 , OR^{a5} , SR^{a5} , $C(O)R^{b5}$, $C(O)NR^{c5}R^{d5}$, $C(O)OR^{a5}$, $OC(O)R^{b5}$, $OC(O)NR^{c5}R^{d5}$, $NR^{c5}R^{d5}$, $NR^{c5}C(O)R^{b5}$, $NR^{c5}C(O)OR^{a5}$, $NR^{c5}C(O)NR^{c5}R^{d5}$, $NR^{c5}S(O)R^{b5}$, $NR^{c5}S(O)_2R^{b5}$, $NR^{c5}S(O)_2NR^{c5}R^{d5}$, $S(O)R^{b5}$, $S(O)NR^{c5}R^{d5}$, $S(O)_2R^{b5}$, and $S(O)_2NR^{c5}R^{d5}$;

each of R^a , R^{a1} , R^{a2} , R^{a3} , R^{a4} , and R^{a5} is independently selected from H, C_{1-6} alkyl, C_{1-4} haloalkyl, C_{2-6} alkenyl, C_{6-10} aryl, C_{3-10} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl- C_{1-4} alkyl, C_{3-10} cycloalkyl- C_{1-4} alkyl, (5-10 membered heteroaryl)- C_{1-4} alkyl, or (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, wherein said C_{1-6} alkyl, C_{2-6} alkenyl, C_{6-10} aryl, C_{3-10} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl- C_{1-4} alkyl, C_{3-10} cycloalkyl- C_{1-4} alkyl, (5-10 membered heteroaryl)- C_{1-4} alkyl, and (4-10 membered heterocycloalkyl)- C_{1-4} alkyl are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from C_{1-4} alkyl, halo, CN, OR^{a6} , $C(O)R^{b6}$, $C(O)NR^{c6}R^{d6}$, $C(O)OR^{a6}$, $OC(O)R^{b6}$, $OC(O)NR^{c6}R^{d6}$, $NR^{c6}R^{d6}$, $NR^{c6}C(O)R^{b6}$, $NR^{c6}C(O)NR^{c6}R^{d6}$, $NR^{c6}C(O)OR^{a6}$, $S(O)R^{b6}$, $S(O)NR^{c6}R^{d6}$, $S(O)_2R^{b6}$, $NR^{c6}S(O)_2R^{b6}$, $NR^{c6}S(O)_2NR^{c6}R^{d6}$, and $S(O)_2NR^{c6}R^{d6}$;

each of R^{b2} , R^{b3} , R^{b4} , and R^{b5} is independently selected from H, C_{1-6} alkyl, C_{1-4} haloalkyl, C_{2-6} alkenyl, C_{6-10} aryl, C_{3-10} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl- C_{1-4} alkyl, C_{3-10} cycloalkyl- C_{1-4} alkyl, (5-10 membered heteroaryl)- C_{1-4} alkyl, or (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, wherein said C_{1-6} alkyl, C_{2-6} alkenyl, C_{6-10} aryl, C_{3-10} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl- C_{1-4} alkyl, C_{3-10} cycloalkyl- C_{1-4} alkyl, (5-10 membered heteroaryl)- C_{1-4} alkyl, and (4-10 membered heterocycloalkyl)- C_{1-4} alkyl are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from C_{1-4} alkyl, halo, CN, OR^{a6} , $C(O)R^{b6}$, $C(O)NR^{c6}R^{d6}$, $C(O)OR^{a6}$, $OC(O)R^{b6}$,

OC(O)NR^{c6}R^{d6}, NR^{c6}R^{d6}, NR^{c6}C(O)R^{b6}, NR^{c6}C(O)NR^{c6}R^{d6}, NR^{c6}C(O)OR^{a6}, S(O)R^{b6}, S(O)NR^{c6}R^{d6}, S(O)₂R^{b6}, NR^{c6}S(O)₂R^{b6}, NR^{c6}S(O)₂NR^{c6}R^{d6}, and S(O)₂NR^{c6}R^{d6};

