their gender. For example, this document provides methods and materials for using sGC agonists or a combination of sGC agonists and PDE5A inhibitors in male patients to reduce calcification of heart valves and/or vessels or to slow progression of aortic sclerosis to calcific aortic valve stenosis. As described herein, sGC agonists such as ataciguat can be used to slow progression of aortic sclerosis to calcific aortic valve stenosis, but such treatment is more effective in males than in females. Having the ability to effectively slow progression of aortic sclerosis to calcific aortic valve stenosis can allow male patients to live longer and happier lives. In some cases, selectively slowing progression of aortic sclerosis to calcific aortic valve stenosis in male patients can allow female patients to avoid unnecessary treatment with sGC agonists. This document also provides methods and materials for using anti-fibrotic agents to treat females identified as having aortic sclerosis. In some cases, such as when calcification is observed after treatment with an anti-fibrotic agent, females can be treated with one or more sGC agonists. The methods disclosed herein also can be used to reduce blood pressure in mammals who have, or who are at risk of having, hypertension, particularly in a supine position. In addition, the methods disclosed herein can include treatment of diastolic dysfunction, mitigation of elevated pulse pressure, and reduction of blood pressure, particularly in a supine position; in some cases, these methods can be carried out on a gender-dependent basis in which males are treated and females are excluded from treatment.

In one example, this document features a method for treating a mammal on the basis of the mammal's gender, where the method includes (a) identifying a mammal as having, or as being at risk of developing, heart valve calcification or vessel calcification, (b) identifying the mammal as a male mammal or a female mammal, and (c) when the mammal is a male mammal, administering a sGC agonist to the male mammal, thereby slowing progression of calcification of a heart valve or vessel within the male mammal, and when the mammal is a female mammal, not administering a sGC agonist to the female mammal and, optionally, administering a treatment that is not a sGC agonist to the female mammal to slow progression of calcification of a heart valve or vessel within the female mammal. In one aspect, the present disclosure provides use of a sGC agonist in the manufacture of a medicament for slowing progression of calcification of a heart valve or vessel in a mammal, said use comprising: (a) identifying a mammal as having, or as being at risk of developing, heart valve calcification or vessel calcification, (b) identifying said mammal as a male mammal, and (c) the sGC agonist is to be administered to said male mammal, thereby slowing progression of calcification of a heart valve or vessel within said male mammal. The mammal can be a human. The sGC agonist can be ataciguat (5-chloro-2-[[(5-chloro-2-thienyl)sulfonyl]amino]-N-[4-(4-morpholinylsulfonyl)phenyl]-benzamide; HMR1766), YC-I (5-[1-(phenylmethyl)-1H-indazol-3-yl]-2-furanmethanol), BAY 58-

include administering an anti-fibrotic agent to the mammals identified as being female mammals.

In still another example, this document features a method for avoiding the unnecessary use of a sGC agonist to treat a mammal having, or at risk of developing, heart valve calcification or vessel calcification, where the method includes identifying the mammal as being a female mammal and as having, or at risk of developing, the heart valve calcification or vessel calcification, and excluding the female mammal from treatment with the sGC agonist based, at least in part, on the female gender of the female mammal. The mammal can be a human. The sGC agonist can be ataciguat, YC-I, BAY 58-2667, BAY 41-2272, BAY-41-8543, BAY 63-2521, CFM-1571, A-350619, vericiguat, praliciguat, olinciguat, bis-heteroaryl pyrazole IWP-051, IW-6463, GSK2181236A, IWP-550, IWP-854, IWP-953, nelociguat, MGV354, BI 703704, S3448, or BAY 60-2770.

This document also features a method for treating a mammal on the basis of the mammal's gender, where the method includes (a) identifying a mammal as having, or as being at risk of developing, aortic sclerosis, (b) identifying the mammal as a male mammal or a female mammal, and (c) when the mammal is a male mammal, administering a sGC agonist to the male mammal, thereby slowing progression of aortic sclerosis to calcific aortic valve stenosis within the male mammal, and when the mammal is a female mammal, not administering a sGC agonist to the female mammal and, optionally, administering a treatment that is not a sGC agonist to the female mammal to slow progression of aortic sclerosis to calcific aortic valve stenosis within the female mammal. In another aspect, the present disclosure provides use of a sGC agonist in the manufacture of a medicament for slowing progression of aortic sclerosis to calcific aortic valve stenosis in a mammal, said use comprising: (a) identifying a mammal as having, or as being at risk of developing, aortic sclerosis, (b) identifying said mammal as a male mammal, and (c) the sGC agonist is to be administered to said male mammal, thereby slowing progression of aortic sclerosis to calcific aortic valve stenosis within said male mammal. The mammal can be a human. The sGC agonist can be ataciguat, YC-I, BAY 58-2667, BAY 41-2272, BAY-41-8543, BAY 63-2521, CFM-1571, A-350619, vericiguat, praliciguat, olinciguat, bis-heteroaryl pyrazole IWP-051, IW-6463, GSK2181236A, IWP-550, IWP-854, IWP-953, nelociguat, MGV354, BI 703704, S3448, or BAY 60-2770. The method can further include administering a PDE5A inhibitor to the male mammal. The method can further include identifying the male mammal as having an elevated plasma level of LPA. The method can include administering an anti-fibrotic agent to the female mammal.

In another example, this document features a method for treating a population of mammals identified as having, or as being at risk for developing, aortic sclerosis,

WHAT IS CLAIMED IS:

1. Use of a sGC agonist in the manufacture of a medicament for slowing progression of calcification of a heart valve or vessel in a mammal, said use comprising:

(a) identifying a mammal as having, or as being at risk of developing, heart valve calcification or vessel calcification,

(b) identifying said mammal as a male mammal, and

(c) the sGC agonist is to be administered to said male mammal, thereby slowing progression of calcification of a heart valve or vessel within said male mammal.

