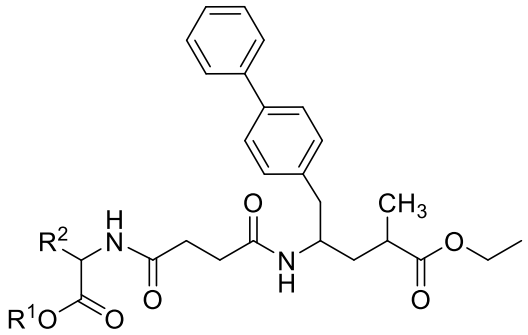
CLAIMS

1. A compound of the Formula (I):



(I)

wherein:

R^1 is H or (C_1-C_4)alkyl;

R^2 is H, (C_1-C_4)alkyl, (C_6-C_{10}) aryl, or 5- or 6-membered heteroaryl comprising 1-3 heteroatoms selected from N, S, and O, wherein the alkyl is optionally substituted with one or more R^3, and wherein the aryl and heteroaryl are optionally substituted with one or more R^4;

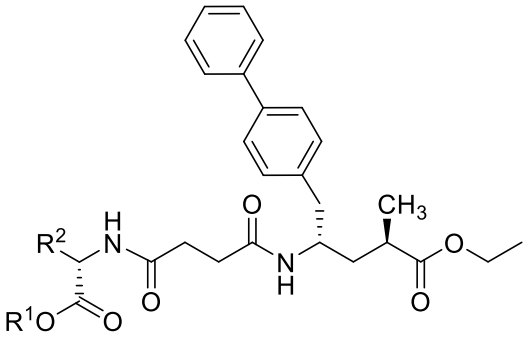
each R^3 is independently at each occurrence -NH_2, (C_1-C_4)alkylamino, (C_1-C_4)dialkylamino, -OH, -SH, -S(C_1-C_4)alkyl, -CO_2H, -$CONH_2$, -NHC(NH)NH_2, (C_6-C_{10}) aryl, or 5- to 10-membered monocyclic or bicyclic heteroaryl comprising 1-3 heteroatoms selected from N, O, and S, wherein the aryl and heteroaryl are optionally substituted with one or more R^5;

each R^4 is independently at each occurrence (C_1-C_4)alkyl, (C_1-C_4)haloalkyl, (C_1-C_4)alkoxy, (C_1-C_4)haloalkoxy, halogen, -NH_2, -OH or CN; and

each R^5 is independently at each occurrence (C_1-C_4)alkyl, (C_1-C_4)haloalkyl, (C_1-C_4)alkoxy, (C_1-C_4)haloalkoxy, halogen, -NH_2, -OH or CN;

or a pharmaceutically acceptable salt thereof.

2. The compound according to claim 1, having a Formula (II):



(II),

or a pharmaceutically acceptable salt thereof.

3. The compound, or a pharmaceutically acceptable salt thereof, according to claim 1 or 2, wherein R^1 is H, ethyl or t-butyl.

4. The compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 3, wherein R^2 is H or (C_1-C_4)alkyl optionally substituted with one to two R^3.

5. The compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 4, wherein R^2 is H or (C_1-C_4)alkyl optionally substituted with -NH_2.

6. The compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 5, wherein R^1 is H, ethyl or t-butyl, and R^2 is H or (C_4)alkyl optionally substituted with -NH_2.

7. The compound of claim 1 selected from:
(4-(((2S,4R)-1-([1,1'-biphenyl]-4-yl)-5-ethoxy-4-methyl-5-oxopentan-2-yl)amino)-4-oxobutanoyl)-L-leucine;
(4-(((2S,4R)-1-([1,1'-biphenyl]-4-yl)-5-ethoxy-4-methyl-5-oxopentan-2-yl)amino)-4-oxobutanoyl)-L-lysine; and
tert-butyl (4-(((2S,4R)-1-([1,1'-biphenyl]-4-yl)-5-ethoxy-4-methyl-5-oxopentan-2-yl)amino)-4-oxobutanoyl)-L-lysinate;
ethyl (2R,4S)-5-([1,1'-biphenyl]-4-yl)-4-(4-(((S)-1-ethoxy-4-methyl-1-oxopentan-2-yl)amino)-4-oxobutanamido)-2-methylpentanoate;
(4-(((2*S*,4*R*)-1-([1,1'-biphenyl]-4-yl)-5-ethoxy-4-methyl-5-oxopentan-2-yl)amino)-4-oxobutanoyl)-*L*-arginine;
(4-(((2*S*,4*R*)-1-([1,1'-biphenyl]-4-yl)-5-ethoxy-4-methyl-5-oxopentan-2-yl)amino)-4-oxobutanoyl)-*L*-histidine;
(4-(((2S,4R)-1-([1,1'-biphenyl]-4-yl)-5-ethoxy-4-methyl-5-oxopentan-2-yl)amino)-4-oxobutanoyl)glycine;
(4-(((2*S*,4*R*)-1-([1,1'-biphenyl]-4-yl)-5-ethoxy-4-methyl-5-oxopentan-2-yl)amino)-4-oxobutanoyl)-*L*-alanine;
(4-(((2*S*,4*R*)-1-([1,1'-biphenyl]-4-yl)-5-ethoxy-4-methyl-5-oxopentan-2-yl)amino)-4-oxobutanoyl)-*L*-valine;
(4-(((2*S*, 4*R*)-1-([1, 1'-biphenyl]-4-yl)-5-ethoxy-4-methyl-5-oxopentan-2-yl)amino)-4-oxobutanoyl)-*L*-phenylalanine;
(4-(((2*S*,4*R*)-1-([1,1'-biphenyl]-4-yl)-5-ethoxy-4-methyl-5-oxopentan-2-yl)amino)-4-oxobutanoyl)-*L*-tryptophan; and