each of R^c, R^d, R^{c1}, R^{d1}, R^{c2}, R^{d2}, R^{c3}, R^{d3}, R^{c4}, R^{d4}, R^{c5}, and R^{d5} is independently selected from H, C₁₋₆ alkyl, C₁₋₄ haloalkyl, C₂₋₆ alkenyl, C₆₋₁₀ aryl, C₃₋₁₀ cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, (5-10 membered heteroaryl)-C₁₋₄ alkyl, or (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, wherein said C₁₋₆ alkyl, C₂₋₆ alkenyl, C₆₋₁₀ aryl, C₃₋₁₀ cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, (5-10 membered heteroaryl)-C₁₋₄ alkyl, and (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from C₁₋₄ alkyl, halo, CN, OR^{a6}, SR^{a6}, C(O)R^{b6}, C(O)NR^{c6}R^{d6}, C(O)OR^{a6}, OC(O)R^{b6}, OC(O)NR^{c6}R^{d6}, NR^{c6}R^{d6}, NR^{c6}C(O)R^{b6}, NR^{c6}C(O)NR^{c6}R^{d6}, NR^{c6}C(O)OR^{a6}, S(O)R^{b6}, S(O)NR^{c6}R^{d6}, S(O)₂R^{b6}, NR^{c6}S(O)₂R^{b6}, NR^{c6}S(O)₂NR^{c6}R^{d6}, and S(O)₂NR^{c6}R^{d6};

each of R^{a6}, R^{b6}, R^{c6}, and R^{d6} is independently selected from H, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₃₋₇ cycloalkyl, phenyl, 5-6 membered heteroaryl, and 4-7 membered heterocycloalkyl, wherein said C₁₋₄ alkyl, C₂₋₄ alkenyl, C₃₋₇ cycloalkyl, phenyl, 5-6 membered heteroaryl, and 4-7 membered heterocycloalkyl are each optionally substituted by 1, 2, or 3 substituents independently selected from OH, CN, amino, halo, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylthio, C₁₋₄ alkylamino, and di(C₁₋₄ alkyl)amino; and

p is 1, 2, or 3;

wherein any aforementioned 4-10 or 4-7 membered heterocycloalkyl group optionally comprises 1, 2, or 3 oxo substituents, wherein each oxo substituent that is present is substituted on a ring-forming carbon, nitrogen, or sulfur atom of the 4-10 or 4-7 membered heterocycloalkyl group, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating or preventing a disease selected from the group consisting of osteoporosis, osteoporosis pseudoglioma syndrome, osteopenia, osteomalacia, renal osteodystrophy, Paget's disease, fractures, and bone metastasis, atherosclerosis, pulmonary hypertension, idiopathic or familial pulmonary hypertension, pulmonary arterial hypertension, including idiopathic pulmonary arterial hypertension, familial pulmonary arterial hypertension, associated pulmonary arterial hypertension,

diabetes, hyperlipidemia, chronic obstructive pulmonary disease, pulmonary embolism, irritable bowel disease, colitis, chemotherapy-induced emesis, diarrhea, carcinoid syndrome, celiac disease, Crohn's disease, abdominal pain, dyspepsia, constipation, lactose intolerance, multiple endocrine neoplasia types I and II, Ogilvie's syndrome, pancreatic cholera syndrome, pancreatic insufficiency, pheochromacytoma, scleroderma, somatization disorder, Zollinger-Ellison Syndrome, liver diseases including chronic liver disease; cancers including liver cancer, breast cancer, cholangiocarcinoma, colon cancer, colorectal cancer, neuroendocrine tumors, pancreatic cancer, prostate cancer, bone cancer, osteosarcoma, chondrosarcoma, Ewings sarcoma, osteoblastoma, osteoid osteoma, osteochondroma, enchondroma, chondromyxoid fibroma, aneurysmal bone cyst, unicameral bone cyst, giant cell tumor, and bone tumors, myeloproliferative syndrome, myelodysplastic syndrome, Hodgkin's lymphoma, non-Hodgkin's lymphoma, myeloma, aplastic anemia, anemia associated with kidney disease, acute lymphocytic leukemia, chronic lymphocytic leukemia, acute myeloid leukemia, and chronic myeloid leukemia.

2. The use of claim 1, wherein said cardiovascular disease is pulmonary arterial hypertension.
3. The use of claim 1, wherein said pulmonary arterial hypertension is associated pulmonary arterial hypertension.
4. The use of claim 1, wherein said gastrointestinal disease is diarrhea or carcinoid syndrome.
5. The use of any one of claims 1-4, wherein the compound is (S)-ethyl 8-(2-amino-6-((R)-1-(5-chloro-[1,1'-biphenyl]-2-yl)-2,2,2-trifluoroethoxy)pyrimidin-4-yl)-2,8-diazaspiro[4.5]decane-3-carboxylate or a pharmaceutically acceptable salt thereof.

6. The use of any one of claims 1-4, wherein the compound is (S)-8-(2-amino-6-((R)-1-(5-chloro-[1,1'-biphenyl]-2-yl)-2,2,2-trifluoroethoxy)pyrimidin-4-yl)-2,8-diazaspiro[4.5]decane-3-carboxylic acid or a pharmaceutically acceptable salt thereof