2. The use of claim 1, wherein said mammal is a human.

3. The use of claim 1 or claim 2, wherein said sGC agonist is:

ataciguat (5-chloro-2-[[(5-chloro-2-thienyl)sulfonyl]amino]-N-[4-(4-morpholinylsulfonyl)phenyl]-benzamide; HMR1766),

YC-I (5-[1-(phenylmethyl)-1H-indazol-3-yl]-2-furanmethanol),

BAY 58-2667 (4-[((4-carboxybutyl)(2-[(4-phenethylbenzyl)oxy] phenethyl)amino)methyl[benzoic]acid hydrochloride),

BAY 41-2272 (3-(4-amino-5-cyclopropylpyrimidin-2-yl)-1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine),

BAY-41-8543 (2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-morpholinyl)-4,6-pyrimidinediamine),

BAY 63-2521 (methyl (4,6-diamino-2-(1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl)pyrimidin-5-yl)(methyl)carbamate),

CFM-1571 (3-[3-(dimethylamino)propoxy]-N-(4-methoxyphenyl)-1-(phenylmethyl)-1H-pyrazole-5-carboxamide hydrochloride),

A-350619 (3-[2-(4-chlorophenylthio)phenyl]-N-(4-dimethylaminobutyl)acrylamide),

vericiguat (methyl (4,6-diamino-2-(5-fluoro-1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl)pyrimidin-5-yl)carbamate),

praliciguat (1,1,1,3,3,3-hexafluoro-2-[({5-fluoro-2-[1-(2-fluorobenzyl)-5-(1,2-oxazol-3-yl)-1H-pyrazol-3-yl]pyrimidin-4-yl}amino)methyl]propan-2-ol),

olinciguat ((2R)-3,3,3-trifluoro-2-{[(5-fluoro-2-{1-[(2-fluorophenyl)methyl]-5-(1,2-oxazol-3-yl)-1H-pyrazol- 3-yl}pyrimidin-4-yl)amino]methyl}-2-hydroxypropanamide),

bis-heteroaryl pyrazole IWP-051 (5-fluoro-2-(1-(2-fluorobenzyl)-5-(isoxazol-3-yl)-1H-pyrazol-3-yl)pyrimidin-4(3H)-one),

IW-6463,

GSK2181236A (1-(6-{2-[({3-methyl-4′-[(trifluoromethyl)oxy]-4-biphenylyl}methyl)oxy]phenyl}-2-pyridinyl)-5-(trifluoromethyl)-1H-pyrazole-4-carboxylic acid),

IWP-550,

IWP-854 (4-(5-fluoro-2-(1-(2-fluorobenzyl)-5-(isoxazol-3-yl)-1H-pyrazol-3-yl)pyrimidin-4-yl)-1-(3-methyl-3H-diazirin-3-yl)-N-(37-oxo-41-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)-3,6,9,12,15,18,21,24,27,30,33-undecaoxa-36-azahentetracontyl)-7,10,13,16-tetraoxa-4-azanonadecan-19-amide),

IWP-953,

nelociguat (methyl (4,6-diamino-2-(1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl)pyrimidin-5-yl)carbamate),

MGV354 ((S)-1-(6-(3-((4-(1-(cyclopropanecarbonyl)piperidin-4-yl)-2-methylphenyl)amino)-2,3-dihydro-1H-inden-4-yl)pyridin-2-yl)-5-methyl-1H-pyrazole-4-carboxylic acid),

BI 703704 ((1R,5S,8s)-3-(4-(5-methyl-2-((2-methyl-4-(piperidine-1-carbonyl)benzyl)oxy)phenyl)thiazol-2-yl)-3-azabicyclo[3.2.1]octane-8-carboxylic acid),

S3448 (2-[[(4-chlorophenyl)sulfonyl]amino]-4,5-dimethoxy-N-[4-(4-thiomorpholinylsulfonyl)phenyl]benzamide), or

BAY 60-2770 (4-[[(4-carboxybutyl)[2-[5-fluoro-2-[[4′-(trifluoromethyl)[1,1′-biphenyl]-4-yl]methoxy]phenyl]ethyl]amino]methyl]benzoic acid).

4. The use of any one of claims 1-3, wherein said medicament is to be administered to said male mammal with a PDE5A inhibitor.

5. The use of any one of claims 1-4, wherein said use further comprises identifying said male mammal as having an elevated plasma level of lysophosphatidic acid (LPA).

6. Use of a sGC agonist in the manufacture of a medicament for slowing progression of aortic sclerosis to calcific aortic valve stenosis in a mammal, said use comprising:

(a) identifying a mammal as having, or as being at risk of developing, aortic sclerosis,

(b) identifying said mammal as a male mammal, and

(c) the sGC agonist is to be administered to said male mammal, thereby slowing progression of aortic sclerosis to calcific aortic valve stenosis within said male mammal.

7. The use of claim 6, wherein said mammal is a human.

8. The use of claim 6 or claim 7, wherein said sGC agonist is ataciguat, YC-I, BAY 58-2667, BAY 41-2272, BAY-41-8543, BAY 63-2521, CFM-1571, A-350619, vericiguat, praliciguat, olinciguat, bis-heteroaryl pyrazole IWP-051, IW-6463, GSK2181236A, IWP-550, IWP-854, IWP-953, nelociguat, MGV354, BI 703704, S3448, or BAY 60-2770.

9. The use of any one of claims 6-8, wherein said medicament is to be administered to said male mammal with a PDE5A inhibitor.

10. The use of any one of claims 6-9, wherein said use further comprises identifying said male mammal as having an elevated plasma level of LPA.