(4-(((2*S*,4*R*)-1-([1,1’-biphenyl]-4-yl)-5-ethoxy-4-methyl-5-oxopentan-2-yl)amino)-4-oxobutanoyl)-*L*-isoleucine;
or a pharmaceutically acceptable salt thereof.

8. The compound of claim 7 which is (4-(((2S,4R)-1-([1,1’-biphenyl]-4-yl)-5-ethoxy-4-methyl-5-oxopentan-2-yl)amino)-4-oxobutanoyl)-L-leucine or a pharmaceutically acceptable salt thereof.

9. The compound of claim 7 which is (4-(((2*S*,4*R*)-1-([1,1'-biphenyl]-4-yl)-5-ethoxy-4-methyl-5-oxopentan-2-yl)amino)-4-oxobutanoyl)-*L*-histidine or a pharmaceutically acceptable salt thereof.

10. A pharmaceutical composition comprising a compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable carriers.

11. A combination comprising a compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, and one or more therapeutically active agents.

12. The combination according to claim 11, wherein the therapeutically active agents are selected from HMG-Co-A reductase inhibitor, an angiotensin receptor blocker, a calcium channel blocker, an endothelin antagonist, a renin inhibitor, a diuretic, an ApoA-I mimic, an anti-diabetic agent, an obesity-reducing agent, an aldosterone receptor blocker, an endothelin receptor blocker, an aldosterone synthase inhibitor, a CETP inhibitor, and a phosphodiesterase type 5 (PDE5) inhibitor.

13. The combination of claim 12, wherein the combination comprises an Angiotensin Receptor Blocker selected from valsartan, candesartan, losartan, irbesartan, telmisartan, olmesartan, eprosartan, fimasartan, and azilsartan, or a pharmaceutically acceptable salt thereof.

14. A compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, for use as a medicament.

15. Use of a compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a disorder or disease selected from hypertension, resistant hypertension, pulmonary heart disease,

pulmonary hypertension, pulmonary arterial hypertension, isolated systolic hypertension, peripheral vascular disease, heart failure, heart failure with preserved ejection fraction (HF-PEF), heart failure with reduced ejection fraction (HF-REF), mitral stenosis and regurgitation, left ventricular hypertrophy, angina, renal insufficiency, renal failure, diabetic nephropathy, non-diabetic nephropathy, contrast-induced nephropathy, nephrotic syndrome, glomerulonephritis, scleroderma, glomerular sclerosis, proteinuria of primary renal disease, renal vascular hypertension, diabetic retinopathy and end-stage renal disease (ESRD), endothelial dysfunction, diastolic dysfunction, cardiomyopathy, hypertrophic cardiomyopathy, diabetic cardiomyopathy, supraventricular and ventricular arrhythmias, cardiac dysrhythmia, atrial fibrillation (AF), new onset of atrial fibrillation, recurrent atrial fibrillation, cardiac fibrosis, atrial flutter, detrimental vascular remodeling, plaque stabilization, myocardial infarction (MI), renal fibrosis, polycystic kidney disease (PKD), renal failure, cyclical oedema, Menière's disease, hyperaldosteronism, hypercalciuria, ascites, glaucoma, menstrual disorders, preterm labor, pre-eclampsia, endometriosis, and reproductive disorders, asthma, obstructive sleep apnea, inflammation, leukemia, pain, epilepsy, affective disorders, depression, psychotic condition, obesity, gastrointestinal disorders, wound healing, septic shock, gastric acid secretion dysfunction, hyperreninemia, cystic fibrosis, restenosis, type-2 diabetes, metabolic syndrome, diabetic complications, atherosclerosis, and male and female sexual dysfunction.

16. The use according to claim 15, wherein the disease or disorder is selected from hypertension, pulmonary hypertension, isolated systolic hypertension, resistant hypertension, peripheral vascular disease, heart failure, heart failure with preserved ejection fraction (HF-PEF), heart failure with reduced ejection fraction (HF-REF), or pulmonary arterial hypertension.

17. The use according to any one of claims 15 to 16, wherein the compound is used together, concomitantly or sequentially with an Angiotensin Receptor Blocker, or a pharmaceutically acceptable salt thereof.

18. The use according to claim 17, wherein the compound is used together, concomitantly or sequentially with an Angiotensin Receptor Blocker selected from valsartan, candesartan, losartan, irbesartan, telmisartan, olmesartan, eprosartan, fimasartan, and azilsartan, or a pharmaceutically acceptable salt thereof.

19. The use according to claim 18, wherein the compound is used together, concomitantly or sequentially with valsartan, or a pharmaceutically acceptable salt thereof.